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Original Article

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Comparison of Ropivacaine and Ropivacaine with Clonidine for Caudal Analgesia in Pediatric Patients for Lower Abdominal Surgeries

S Balasubramanian[1], K Sanmugapiriya[2], K Sureshkumar[1], A Arulmani[3], A Sivashanmugam[3]

[1]Associate Professor, Department of Anaesthesiology, Sri Manakula Vinayagar Medical College and Hospital, Puducherry, India, [2]Senior Resident, Department of Anaesthesiology, Sri Manakula Vinayagar Medical College and Hospital, Puducherry, India, [3]Post-graduate Student, Department of Anaesthesiology, Sri Manakula Vinayagar Medical College and Hospital, Puducherry, India

Abstract

Background: The objective of this study was to compare the duration of anesthesia, hemodynamic parameters, sedation, and side effects between ropivacaine and ropivacaine with clonidine in patients undergoing lower abdominal surgeries by caudal anesthesia.

Methods: A total of 60 patients aged 3-6 years with ASA Grade I-II were enrolled in this study. They were randomized to receive either ropivacaine (0.1% - 1 ml/kg) or ropivacaine with clonidine (0.1% - 1 ml/kg with 1 mcg/kg) in caudal analgesia. Hemodynamic parameters heart rate (HR), systolic blood pressure (SBP) and diastolic blood pressure (DBP), and oxygen saturation (SpO^2) were recorded during and after the procedure. The duration of analgesia and sedation score was noted in the post-operative period.

Result: The two groups were comparable with regards to age, gender, weight, type and duration of the surgery with the $P < 0.05$. There was a significant fall in HR, SBP, and DBP in group RC when compared to group R. The duration of analgesia was significantly prolonged in group RC with a mean duration of analgesia for 480 min. There were no significant differences in sedation score in the two groups. No obvious side effects, such as respiratory depression, hypotension, bradycardia, nausea, vomiting, and urinary retention, were noted.

Conclusion: Addition of clonidine 1 mcg/kg to 0.1% ropivacaine for caudal analgesia significantly prolongs the duration of analgesia in the post-operative period with minimal changes in the hemodynamic parameters without any side effects. Therefore, we conclude that 0.1% ropivacaine with 1 mcg/kg clonidine has better post-operative analgesia when compared to plain ropivacaine.

Key words: Analgesia, Caudal, Clonidine, Hemodynamic, Ropivacaine

INTRODUCTION

Pain is an unpleasant sensation which is only experienced and not expressed, especially in children. The concept of intra and post-operative pain relief in children has improved in the recent years. In pediatric patients even though general anesthesia is the commonly used technique, but regional anesthesia is the cornerstone of modern anesthesia.

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Caudal analgesia is the most commonly performed regional anesthesia as it is the most reliable and safe technique in pediatric patients. Complications in general anesthesia are rare due to modern anesthetic agents, but the risk of post-operative apnoea is significant, especially in infants born preterm and operated on before 46 weeks of post-conceptual age.[1] Therefore, caudal analgesia with sedation and spontaneous breathing is a safe alternative. Single shot caudal analgesia is useful for surgeries lasting <90 min.[2]

Epidural catheter insertion is needed for surgeries lasting more than 90 min, but the placement of the catheter in

Corresponding Author: K Sanmugapiriya, 7, Nethaji St., Sorna Nagar, Ariyankuppam, Puducherry - 605 007, India. Phone: +91-9944337900. E-mail: piriyakannan@gmail.com

caudal space is time-consuming, more expensive also adds to the risk of infection and tends to prevent early mobilization.[3] The search for the ideal adjuvant and a local anesthetic with wide margin of safety, minimal motor blockade, and prolonged period of analgesia continues until date.[4]

Ropivacaine has been extensively used for regional anesthesia in adult and older children[5] due to its wider margin of safety than bupivacaine with lower potential for central nervous and cardiovascular side effects. Ropivacaine has greater sensory and fewer motor effects, and this could allow rapid mobilization after surgery[6,7] when compare to bupivacaine. Recent studies have showed that reducing the concentration of ropivacaine would provide an additional margin of safety as well as reduces the incidence of the unwanted motor blockade.[8] Addition of adjuvants such as epinephrine, opioids, ketamine, and alpha 2 agonist prolongs the duration of caudal analgesia.[9-11] Opioids have the risk of delayed respiratory depression.

Clonidine, an α_2 adrenergic agonist, prolongs the analgesia by non-opioid mechanism such as by stimulating the descending noradrenergic medulla-spinal pathways and inhibiting the release of nociceptive neurotransmitters in the dorsal horn of spinal cord.[12]

Therefore, we did a prospective, randomized, double-blind study to compare the analgesic effects and side effects of ropivacaine and when ropivacaine added to clonidine for caudal analgesia in children undergoing lower abdominal surgeries.

METHODS

After obtaining proper informed consent from parents and approval of the Institutional Ethical Committee. 60 ASA I-II patients, age group of 3-8 years scheduled for lower abdominal surgeries, were included. Patients having bleeding disorders, neuromuscular diseases, infections, and bony abnormalities of the spine were excluded from the study. 60 children were randomly allocated into two groups. Group R received ropivacaine 0.1% 1 ml/kg via the caudal route. Group RC received 1 ml/kg of 0.1% of ropivacaine and clonidine 1 mcg/Kg in the same route.

All the health care providers providing direct patient care, the subject and their parents were blinded to the caudal medications administered. All the medications were prepared by the anesthetist who is unrelated to the study, and the volume of drug contributed by clonidine being insignificant blinding could be done easily. Caudal placement of the drug was given by another person who was also blinded.

All children of both the groups were pre-medicated with 0.5 mg/kg of midazolam orally. In the operating room, monitors were attached, and the baseline reading of heart rate (HR), systolic blood pressure (SBP) and diastolic blood pressure (DBP), oxygen saturation (SpO^2) were recorded. Inhalational induction was done with 8% sevoflurane in oxygen, and intravenous access was secured. Fentanyl 2 mcg/kg was administered intravenously for analgesia. The airway was maintained using a face mask, laryngeal mask airway, or endotracheal tube according to anesthesiologist choice, and the anesthesia was maintained with 1-2% sevoflurane in O_2-N_2O.

After induction, the children were placed in the lateral decubitus position the caudal space was identified, and the appropriate drug was injected as per the group using a 23 G Hypodermic needle. Total volume is being constant at 1 ml/kg in both the groups. After placing a caudal block, the patient was turned supine. The anesthesia was maintained with 1-2% sevo in a mixture of 66% N_2O and 33 % O_2. The surgical incision was made 5 min after caudal placement of the drug, and the duration of the surgery was noted. Intravenous fluids (isolyte-P) were administered according to body weight and the fasting status. Intra operative continuous monitoring of HR, SBP, DBP, SpO_2 was undertaken throughout the surgical procedure, and the record was made at 10 min interval until the end of the surgery and subsequently was monitored for 2, 4, 6, 8, 10, 12, and 24 h in the post-operative period.

The time from the caudal placement of the drug to the first recording of an FLACC scale >3 was taken as the duration of analgesia. Rescue analgesia was provided with paracetamol suppository 20 mg/kg (Table 1).

Respiratory depression was defined as a decrease in SpO_2 to <93% and was treated with oxygen by mask 6 L/min. Hypotension was defined as a decrease in mean arterial blood pressure to <30% from the baseline and was treated with a bolus of 10 ml/kg crystalloid. Bradycardia was defined as HR <15% from the baseline and was treated with 10 mcg/kg of atropine. The sedation score was graded as 0 for awake, 1 for mild (arousable by voice), 2 for moderate (response to physical shake), and 3 for severe (unarousable). The sedation score was noted every 15 min up to 2 h in post-anesthesia care unit.

RESULTS

Statistical analysis was performed with Students unpaired *t*-test, Mann-Whitney U test, and heterogeneity Chi-square test.

Students *t*-test and Chi-square test for independent samples were used to compare the difference in age, sex, weight and duration of surgery. The quantitative data were expressed in terms of mean and standard deviation. The statistical analysis was done using SSPS version-20 software. The information collected regarding all the cases were recorded in the master chart. The mean, standard deviation, χ^2, *P* values were calculated. The $P < 0.05$ was taken to denote significant relationship.

The demographic data such as age, gender, weight, duration of surgery were comparable in both the group shown in Table 2. The mean HR and blood pressure noted at 10 min interval in the intraoperative period and 2, 4, 6, 8, 10, 12, and 24 h in the post-operative period were lowered in group RC when compared to group R (Graphs 1-3). However, none of the children in group RC were treated for hypotension and bradycardia as per the criteria defined in our study. The mean duration of analgesia was 232 mini in group R and 489 min in group RC (Graph 4). The duration of analgesia was significantly prolonged in group RC compared to group R with the significant *P* value of 0.000. Post-operative sedation score showed no statistically significant (Table 3).

DISCUSSION

We conducted this prospective, randomized study in an attempt to evaluate whether administration of clonidine to a commonly administered balanced anesthetic regimen improves the post-operative analgesia in pediatric patients undergoing lower abdominal surgeries.

Caudal analgesia is the most frequently used regional anesthesia in pediatric patients. Bupivacaine is the most

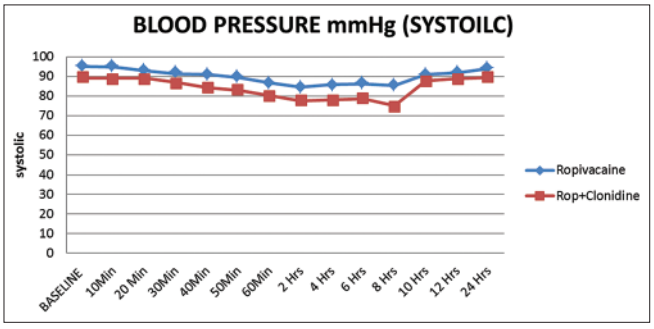
Table 1: FLACC scale

Parameter	0	1	2
Face	No expression	Occasional grimace	Frequent to constant quivering chin
Legs	Normal position or relaxed	Uneasy restless, tense	Kicking or leg drawn up
Activity	Lying quite	Squirming, shifting back and forth, tense	Ached, rigid, or jerking
Cry	No cry	Moans or whimpers	Crying steadily
Consolability	Content, relaxed	Reassurance, hugging	Difficult to console

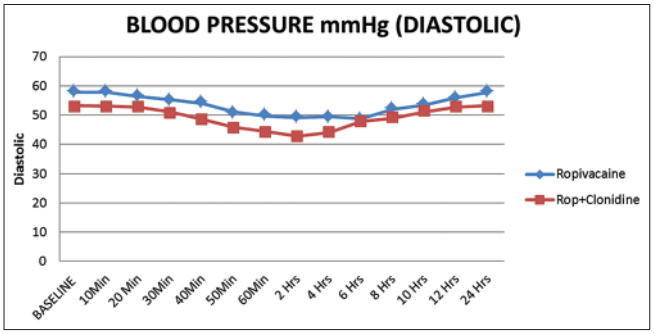
Score 0: No pain, 1-3: Mild pain, 4-7: Moderate pain, 8-10: Severe pain, FLACC: Face, Legs, Cry, Consolability

Table 2: Demographic data

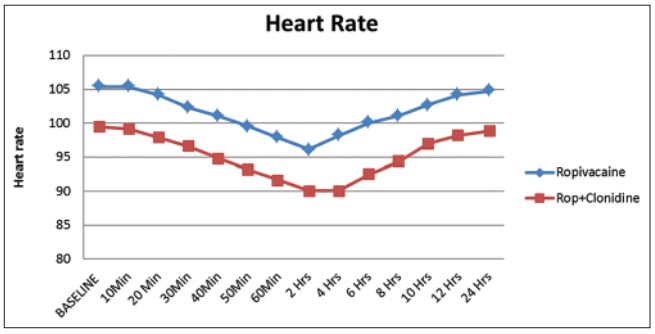
Parameters	Group R (*n*=30)	Group RC (*n*=30)
Age (years)	4.37±1.47	4.90±1.58
Gender		
M%/F%	67/33	80/20
Weight (kg)	17±5.19	18.63±4.61
Duration of surgery (mins)	37±10.55	31.83±16



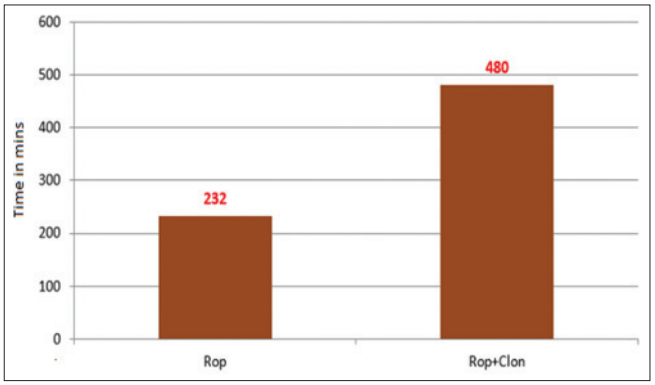
Graph 1: Mean systolic blood pressure



Graph 2: Mean diastolic blood pressure



Graph 3: Mean heart rate



Graph 4: Mean duration of analgesia

Table 3: Sedation score

Time	Group R (*n*=30)	Group RC (*n*=30)	*P* value
Base line	2	2	1.0009
15 min	2	2	1.000
30 min	2	2	0.317
45 min	2	2	1.000
60 min	2	2	0.741
75 min	1	2	0.305
90 min	1	1	0.201
105 min	1	1	0.246
120 min	1	1	0.592

commonly used local anesthetic in caudal analgesia but recently ropivacaine has proved to be more appropriate in pediatric age group due to its similarity in the duration of action to bupivacaine with the lesser motor blockade and less cardiotoxicity. Brockway *et al.*, reported that ropivacaine produces slower onset with less intense motor blockade when compare to a similar concentration of bupivacaine. Luz *et al.*, stated that reduction in the concentration of ropivacaine ensures an additional margin of safety and a reduction in the incidence of the unwanted motor blockade. Bosenberg *et al.*, demonstrated that 0.1-0.2% of ropivacaine produces a satisfactory post-operative analgesia and a concentration of 0.3% or more produces a denser motor blockade and only minimal improvement in the post-operative pain relief. And hence, the reason for selecting 0.1% as the concentration of ropivacaine in the study of the current debate. Several other recent studies have hypothesized that inherent vasoconstrictor activity of ropivacaine, when compared to other local anesthetics, enhances the duration of analgesia. Several agents have been tried as an adjuvant to local anesthetics to enhance the duration of analgesia of which fentanyl, morphine, ketamine, neostigmine, and clonidine deserves a mention. Shukula *et al.*, proposed the use of clonidine as an additive than fentanyl in the view of safety profile as fentanyl causes confusion, itching, nausea, vomiting, and severe respiratory depression. Constant *et al.*, concluded that addition of fentanyl as caudal adjuvant causes vomiting and transient oxygen desaturation when compared to clonidine which has better safety profile as a caudal adjuvant. Vetter *et al.*, concluded that clonidine is preferable to opioids in caudal analgesia also in view of its safety profile since opioids produce nausea, vomiting, and respiratory depression. Almender *et al.*, showed that the incidence of post-operative nausea and vomiting was 30% higher in those who received neostigmine as a caudal additive.

Clonidine, an α2 agonist, has been used as additive to local anesthetics, e.g., Bupivacaine. It has been widely used as an adjuvant to local anesthetics to enhance the quality of analgesia in the post-operative period. So, from the above studies, we decided to take clonidine as a caudal additive along with ropivacaine with better safety profile. The dose of clonidine was based on the study conducted in the pediatric population though no ideal dose of clonidine via the caudal route is yet recommended. A volume of 1 ml/kg was chosen for both the groups because only sub-umbilical surgeries were included in the study. The sub-umbilical surgeries require T_{10} and below levels for analgesia.

All the children were pre-medicated with oral midazolam 0.5 mg/kg 30 min before the caudal block to avoid confounding effects in the evaluation of sedation score post-operatively. We have used FLACC scale to evaluate the pain post-operatively as it is easy to use and it gives us an objective evaluation.

In our study, a mixture of 0.1% ropivacaine with 1 mcg/kg of clonidine has been used to improve the duration and quality via the caudal route. Different doses of ropivacaine along with clonidine 1-2 mcg/kg has been studied in children for a single shot caudal epidural so as to enhance the quality of analgesia in the post-operative period. Ivani *et al.*, state that addition of clonidine 2 mcg/kg to ropivacaine 0.1% provides an increase in duration of analgesia when compared with plain ropivacaine 0.2%. In 2010, Bajwa *et al.*, found that the mean duration of analgesia was 8.5 h with 0.25% plain ropivacaine and 13.4 h with ropivacaine and clonidine 2 mcg/kg which was significantly prolonged. In 2012, Manickam *et al.*, found that mean duration of analgesia was 243.37 min with 0.1% ropivacaine and 590.25 min with 0.1% of ropivacaine with 1 mcg/kg clonidine and 388,25 min with 0.2% ropivacaine. In our study, we found that caudal ropivacaine alone provides an excellent analgesia in the early post-operative period, with the effect lasting a few hours (232 min) of caudal placement of drug. However, the addition of clonidine prolongs the mean duration of analgesia for 480 min. The addition of clonidine prolongs the duration of analgesia due to several mechanism. The anti-nociceptive action is due to the direct suppression of the spinal cord nociceptive neurons. Clonidine also cross the blood brain barrier and interacts with $\alpha_2$adrenoreceptors at spinal and supra-spinal sites to provide analgesia. It also suppresses the neurotransmission in peripheral sensory Adelta and C fibers. It acts on α-2β adrenoceptors located at the peripheral vascular smooth muscles causes vasoconstriction.

Luz *et al.*, found that using 0.1% ropivacaine in caudal anesthesia was less effective in providing post-operative as it also acts only for a shorter duration when compared to 0.2% ropivacaine and 0.2% bupivacaine. Clonidine causes dose-dependent post-operative sedation in children. In our study, the post-operative sedation score was not statistically significant with the *P* value of >0.05. The finding in our study is almost similar with the observation of Bajwa *et al.*,

and Laha *et al.*, as the post-operative sedation was not statistically significant in the patient who received clonidine as an adjuvant to ropivacaine.[13-22]

Regarding HR, epidural clonidine caused bradycardia due to sympathetic predominance. In our study, we found that there was a statistically significant decrease in the HR for the group RC from 40 min to 8 h with the *P* value of <0.05. However, none of the children required drug intervention for decrease in HR as the hemodynamic parameters were not below the defined criteria.

Regarding the mean arterial blood pressure, epidural clonidine causes hypotension due to the inhibition of preganglionic sympathetic fibers. In our study, we found that there was statistically significant fall (*P* value <0.05) in both the systolic and the diastolic BP for Group (RC) from 40 min to 8 h and from 40 min to 4 h, respectively. However, none of the children required drug intervention for hypotension as the hemodynamic parameters were not below the defined criteria.

CONCLUSION

The addition of clonidine 1 mcg/kg to 0.1% ropivacaine for caudal anesthesia significantly prolongs the duration of analgesia in the post-operative period with minimal changes in the hemodynamic parameters and without any side effects when compared to 0.1% of plain ropivacaine.

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Original Article

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Clinical utility of Garenoxacin in Lower Respiratory Tract Infections: A Retrospective Analyzes: A Case-Cohort Study

Pravati Dutta[1], Shreyas Lathi[2], K Krishnaprasad[3], Amit Bhargava[4]

[1]Professor, Department of Pulmonary Medicine, VSS Medical College, Burla, Sambalpur, Odisha, India, [2]Assistant Manager, Medical Services, Glenmark Pharmaceuticals Ltd., Mumbai, Maharashtra, India, [3]Deputy General Manage, Medical Services, Glenmark Pharmaceuticals Ltd., Mumbai, Maharashtra, India, [4]Vice President & Head Medical Affairs, Glenmark Pharmaceuticals Ltd., Mumbai, Maharashtra, India

Abstract

Background: In the backdrop of community settings management of lower respiratory tract infections (LRTI) combined with significant comorbidities, exacerbated respiratory disease, recurrence and poor response to first-line antibiotics poses a therapeutic challenge. Antibiotic resistance of common LRTI pathogens including *Streptococcus pneumoniae* reported by Asia-pacific countries is among highest in the world. Newer fluoroquinolones with extended Gram-positive activity symbolize significant advance against penicillin-resistant *S. pneumoniae* (PRSP).

Aim: To assess clinical role of garenoxacin in LRTI.

Methods: Retrospective cohort analyzes of consecutive patients receiving garenoxacin for LRTI under community settings. Baseline demographics including symptoms, medical, and prior antibiotic usage history were noted. Clinical response was interpreted as success or failure specifying significant improvement or persistence of presenting symptoms, respectively. Adverse events requiring treatment withdrawal or alternative therapy were also noted.

Results: Garenoxacin was prescribed for Acute bronchitis (54%) acute exacerbation of chronic obstructive pulmonary disease (22%), Bronchiectasis (13%), and others as 1st line empiric therapy (59%), 2nd line therapy (11%) after failure of azithromycin for LRTI and as continuation therapy (30%) after i.v. antibiotics. Associated high-risk factors were present in 65% cases. Garenoxacin therapy was advised for 5-14 days in all cases established clinical success (100%) with no reported cases for serious adverse events. Assessed mean treatment duration for acute bronchitis/CAP and AECOPD were 7.9 and 7.1 days, respectively.

Conclusion: Management of AECOPD or LRTI in settings of significant comorbidities remains a therapeutic challenge. Garenoxacin a distinguished des-fluoroquinolone essays clinical advantage against PRSP and AECOPD/LRTI management, especially in the context of inadequate response to first-line therapy.

Key words: Exacerbation of chronic obstructive pulmonary disease, Fluoroquinolone, Lower respiratory tract infections, *Streptococcus pneumoniae*

INTRODUCTION

Lower respiratory tract infections (LRTI) are an extensive universal health problem. In terms of disease burden LRTI amounts to 94,037,000 disability-adjusted life years (DALYs) lost globally according to the World Health Organization report and accounts for about 20% of total mortality due to infectious diseases in India.[1,2]

LRTI is defined as an acute illness of ≤21 days presenting with a cough and one of the symptoms such as sputum production, dyspnea, wheeze, and chest pain/discomfort having no other explanation for symptoms. LRTI is broad term encompassing mainly acute bronchitis, CAP, acute exacerbation of chronic obstructive pulmonary disease (AECOPD), and acute exacerbation of bronchiectasis.[3]

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Corresponding Author: Dr. Shreyas Lathi, 2nd Floor, Glenmark House, BD Sawant Marg, Andheri(E), Mumbai - 400 099, Maharashtra, India. Phone: +91-7768071308/9850471045. E-mail: Shreyas.Lathi@glenmarkpharma.com

Acute purulent bronchitis is characterized by infection of bronchial tree resulting into reversible bronchial inflammation, bronchial edema, and mucus formation.[4] CAP is more severe infection than acute bronchitis having prolonged symptom course and higher risk for complications. Clinical diagnosis of CAP is made when symptoms of acute LRTI are present for <1 week; at least one systemic feature present like fever, chills, rigor; new focal sign on chest examination, and no other possible explanation for the symptoms.[2] COPD exacerbation and Bronchiectasis exacerbation compels adverse impact on systemic inflammation, lung functions, exercise performance, quality of life, associated comorbidities effecting higher morbidity and mortality rates; warrants management with antibiotic therapy along with other therapies. AECOPD is defined as the acute change in patient's baseline dyspnea, cough, or sputum beyond normal variability requiring a change in therapy according to the American Thoracic Society and European Respiratory Society (ERS). Bacterial infections are responsible for 70-75% cases. Bronchiectasis means permanent dilation of the bronchi and bronchioles due to the destruction of the muscles and elastic connective tissue triggered by an infection. Bronchiectasis exacerbations are defined as worsening of ≥4 symptoms such as sputum with the cough, dyspnea, fever, wheezing, physical resilience, fatigue, lung function, and radiological signs of infection.[5-9]

In community setup, common causative pathogens of LRTI includes Gram-positive, Gram–negative, and atypical. ERS, in collaboration with European Society for clinical microbiology and infectious diseases (ESCMID), recommends amoxicillin + clavulanate, fluoroquinolones and macrolides (in countries with low resistance) for the management of LRTI.[3]

Garenoxacin, a unique fluoroquinolone, lacks fluorine atom at C6 position which was thought to be essential, unlike traditional quinolones. Garenoxacin owing to unique substitutions at the 6th, 7th, and 8th position in quinolone ring essays lower MIC_{90} and higher AUC/MIC_{90} ratio governing higher potency, killing power, lower susceptibility to efflux, and resistance mechanisms against prevailing respiratory Gram-positive/negative and atypical pathogens including *Streptococcus pneumoniae* compared to other fluoroquinolones.[10,11]

The current study was directed to evaluate the clinical performance of Garenoxacin for the management of LRTI.

METHODS

A case series cohort involving consecutive patients requiring fluoroquinolones or garenoxacin for LRTI were analyzed, where cases were treated for LRTI at primary care center between July and September 2014. Database of all adult patients treated for LRTI at the respiratory clinic was inspected to identify cases. Diagnosis made by attending physician was noted. Furthermore, epidemiological data, demographic data, medical history, treatment history including prior use of antibiotics or fluoroquinolone, clinical response, and adverse event data were collated for analysis. Therapeutic response was adjudged as clinical success specifying complete resolution/significant improvement or failure specifying no significant improvement/persistence of symptoms with therapy. Serious adverse event (SAE) was defined as serious medical abnormality or hospitalization, disability, death, congenital anomaly. It was confirmed for any SAE to be reported to regional or central pharmacovigilance center.

Statistical Analyzes

Descriptive statistics was used to tabulate the data with percentage rate calculated for all categorical nominal and ordinal data variables.

RESULTS

During the rainy season month of July to September 2014, LRTI cases involving garenoxacin for management were distinguished and further analyzed.

Baseline Demographics

Analyzed 46 cases (Table 1) included male (71%), female (29%)with presenting complaints of fever (80%), cough (54%), dyspnea (44%), cough with expectoration (30%), chest pain (26%), swelling (26%), itching (9%), weakness (7%), rhinitis (2%), oral ulcer (2%), dysphagia (2%), anorexia (2%), and pulmonary edema (2%). In addition,

Table 1: Baseline demographic parameters of the study (*n*=46)

Average age	48 years
Average weight	49.4 kg
Study details	**Number of patients *n* (%)**
Gender	
Males	32 (71)
Females	13 (29)
Concomitant significant comorbidities	
Past history of tuberculosis	14 (31)
Hypertension	7 (15)
Type 2 diabetes	6 (13)
Dyslipidemia	3 (7)
Bronchial asthma	3 (7)
Cardiovascular disease	2 (4)
Hypothyroidism	1 (2)
Concomitant risk factors	
Smoking	8 (17)
Alcohol	6 (13)
Hospitalization history in past 3 weeks	4 (9)

22% cases were sputum culture positive with *S. pneumoniae* being most commonly isolated bacteria. Concomitant significant comorbidities and risk factors present in 65% cases. Concurrent medications included mucolytic, inhaled bronchodilator, inhaled corticosteroid, oral hypoglycemic, anti-hypertensive, and hypolipidemic agents and others.

Clinical Results

Study cases (*n*=46) as diagnosed by physician incorporated as Acute bronchitis (54%), AECOPD (22%), Bronchiectasis (13%), pyopneumothorax (4%), Empyema (4%) and Pharyngitis/Tonsilitis (2%), highlighted in Figure 1. Garenoxacin was administered to these cases at a dose of 400 mg daily for 5-14 days. Complete resolution or significant improvement was noted for the majority of symptoms. Furthermore, laboratory data were available for 47% cases demonstrated notable improvement in total leukocyte and neutrophil count at day 5 of therapy compared to day 0. Clinical success was documented in 100% case with no reported case of therapy failure (Figure 2). All of the cases at day 5 of evaluation documents 96% clinical success signifying early clinical response with Garenoxacin therapy.

Garenoxacin was preferred as 1st line empiric therapy in 59% cases, 2nd line therapy after failure of Azithromycin for LRTI in 11% cases and as continuation therapy, i.e., switch over after piperacillin + tazobactum (17%), meropenem (7%), and other beta-lactam + beta-lactamase inhibitor combinations (6%) mainly for empyema, AECOPD and bronchiectasis in total 30% cases (Figure 3). Assessed mean duration of Garenoxacin therapy included 7.9 & 7.1 days for Acute bronchitis, AECOPD respectively as highlighted in Table2.

Safety Profile

None of the cases reported any adverse event or SAE requiring discontinuation of therapy or hospitalization.

DISCUSSION

Overwhelming morbidity and mortality of LRTI are representative of global health barrier posed by them. In community setup, common etiology of LRTI is Gram-positive/negative pathogen, especially *S. pneumoniae* most common pathogen succeeded by *Haemophilus influenzae*, *Moraxella catarrhalis*, *Staphylococcus aureus*, and atypical pathogens.[3]

In India, COPD a gradually progressive disease estimated to account for 22.2 million cases by 2016, disease burden rise of about 30% compared to 2006. In terms of Global burden, COPD will be the 7th leading cause of DALYs lost by 2030. COPD accounts for 56% of total health care costs due to respiratory diseases. In India, estimated economic burden of COPD is ≈35,331 crores which can be reduced to only 4,135 crores if we follow national and international treatment guidelines.[12,13]

AECOPD is defined as the acute change in patient's baseline dyspnea, cough, or sputum beyond normal day to day variations requiring a change in therapy. In India, estimated AECOPD burden is about 0.9 million

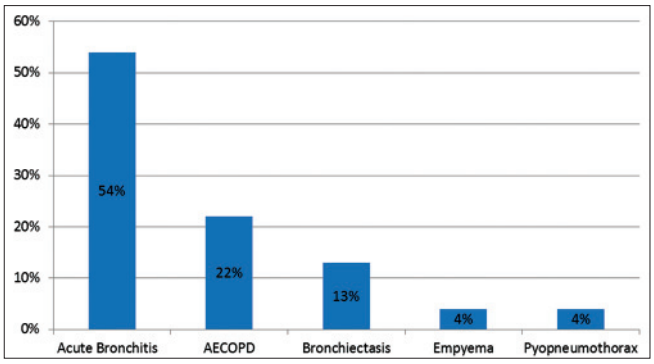

Figure 1 : Study cases (*n*=46) as diagnosed by physician

Mean Treatment Duration (days) with Garenoxacin Therapy		Clinical success with Garenoxacin Therapy at Day 7
Acute Bronchitis	7.9	
AECOPD	7.1	
Bronchiectasis	10.8	

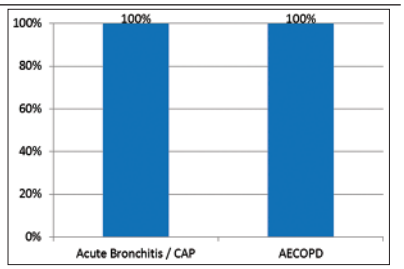

Figure 2: Clinical success with Garenoxacin therapy at day 7

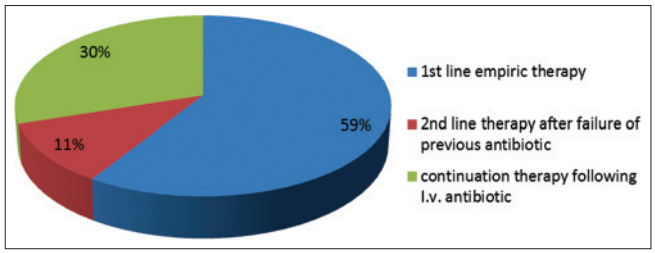

Figure 3 : Garenoxacin Therapy Preference

Table 2: Preferred treatment duration for Garenoxacin in patients with LRTI

Days	Acute bronchitis (*n*=24) (%)	AECOPD (*n*=10) (%)
≤5	4 (17)	1 (10)
6-10	19 (79)	9 (90)
11-14	1 (4)	0 (0)

AECOPD: Acute exacerbation of chronic obstructive pulmonary disease, CAP: Community-acquired pneumonia

by 2016. Following hospitalization, AECOPD reports 5-year mortality rate of about 50%. AECOPD leads to an accelerated rate of lung function decline requiring several weeks to recover. RTIs are most common cause of AECOPD precipitation.[12,13] In India, *Klebsiella pneumoniae*, *S. pneumoniae*, *S. aureus,* and *Pseudomonas aeruginosa* are common pathogen isolated form AECOPD patients.[14-16] The treatment goal should be to minimize the impact of current episode and prevent future exacerbations. Global initiative for lung disease (GOLD) guidelines recommend pharmacotherapy with bronchodilators, corticosteroids, and antibiotics for AECOPD. Systemic antibiotics reduce recovery time, improves lung function (FEV_1) and arterial hypoxemia (PaO_2), reduce relapse rate, treatment failure, and length of hospital stay in AECOPD. A systemic review reports 77% reduction in short-term mortality, 53% reduction in treatment failure with antibiotics and supports antibiotics usage in moderate or severe AECOPD. GOLD guidelines recommend antibiotic usage in AECOPD patients with 3 cardinal symptoms such as increase in dyspnea, sputum volume, and sputum purulence for duration of 5-10 days.[12,13]

A meta-analysis involving 19 randomized controlled trials (RCTs), and a therapeutic outcome probability model considers fluoroquinolone (moxifloxacin, levofloxacin) and amoxicillin + clavulanate equivalent with highest predicted efficacy for the management of AECOPD and acute exacerbation of chronic bronchitis (AECB).[17,18] Compared to respiratory quinolones combination of amoxicillin + clavulanate requires longer therapy duration (i.e., 10 days compared to 5 days of quinolones) with higher reports of gastrointestinal intolerance especially at higher dosages.[3]

Amoxicillin + clavulanate is recommended as 1st line therapy by ERS and ESCMID guidelines for LRTI management.[3] Clinical trial data are presented as the following format, reported efficacy parameter (sample size, efficacy evaluated at therapy day, the dosage of antibiotic). Randomized, double-blind, comparative controlled studies with amoxicillin + clavulanate for AECOPD/AECB management reports 88.8% success rate (728, day 7-14, 500/125 mg thrice daily, 7-14 days);[19] 93.2% clinical success (600-500/125 mg thrice daily, 7 days); 87% clinical cure (287, day 10, 875 mg twice daily, 10 days);[20] 74.1% cure (310, day 9-11, 500/125 mg thrice daily, 8 days).[21]

Moxifloxacin, a 4th generation fluoroquinolone, according to a recent meta-analysis involving 11 RCTs is considered clinically equivalent and bacteriologically superior to comparator agents for AECOPD management.[22] A analysis of 4 comparative studies for AECB/AECOPD reports 89% clinical response with Moxifloxacin.[23] In randomized, double-blind, comparative controlled studies for AECOPD/AECB management moxifloxacin reports 89% clinical resolution (491, day 5, 400 mg once daily, 5-10 days);[24] 86.3% clinical cure rate at day 7 (345, day 10 ± 3, 400 mg once daily, 7 days);[25] and 83-87.6% clinical success (MOSAIC study) (730, day 7-10, 400 mg once daily, 5 days).[26] AVANTI a prospective, observational study involving 2536 AECB/AECOPD patients reported 93.2% improvement at 5 days.[27]

Levofloxacin, a 3rd generation fluoroquinolone, in randomized, double-blind, comparative controlled studies for AECOPD/AECB management reports 82.8% clinical success rate (532, day 5, 500 mg once daily, 5 days);[28] 93% complicated/79.2% uncomplicated cases (763, day 3/5, 750 mg once daily, 3/5 days);[29] 82.8% clinical success (511, day 10, 500 mg once daily, 7 days);[30] and 96.5% cured (346, day 7, 500 mg once daily, 7 days).[31]

Though the novel respiratory fluoroquinolones offer substantial superior clinical benefit, their success has often been hampered by the presence of penicillin-resistant *S. pneumoniae* (PRSP) and quinolone-resistant *S. pneumoniae* (QRSP) strains in circulation. These strains are often resistant to multiple antibiotic classes.[3] For AECOPD/AECB management, a randomized, double-blind (MAESTRAL) study involving 1372 patients reports failure rate of 22% with amoxicillin + clavulanate (875/125 mg twice daily, 7 days), 20.6% with moxifloxacin (400 mg once daily, 5 days) at 8 weeks and an observational study involving 260 patients reports 12.5% failure rate with both amoxicillin + clavulanate /moxifloxacin at 4 week.[32,33]

A recent study reports worldwide 15-30% *S. pneumoniae* are multidrug-resistant, i.e., resistant to ≥3 antibiotic classes.[34] An Asian surveillance of CAP patients reports 52.6% *S. pneumoniae* non-susceptible to penicillin.[35] A surveillance from the United States reports rise of penicillin-resistant invasive *S. pneumoniae* serotype 19A from 6.7% in 1998 to 35% in 2005.[36] A PROTEKT surveillance study from the United states involving 39,495 isolates reports 21.2% isolates resistant to penicillin.[37] Global surveillance studies report 10-30% *S. pneumoniae* isolates harbors first step mutations conferring low-level fluoroquinolone resistance.[38] A multicenter study from Hong Kong reports 13.3% Levofloxacin and 8.9% moxifloxacin resistance with *S. pneumoniae*.[39]

Garenoxacin a des-fluoroquinolone with novel structure essays lower MIC_{90} and higher AUC/MIC_{90} ratio amounting to higher potency, killing power and lower susceptibility to resistance mechanisms against extensive Gram-positive/negative and atypical pathogens including *S. pneumoniae*, *H. influenzae*, and *M. catarrhalis*.[10,11]

A prescription event monitoring study involving 11,698 patients comprised of 39% AECB patients reports 91.3% clinical success with Garenoxacin.[40] A review of RCTs by Takagi *et al.* reports 93% efficacy with Garenoxacin in AECB patients.[10]

According to various *in vitro* studies, Garenoxacin demonstrates lower MIC_{90} against PRSP compared to moxifloxacin and levofloxacin. Garenoxacin demonstrates lower MIC_{90}, higher AUC/MIC_{90} ratio, shorter time required to achieve 99.9% killing against *S. pneumonia* mutants with single, double, or triple mutations in quinolone resistance determining region, i.e., QRSP and lower tendency to select resistant clones signifying better activity compared to moxifloxacin, levofloxacin against QRSP.[41-47] A review of RCTs by Takagi *et al.* reports 89% efficacy with Garenoxacin against PRSP.[10]

An *in-vitro* study involving 14,665 pneumococcal strains reports 8-32-fold greater activity with Garenoxacin compared to Levofloxacin, inhibition of >99.9% strains and>99.9% activity against *S. pneumoniae* strains resistant to 6 drug classes.[48] Another *in-vitro* study involving 18,887 *S. pneumoniae* isolates reports Garenoxacin potency of 16-32-fold superior than levofloxacin and 2-fold superior than Moxiflxoacin.[49]

Garenoxacin offers comprehensive efficacy of 91-96% against RTI with better safety profile established over ≈20,000 patient indexes. Garenoxacin shows efficacy of ≈94% against β-lactam or macrolide-resistant *S. pneumoniae* in clinical trials.[10,50]

In the present study associated with comorbidities or risk factors were present in 65% cases which included mainly past history of Tuberculosis, Tye 2 DM, Hypertension, Smoking or Alcoholism. Past history of tuberculosis was present in AECOPD or Bronchiectasis cases mainly, and none of the patients were diagnosed to have active tuberculosis or were on concurrent anti-tuberculous therapy. Current retrospective analyzes report 100% clinical success with Garenoxacin for the LRTI management.

Current retrospective analyzes findings are exploratory and need to be further confirmed in multicenter, randomized, double-blind clinical trial for AECOPD.[30,51]

CONCLUSION

AECOPD, a cause of significant health burden leads to very high mortality post hospitalization. RTIs are most common cause precipitation of exacerbation in COPD patients with *S. pneumoniae* as the most common responsible pathogen. Widespread use of beta-lactams governs rising prevalence of PRSP. Fluoroquinolones remain preferred agents for the management of AECOPD, especially with associated significant comorbidities and risk factors. Garenoxacin des-fluoroquinolone with unique structure exhibits lower MIC_{90} signifying better activity against common respiratory pathogens including PRSP, QRSP, and AECOPD or LRTI management compared to levofloxacin and moxifloxacin.

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Original Article

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Duplication Renal Anomalies in Children: A Single Centre Experience

Sriram Krishnamoorthy[1], Shivraj Barath Kumar[2], Ramesh Babu[3]

[1]Professor, Department of Urology, Sri Ramachandra Medical College & Research Institute, Chennai, Tamil Nadu, India, [2]Post-graduate Student, Department of Urology, Sri Ramachandra Medical College & Research Institute, Chennai, Tamil Nadu, India, [3]Professor, Department of Paediatric Urology, Sri Ramachandra Medical College & Research Institute, Chennai, Tamil Nadu, India

Abstract

Introduction: Duplication anomalies are one of the most common congenital anomalies of the urinary tract. The overall incidence of duplex kidneys is 1% of all live births. With routine antenatal screening by obstetricians becoming a common practice these days, more and more of such conditions are being detected antenatally

Purpose: Duplication anomalies of the kidneys are congenital anomalies, characterized by the presence of two separate pelvi-calyceal units. They may be associated with or without duplication of ureters. The overall incidence of duplex kidneys is 1% of all live births.

Materials & Methods: This was a retrospective audit on patients with duplication anomalies of the kidneys. All children with such duplication anomalies, who were admitted in our institution, were included in our study.

Results: Forty-two children were diagnosed to have duplication anomalies over a period of 11 years from 2004 to 2014. Nineteen children, who fitted well in our inclusion criteria and needed surgical intervention, were included in our study. Recurrent UTI was the most predominant mode of presentation. More than 50% of children needing surgical intervention (*n*=10) had presented with febrile UTI, recurrent break through infections necessitating multiple repeated admissions and a progressive deterioration of renal function. Ureterocele of the upper moiety was the most common anomaly observed in 10. Of these, two children had associated non-functioning upper moiety and underwent Hemi Nephrectomy.

Conclusion: Duplication anomalies require a systematic evaluation with all available armamentarium. Management of these conditions is tailor made based on the type of anatomy and function. A minimally invasive option is often successful in a majority of such patients. A systematic approach looking for specific objective ultrasound parameters will be helpful in diagnosis of children with duplication renal anomalies. High index of suspicion often leads to earlier detection and an earlier post natal intervention.

Key words: Duplication anomaly; Ectopic ureter; Hemi Nephrectomy; hydronephrosis, Ureterocele

INTRODUCTION

Duplication anomalies are one of the most common congenital anomalies of the urinary tract. The overall incidence of duplex kidneys is 1% of all live births.[1] It also accounts for 7.2% of patients with congenital urinary tract anomalies.[2] With increasing usage of antenatal screening by obstetricians, more and more of such conditions are being detected antenatally.[3]

Duplication anomalies of the kidneys are congenital anomalies, characterized by the presence of two separate pelvicalyceal units. They may be associated with or without duplication of ureters.

Despite being one of the most common anomalies of the kidney, this condition is grossly under reported most of the times, owing largely to many of the cases that are either missed out during routine antenatal screening and/or as they remain largely asymptomatic in the early postnatal period.[4] However, the risk of renal infection in children is increased by 20 folds with advancement in age.[5] Many

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Corresponding Author: Ramesh Babu, Department of Paediatric Urology, Sri Ramachandra Medical College, Chennai - 600 116, Tamil Nadu, India. Phone: +91-9840359062. E-mail: drrameshbabu1@gmail.com

of these children develop serious complications in their childhood or in the early adolescent period with recurrent breakthrough urinary tract infections, urinary incontinence or progressive deterioration of renal function, needing some form of medical or surgical intervention.[6]

The traditional classification of the duplex system into complete (two ureters) and incomplete (Y-shaped ureters) is based on intravenous urogram. With the advent of computed tomography (CT) urography, based on the radiological features of both the moieties, Rui defined a new classification. Here, the duplex kidney was classified into five types which can be depicted by CT urography prior to management that could facilitate in selecting an appropriate mode of treatment.[7] However, magnetic resonance urography (MRU) has largely revolutionized the understanding of the complexity of pelvicalyceal anatomy, and the most comprehensive morphologic and functional evaluation of duplex systems can be achieved using MRU.[8]

The purpose of this article is to retrospectively audit the various duplication anomalies of the kidneys that we have come across in our institution and also to highlight their various modes of presentation, the various modalities of treatment offered and their long-term follow-up.

MATERIALS AND METHODS

This was a retrospective audit on patients with duplication anomalies of the kidneys. All children with duplication anomalies of the kidneys, who were admitted to Sri Ramachandra Medical College and Research Institute and subsequently underwent surgical correction of these anomalies, were included in our study.

Those children with recurrent urinary tract infections, life-threatening urosepsis or having intractable symptoms or progressive deterioration of renal function were subjected for surgical intervention.

Children with associated neurovesical dysfunction or those who presented with life-threatening urosepsis needing emergency temporary diversion procedures or those with the duplex system not needing any form of surgical intervention and those who had not turned up for a regular post-operative follow-up were all excluded from our study.

The pre-operative evaluation included Voiding cystourethrogram (VCUG), Intravenous urogram, CT assisted urogram, Nuclear Scintigraphy, and Magnetic Resonance Urogram whichever we felt as required and appropriate. All these patients were followed up

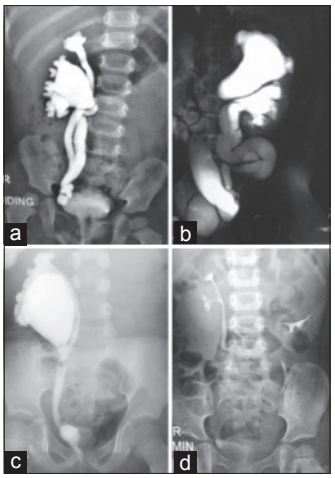

Figure 1: Describes the various types of duplication anomalies encountered in our study. (a) Vesico-ureteral reflux with both moieties functioning - underwent common sheath reimplant, (b) Ureterocele with functioning upper moiety - underwent endoscopic incision, (c) Lower pole PUJ with functioning moiety - underwent uretero-pyelostomy, (d) Non-functioning upper pole with ectopic ureter - underwent lap heminephrectomy

postoperatively with urine culture, ultrasound abdomen, and nuclear scintigraphy. VCUG was done in children with persistent urinary tract infections. The management of cases was individualized based on the anatomy and functioning status of the moieties.

RESULTS

A total of 42 children were diagnosed to have duplication anomalies over a period of 11-year from 2004 to 2014. Of these 19 children, who needed surgical intervention were included in our study.

Female children were more commonly involved than males, with the female to male ratio being 1.4-1. The mean age of presentation was 38 months, with the youngest presenting at 7 months and the oldest being 10 years of age. The median age of presentation was 36 months. Table 1 summarizes the details of all the 19 patients who had undergone surgical intervention.

Two patients had bilateral VUR, and one had unilateral VUR. All three underwent common sheath reimplantation. Duplication anomaly was seen almost equally on both sides, with the left ureter showing duplication in 10 children. Figure 1a-d gives examples of the various types of duplication anomalies that we had managed in our study.

Recurrent UTI was the most predominant mode of presentation. More than 50% of children needing surgical intervention (n = 10) had presented with febrile UTI, recurrent breakthrough infections necessitating multiple

Table 1: Patient characteristics, management, and follow-up of all children managed surgically

S. No.	Age (in months)/ gender	Laterality	Presenting complaints	USG/MCU/IVU/CT/MRI/RENOGRAM	Surgical management	Follow-up (at 1 year)
1	60/F	L	Constant dribbling	Left ectopic ureter from non-functioning upper pole; no VUR into left lower/right	Lap upper pole HN	Preserved left lower pole function
2	11/F	L	Recurrent UTI	Ureterocele from non-functioning upper pole; no VUR into left lower/right	Lap upper pole HN	Preserved left lower pole function
3	10/M	L	Antenatal HN	Left duplex; ureterocele from functioning upper moiety; no VUR in any	TUI	Preserved left lower pole function; grade 2 VUR following incision; no UTIs
4	7/F	L	Antenatal HN	Left duplex; ureterocele from non-functioning upper moiety; no VUR	Lap upper pole heminephrectomy	Loss of function in left lower pole also at follow-up/no intervention; no UTIs
5	48/M	L	Recurrent UTI	Ureterocele from functioning upper pole; no VUR	TUI	No further UTIs; no VUR
6	120/F	L	Constant dribbling	Left ectopic ureter from functioning upper pole; no VUR into left upper/right	Uretero-pyelostomy left upper pole to lower pole; Ectopic ureter from left upper pole excised as low as possible	No UTIS, no more dribbling
7	72/M	R	Antenatal HN and recurrent UTI	VUR with non-functioning lower pole right; no VUR on left	Lap right lower pole heminephrectomy	Preserved right upper pole function; no further UTIs.
8	48/F	R	Recurrent UTI	Right sided duplex with VUR and both upper and lower functioning on right side/no VUR on left	Right common sheath reimplantation	No further UTIs
9	24/M	R	Recurrent UTI	Ureterocele from functioning upper pole; no VUR	TUI	No further UTIs; grade 3 VUR into upper pole; stable/no intervention
10	12/F	L	Antenatal HN	Left duplex; ureterocele from functioning upper moiety; no VUR in any	TUI	Preserved left lower pole function; No VUR following incision; no UTIs
11	36/M	BL	Recurrent UTI	Bilateral duplex with VUR and both upper and lower functioning	Bilateral common sheath reimplantation	No further UTIs
12	48/F	BL	Recurrent UTI	Bilateral duplex with VUR and both upper and lower functioning on both sides	Bilateral common sheath reimplantation	No further UTIs
13	60/M	L	Recurrent epidydymo orchitis	Left ectopic ureter from non-functioning upper pole opening in verumontanum; grade 2 VUR into left lower/right	Lap upper pole heminephrectomy	Preserved left lower pole function; no UTIs; VUR managed conservatively
14	24/F	R	Antenatal HN	Ureterocele from functioning upper pole; no VUR	TUI	No further UTIs; grade 1 VUR; no UTIs
15	12/F	L	Antenatal HN	Ureterocele from functioning upper pole; grade 2 VUR lower pole	TUI	No further UTIs; Grade 1 VUR settled during follow-up; no UTIs
16	48/F	R	Constant dribbling	Right ectopic ureter from non-functioning upper pole; no VUR into right lower/right	Lap upper pole heminephrectomy	Preserved right lower pole function
17	36/M	L	Recurrent UTI	Ureterocele from functioning upper pole; no VUR	TUI	No further UTIs; no VUR
18	48/M	R	Recurrent UTI	Incomplete duplication; Lower pole PUJ; preserved function; VUR into common ureter left	Lower to upper Pyelo ureterostomy and left ureteric reimplantation	No Further UTI s
19	10/F	R	Antenatal HN	Ureterocele with functioning upper pole	TUI	No further UTIs. No VUR

M: Male, F: Female, R: Right; L: Left; BL: Bilateral, UTI: Urinary tract infections, HN: Hydronephrosis, VUR: Vesico-ureteral reflux, USG: Ultrasonogram of abdomen, CT: Computed tomography, IVU: Intravenous urogram, MCU: Micturating cystourethrogram, MRI: Magnetic resonance imaging, TUI: Transurethral incision, HN: Heminephrectomy

repeated admissions and a progressive deterioration of renal function. Those children who were antenatally diagnosed to have hydronephrosis and subsequently followed up in the postnatal period constituted the second most common mode of presentation (n = 6). All four children with ectopic ureter had incontinence of urine needing surgical intervention, but one of them, a 5-year-old male child had recurrent epididymo-orchitis, needing heminephrectomy.

Ureterocele of the upper moiety was the most common anomaly observed in 10 patients. Of these, two children had associated non-functioning upper moiety and underwent heminephrectomy.

All patients were symptom-free at the end of 1 year. None of the patients had any complication either during the procedure or thereafter. Four patients had reflux into the upper moiety following endoscopic incision. But none of

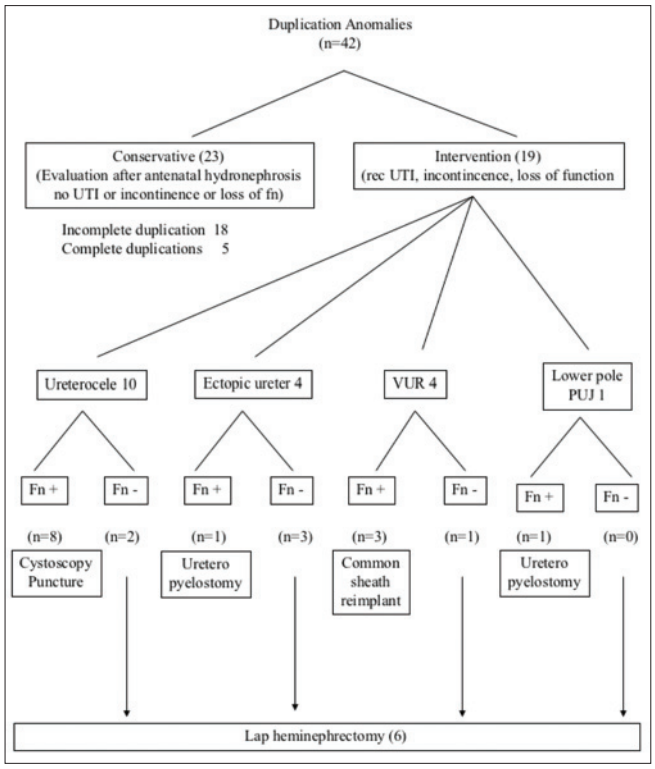

Figure 2: Algorithm giving an overview of management of all patients with duplication anomalies

them required intervention, as there were no breakthrough infections in any of these patients. One child had a slight decrease in upper moiety function after incision but is being followed up, as she is asymptomatic. One child, who underwent upper pole heminephrectomy, had a decrease in function of the lower moiety as well. As she did not have any symptoms, she has been kept under close monitoring. None of our children had any problems with the remnant stump after heminephrectomy. The flow chart in Figure 2 summarizes the details of the management of all patients with duplication anomalies.

DISCUSSION

The routine use of antenatal ultrasound screening in the second trimester has significantly increased the detection of various congenital anomalies in the fetuses. In one of the largest studies on more than 7000 fetuses, the urinary tract anomalies constituted 17.3% of the total fetal anomalies.[9] Duplication of the renal pelvis and ureters is the most common urogenital anomaly.[10] The overall reported incidence of duplication of upper urinary tract is 0.7-1%, and the most common anomaly associated with duplex system is vesico-ureteric reflux.[11]

The development of the duplex system is known to be due to an additional ureteral bud arising from the mesonephric duct and meeting the renal blastema at a separate site from the original bud.[12] It is not uncommon to have more than one renal abnormality in patients with the duplex system. In cases of complete duplication, the ureters enter the bladder in contrast to the moieties that they drain. The orifice of the upper moiety is characteristically located medial and caudal than the orifice of the lower moiety that is located cranial and lateral. This relationship is so consistent that it is called, Weigert-Meyer rule, which is seen to be obeyed in more than 90% of the cases.[13]

In one of the series of excretory urograms performed in 1716 children and 3480 adults to find out the overall incidence and complications of renal duplication anomalies, Privett *et al.* observed that the duplication anomalies were present in 1.8% of the general population, and females were twice as commonly involved as males.[14] In our study, nearly 60% of the patients were females and bilateral in 10% of the cases.

With an ever increasing awareness in doing routine antenatal screening ultrasounds these days, more and more of these asymptomatic duplex anomalies are being diagnosed. Whitten *et al.* had observed that the use of routine antenatal ultrasound has considerably increased in the recent years, resulting in increased diagnosis of such malformations of the kidneys.[4] From their retrospective audit of all patients who had antenatal USG, they were able to identify and classify the likelihood of duplex kidney based on objective ultrasound parameters. In their study, they were able to correctly diagnose the condition in as high as 75% of the cases using such prognostic features. In our series, 7 children were diagnosed antenatally (about 37%) and treated appropriately.

Ureteroceles have been one of the most common associated anomalies in patients with duplex systems. Godinho reports 4 cases of fetal ureterocele diagnosed at a mean gestational age of 23 weeks.[15] Yong observed that ectopic ureteroceles were frequently associated with ureteral duplication.[16] In their retrospective study on the post-operative results on 39 patients in 12 years' period, they observed that the median age at operation (common sheath reimplantation) was 16 months. In our study, the mean age at common sheath reimplantation was 44 months. 10 out of 19 children had ureteroceles in our study, and all of them were intravesical. Eight of them benefitted with endoscopic transurethral ureterocele incision. Two had non-functioning upper moiety and underwent upper moiety heminephrectomy.

The management of asymptomatic ureteroceles in the duplex system has always been a challenging task. The management depends on whether it is intravesical or extravesical, functional status of the upper moiety and

presence of associated reflux in the lower moiety. The endoscopic incision is the widely accepted appropriate treatment for a completely intravesical ureterocele.[17] Sander observed a higher need for second surgery in children undergoing endoscopic incision of ureteroceles in the duplex system.[18,19] In our study, 4 children had mild reflux following incision, but were asymptomatic and followed up with conservative measures.

In a select group of patients, non-surgical expectant treatment of antenatally detected ureteroceles has also been an accepted protocol. Shankar *et al.* observed in his study that in those with duplex system ureteroceles, 27% of them were asymptomatic and were followed up for 8 years and none of them required surgery or developed urinary tract infections.[20] In our series also, ureteroceles that were asymptomatic were followed up conservatively.

Uretero-pyelostomy or uretero-ureterostomy is a feasible option in a select group of patients with the duplex system and functioning moieties in whom the existing function of the moieties needs to be preserved. Choi and Oh, in their series of 63 children with complete duplex system concluded that uretero-ureterostomy had been the most successful nephron-sparing additional surgery, especially if the upper moiety is salvageable. Similar views were echoed by various other authors as well.[19,21] In our series, two children were benefitted by uretero-pyelostomy (one for ectopic ureter and the other for pelvi-ureteric obstruction of lower moiety) with an excellent long-term follow-up.

The management of non-functioning moieties has been a relatively easy task. Laparoscopic heminephrectomy has been the standard treatment of poorly functioning moiety. It is a relatively safe mode of treatment, reproducible with relatively low morbidity and better treatment outcomes.[22] Traditionally, the majority preferred a transperitoneal approach, but the retroperitoneal approach is a relatively new and well-tolerated minimally invasive approach despite being technically demanding.[23] The robotic transperitoneal approach is fast catching up and is now considered as an acceptable modality of treatment. Malik noted that robotic-assisted heminephrectomy provided comparable results in regard to complication rate and renal function of the remnant moiety.[24] In their comprehensive review of robot-assisted laparoscopic urology procedures, Song SH supported the view that despite a high purchase and maintenance cost involved, robotic technology has been a technically feasible and safe approach, especially for managing complex duplication anomalies.[25]

On the other hand, heminephrectomy is not without complications. Gundeti *et al.*, in his study on assessment of functional outcome 101 patients following heminephrectomy, observed that there was a mild decrease in the function of the remaining moiety in more than 50% of the patients.[26] Dalsan *et al.* reiterated the need for following up all remnant moieties with nuclear scintigraphy even though the extent of functional damage is subtle.[27] Complete ureterectomy along with heminephrectomy also has its own drawbacks. The risk of injury to the good ureter may outweigh the benefits of complete ureterectomy.[28] It's prudent to leave behind a distal ureteric stump in such cases.

Leclair reiterated that the possibility of vascular damage to the remaining moiety warranted a very cautious dissection of the renal pedicle. One should not hesitate to convert if clear visualization of vascular anatomy could not be ascertained.[29]

Hisamatsu observed that recurrent infections after heminephrectomy were all treatment outcomes based on the initial surgical approach to ectopic ureterocele rather than isolated problems associated with a distal ureteral stump. They concluded that total ureterectomy is unnecessary at the time of heminephrectomy for a poorly functioning moiety because the distal ureteral stump rarely causes a problem.[30] In our series, we left behind a distal ureteral stump in all six cases to avoid injury to the adjacent normal ureter. None of them had complications as a result of this.

Most of the patients with the duplex system are asymptomatic. Many of the antenatally detected patients with duplication anomalies, when they were followed up in the postnatal period, were found to have a rather benign course. Treatment is indicated only when these patients are symptomatic either in the form of recurrent breakthrough infections or if there are clinical signs of deterioration of renal function. The treatment strategies are modified based on the functional status of the moieties, the degree of obstruction and the extent of dilatation of pelvicalyceal system, symptomatic status of ureteroceles, grade of vesico-ureteral reflux, and the site of the insertion of ectopic ureters.

In our institution, all children with antenatal hydronephrosis are followed up in the immediate postnatal period. All children are subjected for repeated periodic ultrasound abdomen, micturating cystourethrograms, and serial DTPA renograms. At any point of time, where if the infection is not settling with conservative measures, or if there is a progression of hydronephrosis or a deterioration of renal function, they are subjected for surgical intervention.

CONCLUSIONS

Duplication anomalies require a systematic evaluation with all available armamentarium. The management of these conditions is tailor made based on the type of anatomy and function. A minimally invasive option is often successful in a majority of such patients. A systematic approach looking for the presence of certain specific objective ultrasound parameters will be very helpful in the diagnosis of children with duplication renal anomalies. A high index of suspicion leads to an earlier detection of these anomalies and offers potential benefits, including earlier postnatal intervention. This considerably decreases the morbidity, risks of recurrent urinary tract infections, and progressive renal deterioration.

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Original Article

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Coronary Artery Bypass Surgery in "Awake" Patient: A Prospective Study

Tumulu Rajmohan Rao[1], Avinash Dal[2], Anil Dronumraju[3], K Kiran Kumar[4], J Ibrahim[5]

[1]Chief Cardiac Anaesthesiologist, Sunshine Hospitals, Secunderabad, Telangana, India, [2]Chief Cardiothoracic Surgeon, Continental Hospital, Hyderabad, Telangana, India, [3]Consultant Cardiothoracic Surgeon, Continental Hospital, Hyderabad, Telangana, India, [4]Consultant Cardiac Anaesthesiologist, Indus Hospital, Visakhapatnam, Andhra Pradesh, India, [5]Chief Cardiac Perfusionist, Continental Hospital, Hyderabad, Telangana, India

Abstract

Background: Advances in cardiac surgery and anesthesia are meant to give better outcomes and faster recovery for the patients. As the rate of success of coronary bypass surgery has been standardized over the years, we are presently attempting to improve early recovery which directly helps in early rehabilitation.

Aim: To see the feasibility of awake cardiac surgery under epidural anesthesia. Single tertiary care medical center. Prospective, randomized, non-blinded clinical study. 10 patients scheduled for awake off-pump coronary artery bypass surgery.

Subjects and Methods: In selected 10 patients epidural catheter was inserted between C7-T3 inter-vertebral spaces 1 day prior to surgery. On the day of surgery, epidural anesthesia was given with bolus dose of 0.05 ml/cm of height of patient of 0.5% bupivacaine and 100 µg of fentanyl. After assessing the level of block, continuous infusion of 0.5% bupivacaine at 3 ml/h was started, and infusion rate was adjusted according to the requirement. Post-operative analgesia was maintained with continuous infusion of 0.125% bupivacaine 4-14 ml/h according to pain score. The epidural catheter was left *in-situ* for 48 h and removed.

Result: Thoracic epidural anesthesia (TEA) without intubation was used in 10 patients undergoing off-pump coronary artery bypass graft surgery, performed successfully through a median sternotomy. The mean surgical time was 113.5 min; average intravenous fluid infusion was 595 ml, one patient required nor-adrenaline infusion during surgery. The requirement of epidural infusion intra-operative and post-operative period was 20 ml and 276 ml, respectively. All patients had an uneventful post-operative course.

Conclusion: The study shows that awake cardiac surgery using only TEA without general anesthesia is feasible and safe.

Key words: Analgesic techniques, Awake surgery, Cardiac, Regional, Thoracic epidural anesthesia

INTRODUCTION

Surgical myocardial revascularization has undergone many changes from the way it was performed in the initial days. Though the initial focus was primarily on mortality and efficacy of the revascularization, the current focus is on the morbidity of the surgical procedure and the pattern of recovery of the patients in the post-operative period.

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Nevertheless, no new procedure and/or technique can ignore the primary aims of the surgery; and keeping this in mind, techniques can be developed, and advances be made to improve the overall result of the surgery. One such advance made is the use of latest anesthesiological techniques, thus facilitating faster recovery of patients by surgery performed under regional anesthesia in a totally conscious patient (conscious coronary artery bypass, CONCAB). Coronary arteries bypass grafting (CABG) in an "awake" patient without endotracheal general anesthesia with high thoracic epidural block was first performed in October 1998.[1] Regional anesthesia with the use of high thoracic epidural anesthesia (TEA) and post-operative analgesia in patients undergoing cardiac surgery leads to stress-response attenuation, improved perioperative analgesia, cardiac sympatholysis, and

Corresponding Author: T Rajmohan Rao, 302-A, Usha Enclave, Navodhaya Colony, Hyderabad - 500 073, Telangana, India. Phone: +91-9701185818. E-mail: rajmohanrao@yahoo.co.uk

improved post-operative pulmonary function.[2-4] Therefore, it appears advantageous to combine the benefits of beating heart surgery with TEA, which enables CABG in the "awake" patient. Similar cases have been reported in the literature in an attempt to ameliorate the morbidity of the CABG procedure.[5-7] This study represents experience in first 10 patients who underwent this procedure.

SUBJECTS AND METHODS

After getting the approval from the ethics committee and informed consent from the patients, who were undergoing off-pump CABG, 10 cases had been selected for "awake CABG surgery." Inclusion criteria and exclusion criteria were defined in Tables 1 and 2, respectively.

During the pre-anesthetic visit, patients were explained about the procedure and its complication along with the routine clinical activity. The epidural catheter was inserted 1 day before surgery in all the patients. The procedure was done in the intensive care unit (ICU). Routine monitoring during epidural catheterization was done with electrocardiogram (ECG), non-invasive blood pressure, and pulse oximetry. Emergency drug tray (atropine, lidocaine, and ephedrine) was prepared and kept. A wide bore peripheral intravenous line was established with either 16 G or 14 G IV cannula. In sitting position, 20 G epidural catheter was inserted through an 18 G Touhy needle in a prominent inter-vertebral space between C7 and T3. Epidural space was identified by loss of resistance method. Only 3 cm of the catheter was kept inside the epidural space, and a sterile dressing was placed, taking care that the catheter was not kinked. The patients were pre-medicated with oral tablets of diazepam (5 mg) and ranitidine (150 mg) the night before surgery; and lorazepam (2 mg) and ranitidine (150 mg) 30 min before shifting to operation theater (OT).

In the OT, patients were connected to the monitor; femoral artery cannulation and Swan-Ganz catheter insertion were done under local anesthesia. Correct placement of the epidural catheter was tested with bolus dose of 2 ml of 0.2% lidocaine with 1:2,00,000 adrenaline. Criteria followed for correct placement were: (1) No rise in heart rate more than 10 beats/min, (2) No rise in systolic blood pressure more than 15 mmHg, and (3) No sign and symptom of the subarachnoid block. We have used 2 ml of test dose which contains 40 mg of lidocaine and 10 μg of adrenaline which is sufficient to recognize the inadvertently placement of the catheter in intravascular or subarachnoid space.[8] After successful test dose, epidural anesthesia was given with bolus dose of total 10 ml of 0.5% bupivacaine (which is 0.05 ml/cm of height of patient[9]) and 100 μg of fentanyl. This combination was given over 15 min through a syringe pump. The level of the block was checked for T1-T6 dermatome by the loss of pinprick and temperature sensation. The surgical skin incision was mid-manubrial which was well below the sternal notch thus avoiding the overlap of cervical dermatomes on the upper thoracic dermatomes. If the patient perceives any pain during skin incision, the surgeon may infiltrate local anesthesia. After assessing the level of block continuous infusion of 0.5% bupivacaine at 3 ml/h was started, and the dose was adjusted according to the requirement. Oxygen was administered through Hudson's mask. The patients' ECG, respiratory rate, pulse oximetry, rectal temperature, arterial pressure, and pulmonary artery pressure were monitored. Arterial blood gases were sampled every 2 h and were found to be satisfactory (Tables 3 and 4). The patients' limbs were strapped to prevent accidental movement during surgery.

Table 1: Inclusion criteria of patients

1	Willing to sign written informed consent document
2	Patients scheduled for elective off-pump coronary artery bypass grafting surgery
3	Stable angina
4	Left ventricular ejection fraction >50%
5	Prothrombin time (INR) <1.5
6	Partial thromboplastin time <45 s
7	Platelet counts >100,000/ml
8	Antiplatelet therapy stopped for 1 week

INR: International normalized ratio

Table 2: Exclusion criteria of patients

1	Emergency operation
2	Known coagulation disorders or recent thrombolytic therapy
3	Unstable angina
4	Heart block
5	Acute myocardial infarction within the previous 7 days
6	Clinically significant associated valvular disease
7	Significant left main disease (LM >50%)
8	Patient on IABP or on ventilator
9	Known neuraxial pathology
10	Infection at the site of epidural catheter insertion
11	Patients participating in other clinical studies
12	Difficult airway

Table 3: Hemodynamic parameter

Parameter	Before TEA	30 min after TEA	2 h after TEA	4 h after TEA	12 h after TEA	24 h after TEA
Heart rate	85.71	63.42	63.14	75.28	77	74.14
ABP-systolic	154	129.85	120.85	129	138.57	135.57
ABP-diastolic	75.57	68	62.14	67.85	73.28	69.71
ABP-mean	105.14	91.14	83.71	92.28	98.14	90
PAP-systolic	26.28	32.57	27.42	31.71	31.85	28.42
PAP-diastolic	14.14	15.85	12.28	16.85	15.57	17
PAP-Mean	18.85	22.85	17.42	21.71	21.85	19

TEA: Thoracic epidural anesthesia, ABP: Arterial blood pressure, PAP: Pulmonary artery pressure

To prevent hypothermia, the room temperature was kept at 22°C, intravenous (IV) fluids (ringer lactate solution IP) were given through on line warmer, and a warming blanket was used to keep the patient warm. After sternotomy, the surgeon carefully harvested the left internal mammary artery (LIMA), using an extrapleural dissection technique without opening the left pleura and radial artery through a vertical incision in the forearm. The lungs and pleura moved less toward the surgeon during harvesting of LIMA as compared to controlled ventilation. Therefore, extrapleural dissection was easier than normal. Heparin injection was administered to keep the activated clotting time around 300 s. In the case of single vessel disease, the LIMA was anastomosed to left anterior descending. In triple and double vessel disease, the LIMA and radial artery were anastomosed together, as a Y-graft. Anastomoses were performed by the standard beating heart technique. Epicardial stability was achieved using octopus 3 tissue stabilizers (Medtronic Inc, Minneapolis, MN). After the anastomosis, protamine was administered to neutralize the heparin. As both the pleurae were intact, only 2 mediastinal chest tubes were placed. The sternum was approximated with 6 steel-wire-sutures and incisions were closed in layers. The patients were hemodynamically stable throughout the procedure (Table 5). Their mean arterial pressure was maintained >70 mmHg with IV fluids (ringer lactate IP), lowering the head end of operation table and infusion of a vasopressor such as ephedrine and nor-adrenaline. During the whole procedure, patients were verbally communicating and listening to the music of their choice.

At the end of the surgery, patients were shifted to the ICU, and post-operative analgesia was maintained with continuous infusion of 0.125% bupivacaine 4 ml/h. Opioids were knowingly avoided in epidural infusions as they cause sedation. The pain relief was assessed by VAS scale. The infusion rate was adjusted depending on the patient's condition. If the patient complains of inadequate pain relief (VAS>4), the rate will be modified providing it had been constant for at least 30 min. Each dose adjustment will consist of 4 mL top-up dose followed by a 2 mL/h increase in infusion rate up to a maximum of 14 mL/h. The rate of epidural infusion will be decreased if the patient complains of paresthesia in dermatome C8 or higher, weakness in upper limbs or the patient is pain-free (VAS<4). The epidural catheter was left *in-situ* for 48 h and removed before the patient was shifted out of ICU; subsequent analgesia was obtained by oral analgesics.

Post-operative monitoring was consist of ECG with automatic ST segment analysis, intra-arterial blood pressure, pulmonary artery pressure, SpO_2, arterial blood gas analysis every 6 h, creatine phosphokinase (CPK-MB), and troponin-T (Trop-T) 6 and 12 h after surgery.

RESULTS

The demographic profile (Table 6) shows all the patients were male, mean age was 54 years, weight 65 kg, 5 of them had single vessel disease, 3 had double vessels, and 2 had triple vessel disease. Their ejection fraction was more than 56%, 4 patients had regional wall motion abnormalities, and 2 had a history of myocardial infraction. 4 patients were actively smoking, 3 patients were alcoholic, 3 patients were diabetic, 2 had renal dysfunction with serum creatinine more than 1.5 mg/dl, 7 patients had treated high arterial pressure, and 2 had the chronic obstructive pulmonary disease.

Desired level of the block from T1 to T6 dermatomes were achieved in 7.1 (4-11) min after infusion of bolus

Table 4: Respiratory parameter

Parameters	Before TEA	30 min after TEA	2 h after TEA	4 h after TEA	12 h after TEA	24 h after TEA
Respiratory rate	17.28	13.71	15.57	18	22	21.71
SpO_2	95	100	100	97.91	97.58	97.57
PaO_2	77.65	167.78	122.08	143.94	126.35	132.07
$PaCO_2$	34.47	43.74	40.7	42.52	39.04	39.91
pH	7.42	7.28	7.28	7.31	7.35	7.39

TEA: Thoracic epidural anesthesia, SpO_2: Peripheral oxygen saturation, PaO_2: Partial pressure of oxygen in arterial blood, $PaCO_2$: Partial pressure of carbon dioxide in arterial blood

Table 5: Result

Complications	Mean	Range (SDEV)
Surgical time (minutes)	113.5	85-145 (20.031)
Time of onset of block (min)	7.1	4-11 (2.071)
Amount of ringer lactate (ml)	595	350-1200 (245.407)
Intraoperative 0.5% bupivacaine (ml)	20	15-28 (4.335)
Post-operative 0.125% bupivacaine (ml)	276	230-350 (30.724)
Ephedrine bolus used		Two case
Nor-adrenaline infusion used		One case

Table 6: Demographic characteristics

Patient variable	Mean	STDEV
Age (y)	54.2	7.763
Sex M:F	10:0	
Weight	65.2	6.413
EF%	56.94	9.745
No of graft	1.7	0.853
	Frequency (%)	
Smoker	40	
Alcoholic	30	
Hypertension	70	
Previous MI	20	
RWMA	40	
Diabetes	30	
COPD	20	
Renal disease	20	

EF: Ejection fraction, MI: Myocardial infraction, RWMA: Regional wall motion abnormality, COPD: Chronic obstructive pulmonary disease

dose. Midline sternotomy and harvesting of internal mammary arteries were successful in all patients; no visible pneumothoraces were seen. Mean operative time was 113.5 min (85-145), number of bypasses was 1.7 (1-3) grafts. 2 out of 10 patients needed ephedrine bolus of 15 mg, and 1 patient needed an infusion of nor-adrenaline (0.02 μg/kg/min) to maintain mean arterial pressure above 70 mmHg. Total amount of IV fluid (ringer lactate) required during the intraoperative period was 595 ml (350-1200). Intraoperatively, the amount of 0.5% bupivacaine and fentanyl including both bolus and infusion dose was 20 ml (15-28), and postoperatively in the ICU 0.125% bupivacaine was of 276 ml (230-350) (Table 5).

Perioperative ECG monitoring with automatic ST segment analysis displayed no signs of myocardial ischemia. The levels of cardiac enzymes CPK-MB and Trop-T were normal (6 and 12 h after surgery). The patients were satisfied with their experience of this anesthetic technique and surgery. There was no major complication found in post-operative period (Table 7). They were discharged on the 5th post-operative day.

DISCUSSION

TEA is used in the post-operative period for alleviating the pain after cardiac surgery. Routinely, the surgery is done with general anesthesia. However, TEA provides excellent conditions for off-pump coronary artery bypass, by causing both coronary artery and systemic artery dilatation. This dilates the LIMA as well as improves collateral blood flow to the heart.[10,11] The hemodynamic condition remains stable during the manipulations of the heart, especially since the hypotensive and myocardial depressive effects of general anesthesia are absent.[12,13] In the case of breathing difficulty, hypoxia, or hypercapnea, a continuous positive pressure ventilation (CPAP) can be administered through a CPAP mask that can be connected to the circle absorber through a Y-connector. The end tidal $C0_2$ probe can be connected to this Y-connector.[12] unlike routine cardiac surgery, the negative pleural pressure is maintained. Thus, it facilitates the extrapleural dissection of the LIMA. There is always a theoretical danger of accidental opening of the pleura leading to pneumothorax and further lung collapse. However, usually the pleural perforation is small; hence, an intercostals chest tube needs to be inserted immediately and connected to continuous low suction through underwater seal to avoid this theoretical danger. The anesthesiologist should also be ready for endotracheal intubation if required. The danger of pleural perforation occurs during LIMA dissection and rarely during sternotomy itself. Deep pericardial stay sutures may be used, but thinner suture material must be used, and only a superficial bite must be taken to prevent the pleura and lung from being damaged. Analgesia after the surgery is good and systemic painkillers are not needed.[14] the patients' pain-free condition improves respiratory movements. Many other complications, which may be secondary to chest wall splinting, were avoided using this method. The risk of epidural hematoma formation in cardiac surgery patients was found to be much less than that of the overall population receiving epidural analgesia.[15] As general anesthesia and mechanical ventilation are totally avoided and excellent pain relief is achieved, the recovery is faster, and hospitalization is shortened.[5] In the right subsets of patients, it is very beneficial. Patients need to be co-operative and consenting for this technique. As patient comfort and co-operation is maximal due to the earlier mentioned advantageous factors, a better effort to recovery and also better patient satisfaction has been found. Long-term studies are thus needed for this procedure to be used as a standard approach. The various advantages offered by this procedure may allow awake CABG (i.e., CONCAB) to compete with interventional catheter-based techniques.

Table 7: Post-operative complications

Complications	No. of cases	Percentage
Intubation	Nil	
ECG changes	2	20
Arrhythmia	1 had ventricular ectopic subsided with amiodarone	10
ST changes	1 (elevated in all leads may be due to pericardial reaction)	10
Trop-T (+ve)	Nil	
Stroke	Nil	
Death	Nil	

ECG: Electrocardiogram, Trop-T: Troponin-T

CONCLUSION

10 patients were subjected to awake coronary artery bypass surgery with the use of TEA. Anesthesia and surgical techniques were modified to make it successful. In today's scenario many people, who are coming for CABG surgery, are not interested to be awake during surgery. It needs more effort to educate the patients about the procedure. The study shows that awake cardiac surgery using only TEA is feasible.

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Original Article

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Relevance of Color Doppler Study for the Assessment of Carotid Arteries of Individuals with Cerebrovascular Disease in Current Practice

A Einstien[1], N Praveen Kumar[2]

[1]Assistant Professor, Department of Radiology, Chettinad Hospital and Research Institute, Chennai, Tamil Nadu, India, [2]Consultant Radiologist, Department of Radiology, KG Hospital, Coimbatore, Tamil Nadu, India

Abstract

Background: Stroke is a major cause of mortality and morbidity. Atherosclerosis of the cranial vessels leading to cerebral infarction accounts for 80% of strokes. Duplex sonography, combining high-resolution imaging and Doppler Spectrum analysis has provided to be popular, noninvasive, accurate, and cost-effective means of detecting and assessing carotid disease. Besides estimating the degree of stenosis, the biggest advantage of sonography is its ability to characterize plaque and identify plaques with a higher risk of embolization.

Aims and Objectives: (1) To evaluate the morphological changes that take place in an extracranial portion of carotid arteries by color Doppler of carotid arteries in patients with cerebrovascular insufficiency. (2) To assess the utility of peak systolic velocity ratio of internal carotid artery and common carotid artery in the quantification of the carotid arterial stenosis. (3) To evaluate the spectral pattern and the color flow pattern in hemodynamically significant carotid artery disease.

Materials and Methods: In this 5-year study, 200 patients who had clinical findings consistent with cerebrovascular insufficiency were selected, and color Doppler examination was done. Findings were recorded and compared with various velocity ratios. Statistical analyzes were made with IBM SPSS software version 20.0.

Results: As the age increased, % of area stenosis increased. As the degree of stenosis increased the various velocities and their respective ratios increased in proportion to the stenosis. The majority of the plaques were located in the carotid bulb, and most of them were hyperechoic.

Conclusion: Duplex ultrasonographic criteria showed a better correlation with actual stenosis when the intervals of the degree of stenosis were 0%, <50%, 50-70%, 70-99%, and 100%. Doppler ultrasound in carotid artery stenosis had a sensitivity of 88% and specificity of 84%.

Key words: Carotid artery plaque, Doppler duplex ultrasonography, Pulse wave analysis, Stenosis, Stroke

INTRODUCTION

Stroke or cerebrovascular disease is a major cause of death, ranking third behind only malignancies and cardiovascular disease. Atherosclerosis of the cranial vessels leading to cerebral infarction accounts for 80% of strokes. Intracranial hemorrhage and subarachnoid hemorrhage account for the remainder. It has been conclusively proven that the risk for major stroke is higher in the first 3 months after transient ischemic attack (TIA).[1-3] Accurate diagnosis of hemodynamically significant stenosis is critical to identify patients who would benefit from surgical intervention.[4-6]

Duplex sonography, combining high-resolution imaging and Doppler spectrum analysis has provided to be popular, non-invasive, accurate, and cost-effective means of detecting and quantifying carotid disease.[7,8] Carotid sonography has largely replaced angiography for suspected extracranial carotid atherosclerosis.[9,10] Besides estimating the degree of stenosis, the biggest advantage of sonography is its ability to characterize plaque and identify plaques with higher risk of embolization.[11-13] With high-resolution

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Corresponding Author: Dr. A Einstien, Chettinad Hospital and Research Institute, SH-121, Rajiv Gandhi Salai, OMR, Kelambakkam, Chennai - 603 103, Tamil Nadu, India. Phone: +91-7299168640. E-mail: einstien.raju@gmail.com

ultrasound, plaque can be characterized into relative risk groups for containing intraplaque hemorrhage which is thought by many to be precursor plaque ulceration.[14,15]

The aims of the study were: (i) To evaluate the morphological and physiological changes that takes place in extracranial portion of carotid arteries by color Doppler of carotid arteries in patients with cerebrovascular insufficiency, (ii) to assess the utility of peak systolic velocity (PSV) ratio of internal carotid artery (ICA) and common carotid artery (CCA) in quantification of the carotid arterial stenosis, and (iii) to evaluate the spectral pattern and the color flow pattern in hemodynamically significant carotid artery disease by Duplex sonography.

MATERIALS AND METHODS

This study was carried out in the Department of Radiology in Rajah Muthiah Medical College and Hospital between October 2010 and September 2012 and in the Department of Radiology in Chettinad Hospital and Research Institute between October 2012 and September 2015. Sonographic examination of carotid arteries was done using Philips EnVisor Version C.0.2 machine with the multi-transducer system using a high frequency 7 MHz color Doppler linear array transducer. The examination was performed with a Doppler angle of 60°.

200 cases referred to the Radiology Department with history, and clinical findings consistent with cerebrovascular insufficiency for Color Doppler of carotid arteries were included in the study. The following data were collected:

- Intima-medial thickness (IMT) of CCA
- PSV of CCA and ICA
- PSV ratio between ICA and CCA
- Plaque characterization on real-time image
- Measurement of vessel lumen from frozen real-time image
- The presence of spectral broadening or turbulence.

The normal Intima-media thickness is <0.8 mm in healthy individuals.[16] As the study was conducted on 200 patients and each one has two carotid arterial systems, the analysis could be considered on the basis of 400 arteries. This made the calculations and observations easier as in some patients the IMT values were different on two sides.

An artery was classified as being affected by plaque if a focal thickening of >1.2 mm was observed in the vessel wall. Each major plaque was considered as a single entity. Therefore, any vessel showing 2 or more such plaques in tandem were considered as separate entities, whereas multiple insignificant small plaques seen in continuity and having a similar morphological appearance on gray scale ultrasonography were considered as a single entity. Statistical analyzes were made with IBM SPSS software version 20.0.

OBSERVATION AND RESULTS

The age of the patients ranged from 35 to 85 years. Out of total 200 patients, 112 were males and 88 females. The maximum number of patients belonged to the age group of 60-69 years, both in case of males (44) and females (36) making a total of 80 out of 100 patients, i.e., 40% of the total. The patients most commonly had TIA (62) followed by Hemiplegia/Hemiparesis (46) and coronary artery disease (30). Other complaints included Amaurosis fugax, vertigo, memory impairment, and confusion.

Six patients had velocities of their carotid arteries in higher ranges suggesting stenosis but no plaque was found in them. Four of them were found to have hyperthyroidism.

The mean age of patients with their arteries free of any plaques or stenosis was 57.04 ± 13.79 years and that of patients showing any evidence of plaques on either or both sides was 63.54 ± 10.72 years. This difference was statistically significant ($P < 0.05$).

20, out of a total of 400, arteries showed complete occlusion. Out of all the arteries in female patients, 104 arteries had 0% stenosis and only 4 had 100% stenosis (Figure 1). Stenosis increased PSV (Figure 2). In male patients, 32 arteries were found to have 100% stenosis, and 152 had 0% stenosis. Male:female ratio in stenosed arteries was 2:1. Females:males ratio was 3:2 for arteries free of any plaque or stenosis. The duplex criteria in relation with directly observed stenosis are illustrated in Table 1.

Out of total 200 arteries, 144 arteries had their IMT within normal limits and 56 above it. In patients who were <60 years of age only 4 arteries out of 74 had IMT

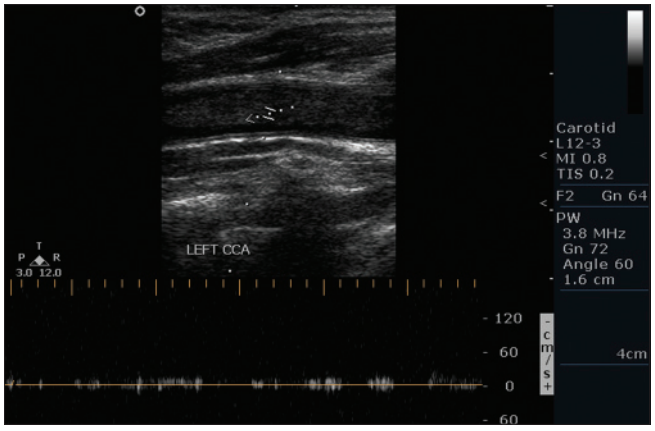

Figure 1: Left common carotid artery occlusion with absence of spectral wave

Table 1: Duplex criteria in relation with directly observed stenosis

% area of stenosis	No. of patients	ICA PSV Cm/sec	ICA EDV Cm/sec	ICA PSV/ CCA PSV	ICA EDV/ CCA EDV	ICA PSV/ CCA EDV
0	92	60.1	26.9	0.85	1.13	2.81
<30	50	69.2	21.6	0.94	1.23	4.20
30-39.9	8	57.95	19.8	0.95	1.48	4-49
40-49.9	16	80.85	26.2	0.90	1.38	4.16
50-59.9	4	127.3	17.05	2.11	1.08	7.98
60-69.9	12	127.5	17.05	2.11	1.08	7.98
70-79.9	4	192.95	31.15	1.53	2.2	7.11
80-89.9	2	389	104	3.74	5.87	21.97
90-99.9	2	282	159	3.55	8.5	15.08
100	Nil	Nil	Nil	Nil	Nil	Nil

EDV: End diastolic velocity, CCA: Common carotid artery, PSV: Peak systolic velocity, ICA: Internal carotid artery

>0.8 mm, whereas in patients >60 years it was 46 out of 124 arteries. Four patients of 80-90 years had their IMT <0.8 mm. The age group of 60-69 had a maximum number of arteries, i.e., 14 which had IMT >0.8 mm.

Out of the total 400 arteries examined 220 plaques were found (Table 2). Plaques were classified in relation to the arterial wall and were labeled as hypoechoic, hyperechoic (Figures 3 and 4), and calcified (Figure 5). 54 out of 220 (26.36%) plaques were hypoechoic, 130 (55.45%) were hyperechoic. The rest were calcified. Plaques with surface irregularity were observed in 58 out of 220 (9.33%). Remaining 130 (60%) were smooth. 16 plaques out of 220 (7.2%) had well-defined hypoechoic areas within them, suggestive of intra plaque hemorrhage.

Out of the total 220 plaques, 100 (45.45%) were located in the region of the bulb, 68 (30.91%) in ICA and 48 (21.82%) in the CCA. Some of the plaques in the region of carotid bulb were seen extending into ICA and external carotid artery (ECA). The location of such plaques was included in the "Bulb" category. Only 4 (2.2%) plaques were seen in ECA, which were separate from the plaque involving the bulb and were considered as a separate entity.

Table 2: Plaque characteristics

Appearance	Hypoechoic	Hyperechoic	Calcified	Total	% age
Smooth	30	70	30	130	71.5
Irregular	24	20	14	58	31.9
Ulcerated	0	32	0	32	17.6
Total	54	122	44	220	100
% age	29.7	67.1	24.2	100	

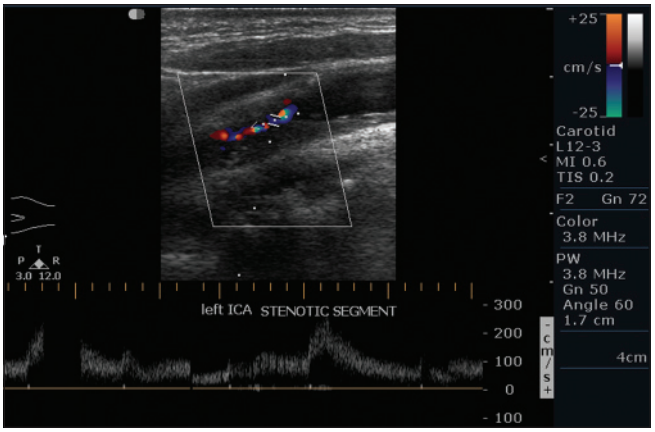

Figure 2: Narrowing of left internal carotid artery showing increased velocity

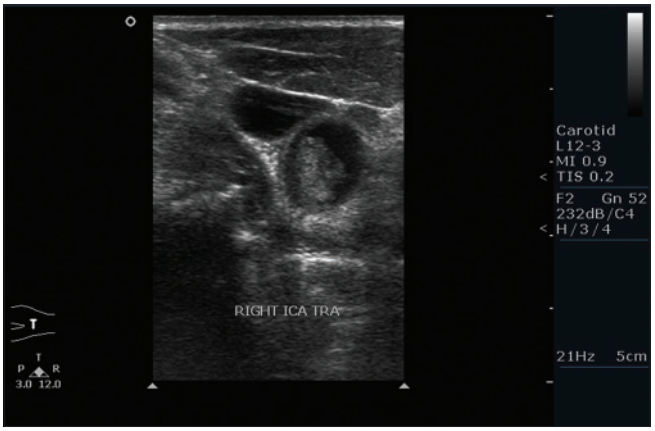

Figure 3: Cross-sectional view of the right internal carotid artery showing eccentric echogenic plaque involving 50% diameter

DISCUSSION

In our study, a maximum number of patients belonged to the age group of 60-69 years. As the age increased, % of area stenosis increased.

The mean IMT both on the right and left side were higher in males than that in females for the age groups, and the mean IMT on the left side was higher than that on the right side. However, these differences were not statistically significant ($P > 0.05$) and may be accounted for by the small number of subjects in our study.

As the degree of stenosis increased the various velocities and their respective ratios (ICA PSV/CCA PSV; ICA end diastolic velocity (EDV)/CCA EDV and ICA PSV/CCA

EDV) increased in proportion to the stenosis, suggesting a positive correlation between them (Table 3). The majority of the plaques were located in the region of carotid bulb, and most of them were hyperechoic.

Duplex ultrasonographic criteria showed a better correlation with actual stenosis when the intervals of the degree of stenosis were 0%, <50%, 50-70%, 70-99%, and 100%. Trying to quantify the stenosis in 10° incremental intervals was particularly inadequate and less sensitive and specific. In our study, Doppler ultrasound in carotid artery stenosis had a sensitivity of 88% and specificity of 84%.

Figure 4: Echogenic plaque in right internal carotid artery delineated by color Doppler

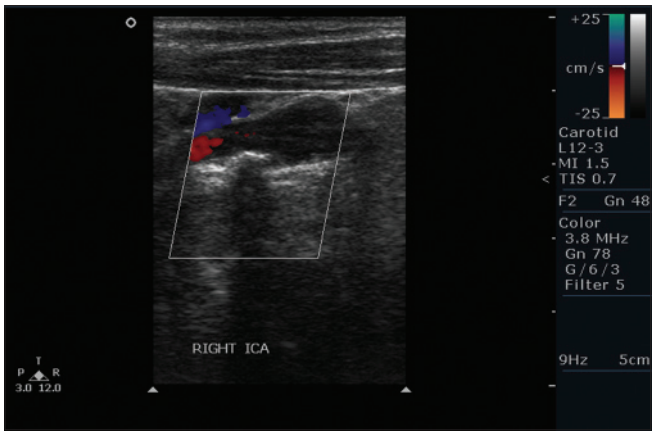

Figure 5: Heavily calcified plaque in right internal carotid artery

Table 3: Relation between degree of stenosis, various velocities and ICA/CCA ratio

Degree of stenosis %	ICA PSV cm/sec	ICA EDV cm/sec	ICA PSV/ CCA PSV
<50	<127.5	<40	<2.1
>80	>282	>104	>3.55

EDV: End diastolic velocity, CCA: Common carotid artery, PSV: Peak systolic velocity, ICA: Internal carotid artery

CONCLUSION

In light of the above findings, the role of carotid Doppler in detecting the site and morphology of atherosclerotic plaque with quantifying the amount of stenosis is very well-justified. In addition, carotid Doppler can also be used to assess the prognosis in potential symptomatic and asymptomatic patients with one or the other risk factor for cerebrovascular disease.

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Original Article

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Association of Maternal Height with Delivery Outcome: A Prospective Study

Alka Garg[1], Lalit Kumar[2], Nikita Garg[3]

[1]Associate Professor, Department of Gynecology & Obstetrics, Rama Medical College, Hapur, Uttar Pradesh, India, [2]Associate Professor, Department of Forensic Medicine and Toxicology, Shri Guru Ram Rai Institute of Medical & Health Science, Dehradun, Uttarakhand, India, [3]Student, Subharti Medical College, Meerut, Uttar Pradesh, India

Abstract

Introduction: In a pregnant woman, maternal height and antenatal estimated fetal weight can influence mode of delivery. The aims and objective of this study were to find out the association between the maternal height and estimated fetal weight and the delivery outcome.

Methods: 125 full term primigravida women without any obstetric and medical complications who were admitted in Rama Medical College, Hapur, Uttar Pradesh for delivery selected randomly for the study. After delivery, 70 women who underwent cesarean delivery formed the study group and 55 women who underwent vaginal delivery formed the control group. These two groups were compared for their maternal heights and antenatal estimated fetal weight using Johnson's formula.

Results: In the present study, mean height of women in the study group was 145.34 cm while that in the control group was 154.02 cm. Out of 44 short statured women (height ≤145 cm), 41 (93.18%) had the cesarean section, and 2 (4.55%) women were delivered vaginally. Estimated fetal weight in the control group was 2845 g while that in the study group was 2928 g.

Conclusions: We conclude that short statured females with larger baby size have the higher incidence of delivery by cesarean section.

Key words: Cesarean section, Fetal weight, Maternal height, Mode of delivery

INTRODUCTION

In a women's life cycle, pregnancy is the most significant and unique stage. This event is regard as "welcome event" for the successful womanhood.[1] In the countries like India, maternal and fetal mortality and morbidity are major health problems. Throughout the world 800 women/day die as a result of preventable causes related to pregnancy and childbirth, in which most of them or near 99% of all maternal mortality contributed by developing countries.[2]

In general, malnourished females tend to have short stature in adulthood; they have high rates of adverse pregnancy outcome such as perinatal mortality and prematurity.[3]

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Several studies from India observed very high rates of low birth weight babies among mothers with height <140 cm[4-6] and 216 g-birth weight variation between short (<143 cm) and tall (>162 cm) mothers.[7] Numerous studies of healthy women from both wealthy and less wealthy countries have shown that shorter maternal height and greater newborn weight associated with increased delivery complications and result in maternal or fetal mortality and morbidity.[8-12] Many studies of maternal anthropometry and pattern of pregnancy outcome recommend the use of anthropometric data like maternal height and weight for screening and its application for betterment for pregnancy outcome.[13]

An important area in which an obstetrician can contribute considerably is the care of pregnant women and for antenatal care is to identify those women with higher risks for problems during pregnancy or delivery they have to ensure that precautionary measures are instituted wherever possible or more intensive medical care is to be arranged. In the developing countries like India, there is a dearth of maternal and child health care services.

Corresponding Author: Lalit Kumar, Department of Forensic Medicine and Toxicology, Shri Guru Ram Rai Institute of Medical & Health Science, Dehradun - 248 001, Uttarakhand, India. Phone: +91-9358507650. E-mail: dr_lalit303@yahoo.com

Antenatal care in rural areas is provided by traditional birth attendants (Dais) and village health workers. To prevent these complications, it is important to develop a simple risk indicator, which is easy to use, reliable, and consistent. Maternal height is one of the simplest measurements to take into consideration. Using these indicators, a specified height is defined and below this attention to be paid to the risk of CPD/contracted pelvis and for the referral to higher centers. The current study was carried out to assess the association of maternal height and estimated fetal weight of women on her obstetric outcome.

METHODS

This study was carried out in Department of Gynecology and Obstetrics, Rama Medical College, Hapur, Uttar Pradesh from 2014 to 2015. It was a cross-sectional, case-control study of 125 full term primigravida women without any obstetric and medical complications who admitted for delivery randomly selected for the study. All the cases were primigravida patients with the gestational age ≥37 weeks who had spontaneous onset of labor. Those pregnancies with medical or obstetric complications or those with fetal anomalies or fetal death or elective Cesarean Section excluded from the study.

After considering these inclusion and exclusion criteria 125 cases elected, out of which 70 cases who underwent emergency cesarean delivery formed the study group, and 55 women who gave birth vaginally formed the control group.

Fetal weight (FW) estimation was done by Johnson's Formula:

FW = (McDonald's measurement - 13) × 155 when the presenting part was at "minus" station

FW = (McDonald's measurement - 12) × 155 when presenting parts at "zero" station

FW = (McDonald's measurement - 11) × 155 when presenting part at plus station

(McDonald's measurement - symphysio-fundal height, FW - in grams if woman weighed more than 91 kg, 1 cm was subtracted from fundal height).

RESULTS

In present study from the Table 1, out of 70 patients from the study group, 8 (11.43%) had the height <140 cm. 32 (45.71%) patients had height in between 141 and 145 cm. 28 (40.00%) had height 146-150 cm. Only 2 (2.86%) patients had the height above 150 cm. In the control group, out of 55 patients, none of the patients belonged to <140 cm. 4 (7.27%) patients in between 141 and 145 cm. While 12 (21.82%) patients in between 146 and 150 cm. 39 (70.91%) had height more than 150 cm. The difference between study group and control group was found to be statistically significant ($P < 0.05$). In the study group, mean height was 145.34 cm, while in the controls it was 154.02 cm.

From the Table 2, authors found in maternal height range of <145 cm among 44 cases, 2 (4.55%) cases from control group delivered spontaneously vaginally, 1 (2.27%)case was undergone instrumental delivery, while 41 (93.18%) cases were undergone cesarean delivery. In the maternal height of 145-150 cm among 40 cases, 17 (42.5%) cases of spontaneous vaginal delivery, 2 (5.0%) case was delivered by instrumental delivery while 21 (52.50%) of cases were undergone cesarean delivery. In the maternal height of ≥150 cm out of 41 cases, 32(78.05%) cases delivered spontaneous vaginally, 1 (2.44%) were required instrumental delivery while 8 (19.51%) cases were required cesarean delivery. Out of all 125 cases in maternal height range, 51 (40.80%) cases were delivered spontaneous vaginally, 4 (3.20%) cases were required instrumental delivery while 70 (56.00%) cases required cesarean delivery. Using Chi-square test, ($P < 0.05$) the difference was found statistically significant.

In the present study, mean estimated weight in the study group was 2928 g while in the control group it was 2845 g. By applying Chi-square test, the difference was found to

Table 1: Distribution of patients according to height (cm) in both the groups

Height (cm)	Study group (*n*=77)		Control group (*n*=55)	
	Cases	%	Cases	%
138-140	8	11.43	0	0.00
141-145	32	45.71	4	7.27
146-150	28	40.00	12	21.82
>150	2	2.86	39	70.91
Total	70	100.00	55	100.00

Table 2: Maternal height and mode of delivery

Height (cm)	Mode of delivery					
	Spontaneous vaginal delivery		Instrumental delivery		Cesarean delivery	
	n	%	*n*	%	*n*	%
≤145	2	4.55	1	2.27	41	93.18
146-150	17	42.50	2	5.00	21	52.50
>150	32	78.05	1	2.44	8	19.51
Total	51	40.80	4	3.20	70	56.00

be significant ($P < 0.05$). Women with lesser height and more baby weight are more likely to go for cesarean delivery (Table 3).

The author concluded from the Table 4 that in the present study in higher maternal height range (>150 cm) and lower estimated fetal weight range (<2.5 kg) almost all babies were delivered vaginally. In the same way, lower maternal height range (<145 cm) and higher estimated fetal weight range (2.5-3.5 kg), almost all (38 out of 39) babies are delivered by cesarean section.

According to Tables 2-4, we can conclude that cases with maternal height range <150 cm and estimated fetal weight range ≥2.5 kg should be referred to advanced or higher hospitals without lacking time. In the present study, in the study group, the incidence of cesarean delivery in women with height 145 cm or less was 32.8%. Whereas those with height more than 145 cm was 23.2% (Table 5).

DISCUSSION

In the present study, the incidence of emergency cesarean delivery in short mothers was 32.8% while that in women with height more than 145 cm was 23.2%. Thus, women who are ≤145 cm have more risk of cesarean delivery when compared to females of more than 145 cm height. In a study by Kathleen *et al*.,[14] women of 146 cm height (−1 SD) relative to another women of 160 cm height (+1 SD) had 2.5 times of higher risk of cesarean delivery. The independent risk for cesarean delivery occurring for a nulliparous and healthy women with no obstetric or clinical abnormality but of 146 cm height (−1 SD) was 2.5 times higher relative to females of 166 cm (+ 1SD) height was clearly established in their study. Thus, women of height <145 cm form a risk group who needs constant observation during their labor for signs of CPD and early referral to higher centers in the event of prolonged labor was needed to avoid a grievous outcome.

In the study, the incidence of cesarean delivery in short mothers was 32.8%. The relative figures of cesarean delivery. However, the current study shows the higher prevalence of cesarean section as compared to Karltreinder,[15] but results of the current series were similar in the comparison with that of Desai *et al*.[16]

Baird[17] postulates that every female has a potential height, which decided by factors such as race, genetics, and geographic distribution. However, there occur certain insults that are exclusively dominant, if it is so during her age of development. As a result of which she becomes short stature or long.

In the present study according to the Table 2, we can conclude that in height range of <145 cm almost all cases were delivered by cesarean section, in height range of 145-150 cm also rate of cesarean section was very elevated, thereafter rate of cesarean section decreased and rate of normal delivery increased. According to the Table 2, cases with height <150 cm was the target population on which consulting doctor have to pay all attention to prevent neglected obstructed labor and undue maternal morbidity.

In the present study, mean estimated weight in the study group was 2928 g while in the control group it was 2845 g. Females with lesser height and larger baby were more likely to go for the cesarean section. Karltreinder[15] mentions that taller females tend to produce heavier children in contrast to the shorter females who tend to produce lighter ones.

Table 3: Distribution of patients according to estimated fetal weight in both the groups

Estimated birth weight (g)	Study group (*n*=77)		Control group (*n*=55)	
	Cases	%	Cases	%
<2.5 kg	3	4.29	8	14.55
2.5-3.5 kg	65	92.86	45	81.82
>3.5 kg	2	2.86	2	3.64
Total	70	100.00	55	100.00

CONCLUSIONS

We concluded that short statured women with larger baby size had the higher incidence of cesarean delivery. In the present study, the mean height of women in the study

Table 4: Maternal height and estimated fetal weight

Height (cm)	Estimated birth weight in kg						Total	
	<2.5		2.5-3.5		>3.5		Study group	Control
	Study group	Control	Study group	Control	Study group	Control		
≤145	2	2	38	1	1	0	41	3
145-150	1	4	20	14	0	1	21	19
>150	0	2	7	30	1	1	8	33
Total	3	8	65	45	2	2	70	55

Table 5: Height and emergency cesarean delivery in study group

Height in cm	Cases	Percentage
<145	41	32.80
>145	29	23.20

group was 145.34 cm while that in the control group was 154.02 cm. Out of 44 short statured women (height ≤145 cm), 41 (93.18%) had cesarean section and 2 (4.55%) women were delivered vaginally. Estimated fetal weight in the study group was 2928 g while that in the control group was 2845 g.

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Original Article

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Awareness, Knowledge and Attitude about Palliative Care, in General, Population and Health Care Professionals in Tertiary Care Hospital

K Saraswathi Gopal[1], P Sai Archana[2]

[1]HOD and Professor, Department of Oral Medicine and Radiology, Meenakshi Ammal Dental College, Chennai, Tamil Nadu, India, [2]Post-graduate Student, Department of Oral Medicine and Radiology, Meenakshi Ammal Dental College, Chennai, Tamil Nadu, India

Abstract

Introduction: Palliative care is an approach that improves the quality of life of patients and their families facing the problems associated with life-threatening terminal illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial, and spiritual (WHO, 2002). An attempt was made to study about the knowledge, attitude, and awareness about palliative care in a tertiary hospital by questionnaire study.

Materials and Methods: A cross-sectional study, conducted at a tertiary care hospital, Chennai. A structured questionnaire was provided to the general population attending the outpatient department and the health care providers including doctors, dentists, and staff nurses. Their awareness, knowledge and attitude toward palliative care were assessed by the answers provided by them.

Results: The awareness and knowledge were very poor among general population when compared to health care providers. Among the health care providers, there was no statistical significance among staff nurse, dentists and medical professional. Both the general population and health care providers were empathetic toward treating sufferers in palliative care and wanted the sufferers to die with dignity until their last.

Conclusion: Awareness and knowledge need to be improved in palliative care especially among general population hence utilization of palliative care could be maximized thereby providing a good quality of life by the sufferers and their families until the end of the journey.

Key words: Attitude, Awareness, General population, Health care professionals, Knowledge, Palliative care

INTRODUCTION

The most countries of the world are experiencing a health transition from communicable diseases to non-communicable diseases. In India too, non-communicable disease has become a major public health challenge, and chronic disease accounts for 53% of all deaths and 44% of disability-adjusted life years lost.[1] With a crude death rate of 6.24/1000 and a population of more than a billion, and total no of people dying every year in India is about 7 million and the majority of them die in misery. The palliative care is an approach that improves the quality of life of these patients and their families facing the problems associated with life-threatening illnesses through prevention and relief of suffering by addressing physical, psychosocial, and spiritual issues.[2] According to the WHO estimates more than 4 million people will benefit from palliative care. <1% of those who need palliative care services have any access to such services in the country. Moreover, the knowledge awareness of palliative and attitude of people referring them to palliative care toward palliate care is very minimal as per various studies hence the aim and objective of my study was to know about the awareness, knowledge and attitude toward palliative care

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Corresponding Author: P Sai Archana, 144/12, Kailash Colony, Annanagar West Extension, Chennai - 600 101, Tamil Nadu, India.
E-mail: Drsai1985@gmail.com

by both health care providers and general population.[3] It is a comprehensive approach where teams work together as one namely family members, palliative care providers, nursing assistants, social workers, physiotherapists, hospice chaplains, volunteers and community to relieve, and ease the pain (physical, mental and spiritual) of the sufferer and offer a support system until their end of life.[4]

MATERIALS AND METHODS

Semi-structured self-designed questionnaires were given to the general population as well as the health care providers attending Meenakshi Ammal Dental College and their awareness, knowledge and attitude toward palliative care was assessed. The questionnaire was tested for its validity and reliability by pilot testing. The study period is from April to June month of 2014, and there were no ethical issues involved. Informed consent was got from the study population in their native languages to avoid language bias. The sampling size was determined by the statistician and sample group consists of both general public and health care professionals (30 staff nurses, 50 dentists and 20 medical practitioners) representing 100 in number in the fields of Medicine and Dentistry and 100, in general, population. The questionnaires were separately given to general population as well as health care providers and their overview of awareness, knowledge and attitude of both groups were assessed. Data were analyzed using SPSS version 15. Chi-square test was used to evaluate the results in both categories (health care providers and general population).

RESULTS

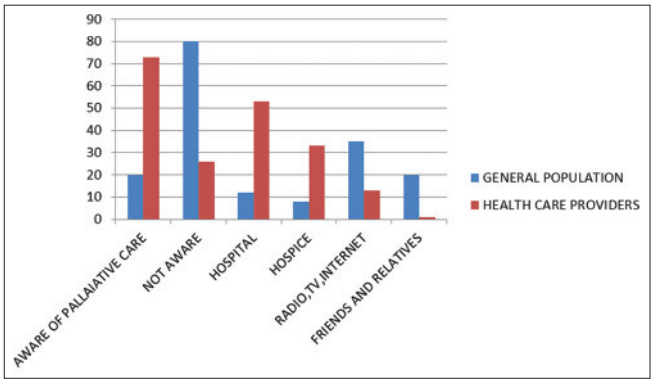
The study group consisted of 100 in general population 100 in health care providers (staff nurses, Medical practitioners and Dentists) and a random sampling method was done. The age group varied from 19 to 62 years in general population, whereas all personnel were between 30 and 50 years in health care providers group. 72% of the general population were males, whereas 44% were males in health care providers. Awareness about palliative care was significantly more in the health care providers group (74%) compared to the general population which was only 20% similarly knowledge regarding services offered and time to intervene (early/late) was very much inadequate in general population than in health care providers. Unfortunately, only 9% of general population and 38% of health care providers were opting to start palliative care early. Interestingly the empathy among general population and health care providers were in par with each other to help the sufferers by providing them physical and emotional support, but only few in both groups were willing to provide financial support. Hence, more awareness and knowledge should be imparted to general population from government and health care professionals by conducting awareness programs to identify and offer palliative care to improve the quality of life.

Awareness

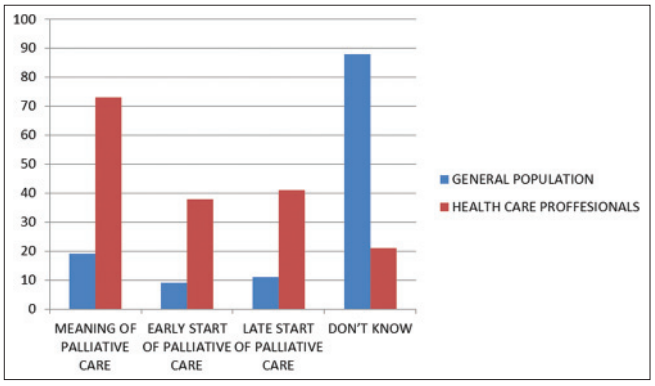
Awareness about palliative care was significantly more in the health care providers group (74%) compared to the general population which was only 20%. There was no statistically significant difference among the awareness of palliative care in the different subgroups of health care providers. The media through which awareness was imparted to the health care providers was through cancer hospital (53%) and hospice (33%), whereas through internet (35%), friends and relatives (20%) in the general population (Table 1 and Graph 1).

Knowledge

Knowledge regarding services offered and time to intervene (early/late) was very much inadequate in general population than in health care providers. Unfortunately, only 9% of general population and 38% of health care providers were opting to start palliative care early (immediately after the diagnosis of terminally ill disease is made), whereas the majority of the population in both the groups did not know about early intervention (Table 2 and Graph 2).



Graph 1: The awareness of palliative care in general population and health care professionals



Graph 2: The knowledge in palliative care by general population and Health care professionals

Table 1: Results regarding the awareness of palliative care in general population and health care professionals

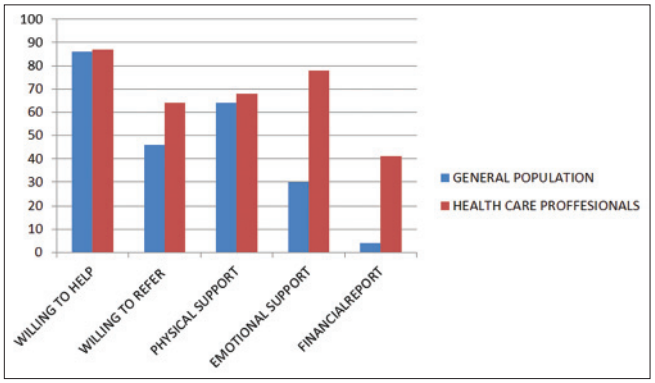
Questions asked about	Health care providers							
	General population		Staff nurses		Medical practitioners		Dentists	
	M	F	M	F	M	F	M	F
Are they aware of palliative care?								
Aware	15	5	1	22	8	6	14	23
Not aware	57	23	1	6	2	4	4	9
Media through which they learnt about palliative care								
A) Hospital	8	4	1	11	8	6	6	21
B) Hospice	3	5	0	12		2	10	9
C) TV, radio, internet	15	20	0	5	2	2	2	2
D) Health education materials	12	8	1	0				

Table 2: Results regarding the knowledge about palliative care by general population and health care professionals

Questions asked about	Health care providers							
	General population		Staff nurses		Medical practitioners		Dentists	
	M	F	M	F	M	F	M	F
What is the meaning of palliative care								
Don't know	4	15	1	19	8	7	16	22
Time to start palliative care	68	13	1	9	2	3	2	10
Early?	6	3	1	16	7	6	3	5
Late?	6	5	1	6	2	2	10	20
Don't know	60	22		6	1	2	5	7

Attitude

Attitude is a paramount feature in utilizing the facilities provided. Interestingly the empathy among general population and health care providers were in par with each other to help the sufferers by providing them physical and emotional support, but only few in both groups were willing to provide financial support. Even though qualities and services provided were known by both the groups, referral to palliative care centers was not done by general population and health care providers (Table 3 and Graph 3).



Graph 3: The attitude toward palliative care by general population and health care professionals

DISCUSSION

Palliative care is an approach that improves the quality of life of patients and their families facing the problem associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual.[4,5]

It is an humanitarian need worldwide for people with life-limiting diseases including cancer, other non-communicable diseases and communicable diseases like HIV/AIDS[4,6] have pain, other symptoms and psychosocial distress which can dramatically decrease quality of life, place a burden on the family's economy and there is little chance of cure.[4] The palliative care services is an exclusive form of holistic treatment which interconnects both sufferers and their families with doctors at hospitals, home based care (maintaining a standard of care at the place of stay for a bedridden patient, through family/community empowerment, and/or home visits by trained teams; usually inclusive of a nurse) as well as the community irrespective of age/religious differences/social status. Ideally, palliative care services should be provided from the time of diagnosis of life-threatening illness, adapting to the increasing needs of cancer patients and their families as the disease progresses into the terminal phase. They should also provide support

Table 3: Results regarding the attitude of palliative care in general population and health care professionals

Questions asked about	Health care providers							
	General population		Staff nurses		Medical practioners		Dentists	
	M	F	M	F	M	F	M	F
Willingness to help to those suffering?								
Yes	63	23	0	2	8	7	15	28
Not answered	9	5			2	3	3	4
Willing to refer to palliative careyes	32	14	1	17	8	8	11	19
No	40	14	1	11	2	2	7	13
Support renderedphysical	48	19	2	16	7	6	12	25
Emotional	72	27	1	18	7	8	16	28
Financial	7	2	0	2	4	3	9	23

to families in their bereavement. In India, currently there are approximately 908 palliative care services delivering palliative care either through home care, outpatient basis or in patient services.[7] These centers are clustered around few areas but, there is extremely limited access to quality palliative care services for vast majority of Indians across the country.

In response to this essential public health need, the Ministry of Health and Family Welfare have initiated activities related to palliative care with a vision of facilitating access to affordable, safe and quality pain relief and palliative care to all those requiring it in the country.[8]

The concept of palliative care and the awareness of available facilities among general population is very much lacking in India as compared with western countries.[9] In our study only 19% are aware of palliative care in the general population group. In our study there was no significant difference in the awareness and knowledge of palliative care among general practitioners, dentists and staff nurses in the health care provider group. The attitude to help the patients physically and emotionally is significantly more in both groups. Hence, the need of the hour is to create awareness about palliative care among public through various medias, internet and health education materials and hospitals should be equipped to cater palliative care needs of patients and a 24 h help line to assist people to get through palliative care can be proposed to bridge the gap between the public and palliative care institutions. Two centers of excellence in the country have been recognized as WHO Collaborating Centers. Thiruvananthapuram (Kerala) has WHO Collaborating Centre for Training and Policy on Access to Pain Relief and Calicut (Kerala) has the WHO Collaborating Centre for Community Participation in palliative care and long term care. The facilities and faculty of these centers may be leveraged for guidance and support in the implementation and monitoring of the tenets of the national program.

The government has recommended the following goals to be achieved in the 4th coming years to increase awareness and reach of palliative care to sufferers:[2,9,10]

1. Improve the capacity to provide palliative care service delivery within government health programs such as the National Program for Prevention and Control of Cancer, cardiovascular disease, diabetes, and stroke; National Program for Health Care of the Elderly; the National AIDS Control Program; and the National Rural Health Mission
2. To ensure the patients to be pain free the availability of opioids for usage should be maintained and should be regulated and prescribed abiding the legal system in our country
3. Increasing the awareness and knowledge to health care providers and general population by introducing palliative care in educational curriculum in both medical and dental fields respectively[5,11,12]
4. Behavioral modifications to be done through education and awareness about palliative care and hence initiatives to be taken for reach of the care to sufferers
5. Encourage and facilitate delivery of quality palliative care services within the private health care centers and primary health care centers in our country
6. Develop national standards for palliative care services and continuously evolve the design and implementation of the National program to ensure progress toward the vision of the program.[4]

If these goals are achieved then the mortality and morbidity due to preventable diseases can be reduced and the terminally ill people will have a better quality of life and the privilege to die with dignity. Usage of technological advancements in the field of medicine by using audiovisual aids and video calling services makes palliative care services and service providers access the area commonly inaccessible and also allow the debilitating patient to access medical care. A study done by Coyle *et al.* demonstrated certain benefits such as limited need for daily physical examination and assessment, screening for a need for a clinical visit or admission, communication assistance to patients who cannot speak or hear and increased satisfaction by the patient and the caregivers.[13-15]

CONCLUSION

Even though percentage of empathy is in par with both general population as well as health care professionals, awareness and knowledge are inadequate to implement changes to reduce morbidity before mortality in palliative care. Hence, we would recommend to start Early intervention and Harness 3 "ness" (Awareness, kindness, persuasiveness) for the success in palliative care by both health care providers and general population till the end of the journey by the sufferers.

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Original Article

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Clinical Study of Carcinoma Thyroid and its Management

T Pramod[1], B S Shivaswamy[2], G Ananth[3], G Rajashekara Babu[4], K Latha[5], K Jagadeesh[6]

[1]Assistant Professor, Department of General Surgery, Sri Devaraj Urs Medical College, Kolar, Karnataka, India, [2]Former Professor and Head, Department of General Surgery, Bangalore Medical College and Research Institute, Bengaluru, Karnataka, India, [3]Assistant Professor, Department of Neurosurgery, Vydehi Institute of Medical Sciences, Bengaluru, Karnataka, India, [4]Associate Professor, Department of General Surgery, Bangalore Medical College and Research Institute, Bengaluru, Karnataka, India, [5]Assistant Professor, Department of Community Medicine, Sri Devaraj Urs Medical College, Kolar, Karnataka, India, [6]Clinical Associate, Department of General and Minimal Invasive Surgery, Indraprastha Apollo Hospitals, New Delhi, India

Abstract

Background: Thyroid carcinoma is one of the common cancers affecting the women in their young age. They vary from being indolent to aggressive cancers. Improvements in diagnostics and understanding the pathophysiology have made the treatment more effective with good long-term results.

Objective: To study the clinical presentation and management of carcinoma thyroid in a tertiary center.

Materials and Methods: 30 patients of histopathologically proven thyroid cancers treated during the period of 2-year from September 2005 to August 2007 were studied. Detailed history and physical findings were noted, along with the investigations and treatment given.

Results: Thyroid carcinoma formed 1.5% of all cancers treated during the period. It formed 15.78% of all thyroid swellings admitted for treatment during the same period. Male:female ratio in this study was 1:5. Most of the cases of carcinoma (86%) were seen in the 21-50 years age group. All patients in this study had a goiter and only 10% of patients presented with lymphadenopathy and hoarseness of voice. Two-thirds of tumors were slowly growing with duration ranging from 3 months to 2 years. Fine-needle aspiration cytology (FNAC) was the common diagnostic test done. Most of the cancers (76.6%) were in Stage I disease. Total thyroidectomy was the most common surgery done, and papillary carcinoma was the most common histopathology seen. Transient hypocalcemia was the most common post-operative complication seen in 20% of patients.

Conclusion: Thyroid cancers affect young adult females presenting as slow growing tumors. Majority of the tumors are papillary type in the early stage with good prognosis. FNAC is a simple test to detect cancer, and total thyroidectomy is the procedure of choice for treatment.

Key words: Fine-needle aspiration cytology, Papillary carcinoma, Radio iodine, Total thyroidectomy, Thyroid carcinoma

INTRODUCTION

Thyroid cancer is the most common endocrine cancer and has the highest mortality among endocrine neoplasms except for ovarian cancer.[1] Even though thyroid cancer is more common in women than in men, death from thyroid cancer is more common in men. Thyroid cancer represents <1% of all malignancies.[2] The cumulative life-time risk of thyroid cancer in Chennai was one in 970 in males and one in 565 in females.[3]

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Thyroid cancers display a wide range of aggressiveness from the more indolent papillary cancer to the uniformly lethal anaplastic cancer. Because of the developments in diagnostic methods and pathophysiological understanding, asymptomatic stages of the disease are detected with increasing frequency, population and patients may be treated more efficiently.

The declining mortality rates are largely due to early diagnosis and effective therapy applied at an early tumor

Corresponding Author: Dr. T Pramod, Department of General Surgery, 2nd Floor, PG Block, Sri Devaraj Urs Medical College, Tamaka, Kolar - 563 101, Karnataka, India. Phone: +91-9844558073. E-mail: pramodthejoram@gmail.com

stage when it is most amenable to surgery and I-131 therapy. Fine-needle aspiration cytology (FNAC) plays an important role in the diagnosis of thyroid cancer and allows the clinician to plan a rational treatment strategy.

The protracted and generally favorable course of well-differentiated carcinomas complicates the evaluation of various treatment methods. There are no long-term prospective studies of the treatment of this disease. The clinical management of the well-differentiated thyroid carcinomas rests on retrospective studies and individual clinical experiences.

Many studies have recommended total or near-total thyroidectomy followed by post-operative I-131 thyroid remnant ablation for most patients with differentiated thyroid carcinoma, regardless of age, and almost everyone preferred long-term T4 therapy to doses sufficient to lower the thyroid stimulating hormone (TSH) levels to 0.01-0.5 μ units/ml. External radiation and chemotherapy play a very important role in the treatment of undifferentiated thyroid carcinoma.

MATERIALS AND METHODS

In this clinical study of thyroid cancers, cases, which were admitted in various surgical units in Victoria hospital, attached to Bangalore Medical College, Bengaluru for a period of 2-year, from September 2005 to August 2007, were studied. A total of 30 cases of histopathologically proven cases of thyroid cancers in all age groups and both sexes were included. Detailed examinations of each case were done and data entered in the proforma case sheet for analytical study.

All patients whose final histopathological diagnoses were proven benign were excluded. Patients whose FNAC revealed follicular neoplasms but the histopathology revealed follicular adenomas were also excluded.

The study required certain investigations to be conducted on the patient viz, routine blood investigations, thyroid profile, radiography of the chest, and neck, FNAC of the thyroid gland and lymph nodes. Ultrasound of the neck was done in all cases to determine whether thyroid swellings are multinodular or solitary nodules and to determine the cervical nodal involvement. Computed tomography scan was done when needed. Indirect laryngoscopy was done in all patients to determine the status of the vocal cords specifically their movements. All the patients underwent surgery after proper consent. Most of the patients were discharged with a clean and healthy wound except a few with post-operative complications.

RESULTS

Thyroid carcinoma formed about 0.17% of all surgical admissions and 1.5% of all cancers admitted during the period. Thyroid carcinoma formed 15.78% of all thyroid swellings admitted to the hospital during the period (Table 1).

No of female patients were 25 and male patients 5. Male:female ratio in this study was 1:5 (Table 2).

In this study, most of the cases (86%) of carcinoma thyroid occurred in the age group of 21-50 years, with the average age being 36 years with a minimum of 19 years and a maximum of 70 years. Only 2 cases (6.6%) were seen after 50 years of age (Table 3).

In this study, all patients (100%) presented with a swelling of the thyroid. Only 10% of patients had hoarseness of voice, which was the most common pressure effect. Features of hyperthyroidism were present in 6.6% of patients. Palpable lymph nodes were present in 10% of cases (Table 4).

Most of the patients (73.3%) presented with symptoms during the past 3 months to 2 years. Only 6.6% of cases had swelling for >5 years. None of the patients had a symptom more than 10 years (Table 5).

Table 1: Incidence

Total no of patients	No of patients	Percentage
Total number of surgical admissions	16897	0.17
Total number of all cancers	1965	1.5
Total number of thyroid cases	190	15.78

Table 2: Sex ratio

Type of carcinoma	Female	Male
Papillary carcinoma	17	4
Follicular carcinoma	6	1
Anaplastic carcinoma	1	0
Medullary carcinoma	1	0
Others	0	0
Total	25	5

Table 3: Age distribution

Age (years)	Papillary	Follicular	Anaplastic	Medullary	Others	Total
0-10	-	-	-	-	-	-
11-20	1	1	-	-	-	2
21-30	5	1	-	-	-	6
31-40	10	2	1	1	-	14
41-50	4	2	-	-	-	6
51-60	-	1	-	-	-	1
61-70	1	-	-	-	-	1
71-80	-	-	-	-	-	-

Two-thirds (66.6%) of the tumors were slow growing, and one-third (33.3%) were fast growing tumors.

22 patients (73.3%) had a firm gland, 7 patients (23.3%) had a hard gland and only 1 patient (3.3%) presented with a soft gland on palpation.

FNAC detected papillary carcinoma in 11 patients (36.6%), follicular neoplasm in 6 patients (20%), and 1 patient each of anaplastic and medullary carcinoma. Rests of the thyroid glands (36.6%) were reported as nodular or colloid goiter (Table 6).

Indirect laryngoscopy was done in all cases. 5 patients (16.66%) showed unilateral vocal cord palsy commonly being on the left side. Bilateral vocal cord movements were equal in the rest of the patients (83.3%).

X-ray neck was done in all the cases. Calcification in thyroid swelling was seen in 2 cases (6.6%) and tracheal deviation in 2 cases (6.6%). Other cases presented as soft tissue swellings (86.6%).

18 patients (60%) presented as multinodular goiter, whereas 12 patients (40%) presented as a solitary thyroid nodule (Graph 1).

Table 4: Clinical features

Clinical features	Number of cases	Percentage
Thyroid swelling	30	100
Dysphagia	1	3.3
Dyspnea	0	0
Hoarseness of voice	3	10
Thyrotoxicosis	2	6.6
Lymph node mass	3	10

Table 5: Duration of symptoms

Duration	Number of cases	Percentage
Up to 3 months	3	10
>3-6 months	7	23.3
>6 months-1 year	6	20
>1-2 years	9	30
>2-5 years	3	10
>5-10 years	2	6.6
>10 years	0	0

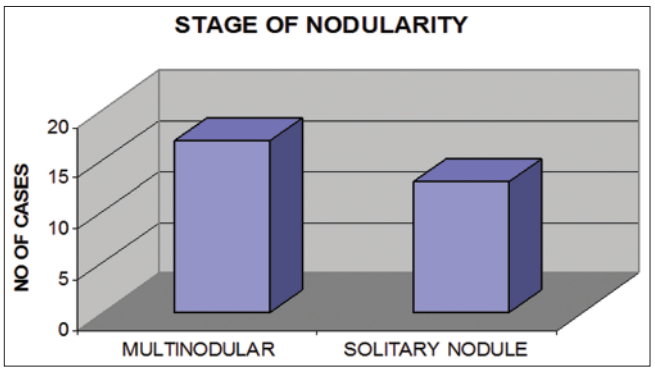
Table 6: FNAC results

FNAC diagnosis	Number of patients	Percentage
Papillary carcinoma	11	36.6
Follicular neoplasm	6	20
Anaplastic carcinoma	1	3.3
Medullary carcinoma	1	3.3
Nodular goiter	9	30
Colloid goiter	2	6.6

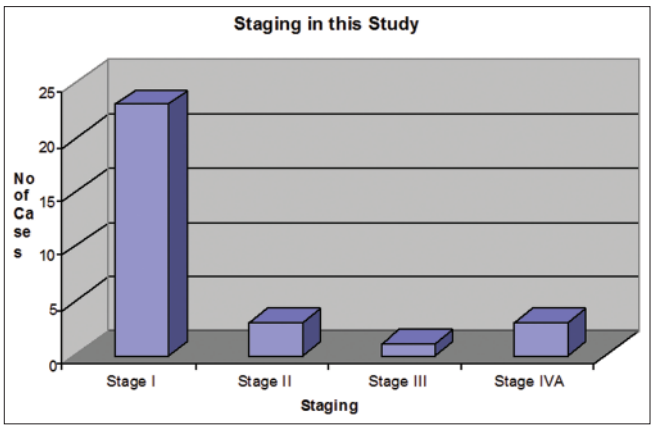
FNAC: Fine-needle aspiration cytology

Most of the cases after investigations and pathological reporting were found to be in Stage I (76.6% of cases). Stage II and IVA was the next commonly seen stage with 10% of cases each in the study (Graph 2).

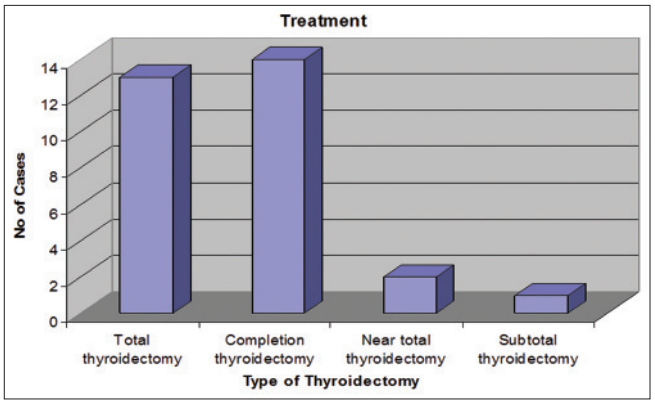
The most commonly performed surgical procedure was completion thyroidectomy in 14 patients (46.6%), followed by total thyroidectomy in 13 patients (43.3%). 2 patients (6.6%) underwent near-total thyroidectomy leaving the thyroid tissue adjacent to the recurrent laryngeal nerve (Graph 3).



Graph 1: Ultrasound results



Graph 2: Staging of carcinoma



Graph 3: Surgical procedure

Patients who were diagnosed as follicular neoplasm by FNAC underwent hemithyroidectomy initially and later a completion thyroidectomy for proven cases.

Patients with FNAC diagnosis as nodular goiter underwent subtotal thyroidectomy followed by completion thyroidectomy later. Only 1 patient underwent subtotal thyroidectomy, as she was low risk for her disease.

The predominant variety of thyroid cancer in our study was papillary carcinoma in 21 patients (70%), and next common was follicular carcinoma in 7 patients (23.3%). None of the other variants of papillary and follicular carcinomas were found in the histopathological study. One patient each of medullary carcinoma and anaplastic carcinoma patients was treated (Graph 4).

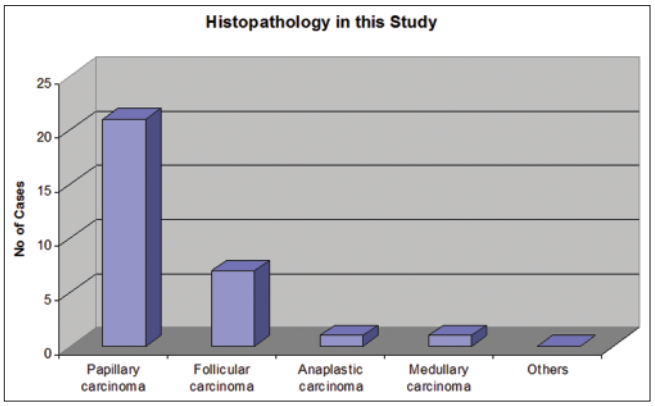
3 patients (10%) presented with lymph node secondaries along with primary in the thyroid. All these patients belonged to papillary carcinoma. None of the other thyroid cancers had cervical lymph node involvement.

2 patients underwent unilateral functional neck dissection. One patient had infiltration of sternocleidomastoid, spinal accessory nerve, and internal jugular vein, who underwent radical neck dissection. 1 patient with medullary carcinoma underwent prophylactic central neck dissection.

All the patients were observed in the immediate post-operative period for any complications. Transient hypoparathyroidism was the most common complication noted in 6 patients (20%). Serum calcium was estimated if the Trousseau's sign (inducing carpopedal spasm by occlusion of the arm with a blood pressure cuff for 3 min) was positive.

All symptomatic hypocalcemic patients were treated with 10 ml of 10% calcium gluconate given slowly intravenously. Less severe cases were treated with oral calcium supplements along with Vitamin D. All patients recovered in the immediate post-operative period. 2 patients (6.6%) had wound infection who improved with antibiotics and dressings. None of the patients had recurrent laryngeal nerve injury postoperatively in our study. No other complications were observed in this study. None of the patients who had immediate post-operative hypocalcemia developed hypocalcemia on a long-term (Table 7).

All the patients with differentiated thyroid cancers were referred to higher centers for radioiodine therapy. One patient who presented with medullary carcinoma was advised a regular follow-up with calcitonin assay. The patient with anaplastic carcinoma was referred for external beam radiotherapy in Victoria hospital. The patient with anaplastic cancer survived for about 6 months.



Graph 4: Histopathology of thyroid carcinoma

Table 7: Surgical complications

Complication	Number of patients	Percentage
Transient hypoparathyroidism	6	20
Wound infection	2	6.6
Recurrent laryngeal nerve palsy	0	0
Others	0	0

The patients with medullary and anaplastic carcinoma treated with total thyroidectomy were started on replacement doses of thyroxine, whereas those with differentiated thyroid cancer were not started on thyroxine, as they were referred for radioiodine ablation.

DISCUSSION

In the US, thyroid malignancies account for 0.6% of male and 1.6% of female malignancies.[4] In India, thyroid malignancies constitute 1.2% and 1.9% of malignancies in men and women, respectively.[5] It is less common in children but still accounts for 1.4% of childhood malignancies. In our study, thyroid carcinoma accounts for 1.5% of all cancer cases. In reality because of the fact that many thyroid cancers never become clinically apparent, and as such are never diagnosed, the true incidence is not known. In an autopsy study, Fukunaga and Yatani reported data from multiple countries that there was an 11% overall incidence of occult thyroid cancer.[6]

Women are affected more than men, and the ratio is somewhere around 3:2, whereas in our study it was 5:1. Surprisingly, a nodule in man is more likely to be malignant than in a woman.

Overall papillary cancer is more common than follicular which is more common than medullary which is more common that anaplastic cancer. In general, papillary carcinoma peaks in early adult life and then gradually decreases in frequency, whereas the incidence of follicular carcinoma tends to peak sometime later. Anaplastic cancer occurs later in life than differentiated cancers.

Exposure to radiation is the only proved thyroid carcinogen. This was first recognized by Duffy and Fitzgerald in 1950.[7] A 10-20 years post radiation latency period was reported earlier, but this has not been noted in the pediatric thyroid cancer cases that have resulted from the chernobyl nuclear disaster in the Ukraine in 1986, where there has been a dramatic increase in such cancers as early as 1989.[8,9] A 3-5 years latency was noted between radiation exposure and tumor development. About 90% of radiation exposed thyroid cancers were found to be papillary thyroid cancers. More recently radiotherapy to the neck in adults resulted in the subsequent development of the anaplastic carcinoma. In addition, thyroid carcinoma is arising as a secondary carcinoma in survivors of Hodgkin's disease.

In countries where there is adequate iodine intake, the well-differentiated thyroid carcinomas constitute 80% of all thyroid cancers. In areas with iodine deficiency, an elective increase in follicular and anaplastic cancers is the rule, but no definite demonstration is made. Chronic stimulation by increased TSH level leads to hyperplasia and possibly carcinomatous degeneration in iodine deficient countries.[10]

Medullary thyroid carcinoma is familial in 10% to 30% of cases. Here, they are part of distinct clinical syndromes - multiple endocrine neoplasia type 2A (MEN 2A), MEN 2B, and familial medullary thyroid cancer (FMTC).

The incidence of malignancy in the thyroid nodule was found to be 3-4%, especially the patients with a history of irradiation, family history, male sex, and rapidly growing tumors.[11] A higher risk of differentiated thyroid carcinoma is found in patients with Graves' disease and cold thyroid nodules, which are more aggressive.

Thyroid cancer most commonly presents as a single neck mass noted incidentally.

A thyroid mass in a child no matter its size or consistency is highly suspicious of malignancy. Regardless of sex, mass in advanced years is likely to be malignant.

Hard and fixed nodules though associated with thyroiditis must be viewed with suspicion for malignancy.

Papillary and follicular carcinomas present as a firm to hard, solitary thyroid nodule, whereas undifferentiated cancer is characterized by a stony hard, irregular nodular gland fixed to the underlying tissues. Solid lesions have a 21% risk of malignancy, cystic 7% and mixed lesions 12%. 5-10% of multiple nodules and 10-20% of solitary nodules are malignant.[12,13]

Papillary carcinoma known for its lymphatic spread presents with cervical lymphadenopathy alone in 20% of cases and thyroid swelling with lymph nodes in 13% of cases. Children and young adults more often have palpable nodal metastases. Many studies reported a 30-40% incidence of cervical nodal metastasis when therapeutic nodal dissections were performed. In medullary carcinoma, metastases are mostly found in the neck and mediastinal lymph nodes and may calcify.[14]

Large multinodular goiters with or without substernal extension can cause tracheal shift or impingement and alteration of the airway. Local compressive symptoms are a rule in the case of anaplastic cancer and can include stridor, dysphagia, dyspnea and even superior vena cava syndrome.

Papillary carcinomas rarely spread by bloodstream, commonly in the skull, spine, and long bones. They can be pulsatile especially the skull. X-ray shows destructive bony lesion.[15]

A serum level of thyroglobulin more than 10 times the upper limit of normal is highly suggestive of cancer.[16] The plasma calcitonin has the most direct diagnostic value in determining the nature of the thyroid mass; it is elevated in almost all patients with MTC.[17,18] Mutation of ret proto-oncogene are associated in 95% of hereditary MTC, MEN 2A, MEN 2B, and FMTC.[19]

Of all the diagnostic methods, FNA and cytological evaluation are the easiest, least expensive, and most accurate method for diagnosing a thyroid nodule, and their value is universally acknowledged.[20,21] The accuracy of this technique depends on the experience of the cytopathologist. It may approach 95%.

Diagnostic ultrasonography using B-mode gray scale provides remarkable anatomic information about the thyroid gland. Because of its simplicity and ability to distinguish between solid and cystic lesions, it is often the first modality to evaluate a thyroid mass in the euthyroid patient. Good quality ultrasound using 7.5-10 MHz transducers provides excellent detail of the superficial gland but requires enough penetration to evaluate posteriorly to the level of the spine. Ultrasonography can detect lesions as small as 3 mm diameter, impalpable nodules, and subtle multinodularity that is not clinically detectable. Punctate or microcalcifications are not common in nodules and repeatedly have high specificity for thyroid cancer (95.2%) but low sensitivity (59.3%) and diagnostic accuracy of 83.3%. They may represent psammoma bodies in papillary cancer.

An elevated or rising thyroglobulin is highly specific and sensitive marker of recurrent follicular thyroid carcinoma.

Calcitonin is a specific and sensitive marker for post-operative monitoring in medullary thyroid carcinoma. Elevated concentrations are seen consistently in metastatic or nodal recurrence and the rising titer over time predicts the disease that may be progressing.

In general, 3 surgical procedures are advocated by experts - hemithyroidectomy, near-total thyroidectomy, and total thyroidectomy.[22]

Total thyroidectomy is the treatment of choice for virtually all patients with papillary thyroid carcinoma (PTC) when post-operative radio iodine therapy is being considered. This basically includes all patients except those with occult PTC (<1 cm). When a total thyroidectomy cannot be performed without injury to the recurrent laryngeal nerve or parathyroid glands, the near-total thyroidectomy is performed, and the small amount or thyroid tissue left behind can subsequently be ablated with radioactive iodine.

80% of patients with PTC have cervical lymph node metastases. The survival rates for patients who are given therapeutic node dissection and prophylactic node dissection are essentially same. Hence, only a therapeutic lymph node dissection is performed. In those patients with palpable lymph node metastases, all the lymph nodes in the central compartment are removed and with evidence of lateral lymph node metastases, a functional neck dissection is performed to remove all the fibrofatty tissue with the lymph nodes, but all the motor (phrenic, vagus, and spinal accessory) and sensory nerves, as well as the sternocleidomastoid and internal jugular vein, are preserved unless invaded by the tumor.[23]

Some experts recommend radio iodine therapy for all patients of PTC except for those with occult papillary, whereas others advocate it only for high-risk patients. The serum TSH levels, amount of residual normal thyroid tissue, the degree of differentiation of the PTC and the patient's age add to affect the amount of radioactive iodine uptake.[24] Most often it is administered 4-6 weeks after thyroidectomy with the patient in the hypothyroid state to maximize TSH-stimulated iodine uptake and whole body iodine retention.

Serum TSH must be elevated to at least 30 mIU/L and negative pregnancy test in women of childbearing age is followed by oral administration of I-131, 30-50 mCi of I-131 (low dose) for low risk, and 100-200 mCi of I-131 (high dose) for high-risk patients. In addition, TSH stimulates thyroglobulin synthesis and secretion and increases radioactive iodine uptake in thyroid cancers, which documents its stimulating role in patients. Hence, patients given an effective thyroxine hormone suppressive therapy (<0.1 mu/ml) have improved survival, lower recurrence rate, and lower mortality.

The follow-up of patients with differentiated thyroid carcinoma includes physical examination, monitoring of thyroglobulin level, I-131 whole body scanning, radiographic imaging, and functional nuclear imaging.

For medullary carcinoma, total thyroidectomy only offers the prospect of definitive cure both in primary and locally recurrent disease, irrespective of the tumor size. All nodes positive MTC without distant metastases clinically are treated by total thyroidectomy with micro dissection of the bilateral central and lateral neck compartments. Calcitonin and carcinoembryonic antigen levels should be assessed at approximately 4 weeks after surgery. A persistent or re-elevating level may indicate locoregional failure or metastases.[25]

Anaplastic carcinoma is devastating, and the treatment results are discouraging. In spite of surgery, radiotherapy, and chemotherapy, almost all the patients die of cancer-related death. The median survival of anaplastic thyroid cancer is 4-5 months.

CONCLUSION

Thyroid cancer is a disease of young adults, constituting about 1.5% of all cancers detected and more commonly seen in females. Most of the cancers present as a slow growing goiter for few months to few years duration. Most of the cancers are of papillary carcinoma type accounting up to 70% of cases. FNAC detects the majority of the cancers and is an important diagnostic test. Thyroid cancers have a good prognosis as most of the patients present as Stage I disease. Lymph nodal involvement is seen in about 10% of patients, and most of the patients require total thyroidectomy with or without lymph node dissection followed by radio iodine ablation as treatment. Prognosis is good for differentiated thyroid cancers and medullary carcinoma, whereas anaplastic carcinoma behaves aggressively and has a poor prognosis.

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Original Article

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Liver Function in Type-2 Diabetes Mellitus Patients

Shipra Mathur[1], Debij Kumar Mehta[1], Sangeeta Kapoor[2], Sushil Yadav[3]

[1]Demonstrator, Department of Biochemistry, Ambikapur Government Medical College, Ambikapur, Chhattisgarh, India, [2]Professor, Department of Biochemistry, Teerthanker Mahaveer Medical College & Research Centre, Moradabad, Uttar Pradesh, India, [3]Demonestrator, Department of Biochemistry, Teerthanker Mahaveer Medical College & Research Centre, Moradabad, Uttar Pradesh, India

Abstract

Background: Diabetes mellitus (DM) is a syndrome of disordered metabolism with abnormally high blood glucose levels (hyperglycemia). In Type-2 DM (T2DM), the loss of direct effect of insulin to suppress hepatic glucose production and glycogenolysis in the liver causes an increase in hepatic glucose production. Hence, this study was intended to determine the status of parameters related to liver function in T2DM patients and compare it with that of controls.

Objectives: To study the activity of serum alanine aminotransferase (ALT), serum aspartate aminotransferase (AST), and serum alkaline phosphatase (ALP) in T2DM patients and compare it with that of normal healthy controls.

Materials and Methods: A total of 30 patients of both sexes suffering from T2DM and 30 age and sex matched normal individuals were selected for the study. The patients with fasting plasma glucose ≥126 mg/dl on 2 occasion were included in the study. Patients with any concomitant diseases which can alter liver function and patient with hepatitis, alcoholic were excluded from the study.

Results: The mean activity of serum ALT (47.86 ± 33.66 U/L), serum AST, (49.7 ± 30.76 IU/L), and serum ALP (115.9 ± 42.65 IU/L) of diabetic patients shows significant difference from that of the normal subjects.

Conclusion: The outcomes of the present study suggest that the liver enzymes (ALT, AST, and ALP) have shown higher activity with T2DM patients than individuals who do not have DM. The most common abnormality seen among these liver enzymes is elevated AST activity.

Key words: Alanine aminotransferase, Aspartate aminotransferase, Alkaline phosphatase

INTRODUCTION

Diabetes mellitus (DM) is often simply considered as diabetes, a syndrome of disordered metabolism with abnormally high blood glucose levels (hyperglycemia). The two most common forms of DM are Type-1 diabetes and Type-2 diabetes (T2DM) both leading to hyperglycemia, excessive urine production, compensatory thirst, increased fluid intake, blurred vision, unexplained weight loss, lethargy, and changes in energy metabolism.

T2DM is a complex heterogeneous group of metabolic conditions characterized by increased levels of blood glucose due to impairment in insulin action and/or insulin secretion. Insulin is the principal hormone that regulates uptake of glucose from the blood into most cells, including skeletal muscle cells and adipocytes.[1] The liver plays a major role in the regulation of carbohydrate metabolism, as it uses glucose as a fuel, it has the capability to store glucose as glycogen and also synthesize glucose from non-carbohydrate sources. This type of role makes the liver more susceptible to diseases in subjects having a metabolic disorder, especially for DM.[2]

In T2DM, the loss of a direct effect of insulin to suppress hepatic glucose production and glycogenolysis in the liver causes an increase in hepatic glucose production.[3] In T2DM, hyperinsulinemia in combination with a high free fatty acid (FFA) flux and hyperglycemia are known to up-regulate lipogenic transcription factors. Moreover, pathways that decrease the hepatic FFA pool, i.e., both FFA oxidation and efflux of lipids from the liver are impaired. The increased availability of FFA, glucose, and insulin contribute to the increase of malonyl-CoA by

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Corresponding Author: Sushil Yadav, Department of Biochemistry, Teerthanker Mahaveer University, Moradabad, Uttar Pradesh, India. Phone: +91-8791391404. E-mail: yadav.sushil4644@gmail.com

stimulating CoA carboxylase that converts acetyl-CoA to malonyl-CoA.[4]

The fatty acids overload the hepatic mitochondrial-oxidation system, leading to accumulation of fatty acids in the liver.[5] These mechanisms finally lead to non-alcoholic fatty liver disease (NAFLD) in T2DM patients. In addition, several studies have also shown an association between NAFLD and features of the metabolic syndrome, including dyslipidemia and DM, stressing the association with insulin resistance as an important feature of NAFLD.

Some authors have considered that NAFLD may be the hepatic component of the T2DM as metabolic syndrome.[6,7] In the majority of cases, NAFLD causes asymptomatic abnormality of liver enzyme levels (including alanine aminotransferase [ALT], aspartate aminotransferase (AST), and alkaline phosphatase (ALP).[8] Of these liver enzymes, ALT is most closely related to liver fat accumulation[9] and consequently ALT has been used as a marker of NAFLD. Serum aminotransferase such as ALT and AST indicate the concentration of hepatic intracellular enzyme that has leaked into the circulation. These are the markers for hepatocellular injury and are used as primary markers.[10]

Numerous studies have identified that hyperglycemia may lead to oxidative stress and glycation reactions. Over time, the initial glycation products undergo intramolecular rearrangements and oxidation reactions (glycoxidation) and ultimately transform into stable so-called advanced glycation end-products (AGEs). AGE-modification of proteins can alter or limit their functional or structural properties, which ultimately can lead to tissue damage as seen in DM. Oxidative stress may also be one of the factors which may alter liver enzymes (ALT, AST, and ALP). ALP is also used for the assessment of the liver function. It reaches extremely high levels in biliary obstruction. The altered ALP activity may reflect an increased hepatic insulin resistance or oxidative stress.[11]

MATERIALS AND METHODS

A total of 30 patients of both sexes suffering from T2DM and 30 age and sex matched normal individuals were selected for the study. Patients whose fasting plasma glucose (FPG) ≥126 mg/dl on 2 occasion were included in the study. Patients with any concomitant diseases which can alter liver function and patient with hepatitis, alcoholic and taking any medicine were excluded from the study.

Estimation of fasting blood serum glucose, ALT, AST, and ALP activity were performed by glucose oxidase-peroxidase method,[12] IFCC kinetic assay, respectively.[13-15]

Calculation

$$\text{Blood glucose } (\text{mg/dl}) = \frac{\Delta A \text{ of test} \times \text{concentrstion of standard } (100\,\text{mg/dl})}{\Delta A \text{ of standard}}$$

Statistical Analysis

Mean±standard deviation was calculated for all the parameters analyzed and were compared by Student's *t*-test (2-tailed) using SPSS. *P*-value considered:
$P < 0.005$ - Significant
$P < 0.001$ - Highly significant

RESULTS

The mean activity of serum ALT (47.86 ± 33.66 U/L), serum AST, (49.7 ± 30.76 IU/L), and serum ALP (115.9 ± 42.65 IU/L) of diabetic patients shows significant difference from that of normal subjects (Table 1 and Figures 1-3).

The prevalence of increased activity of AST was 56.1%, ALT was 19.8% and ALP was 33% in T2DM patients (Table 2 and Figure 4).

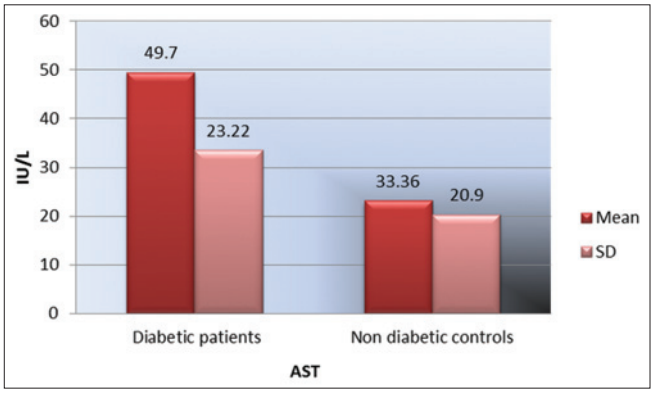

Figure 1: Comparison of serum aspartate aminotransferase activity in diabetic patients and non-diabetic controls

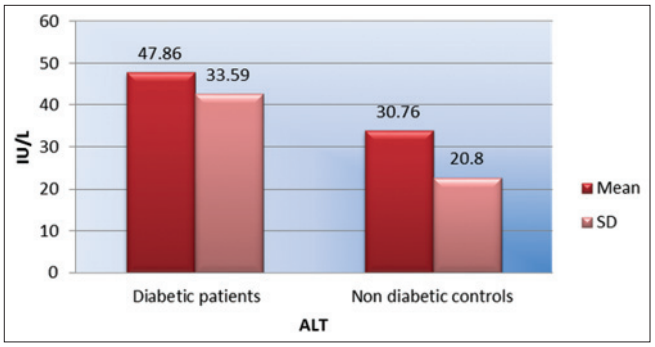

Figure 2: Comparison of serum alanine aminotransferase activity in diabetic patients and non-diabetic controls

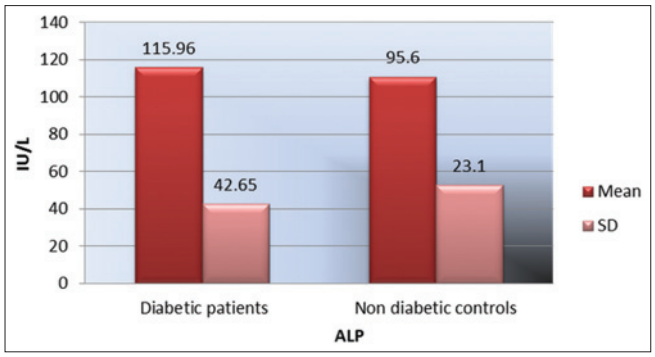

Figure 3: Comparison of serum alkaline phosphatase activity in diabetic patients and non-diabetic controls

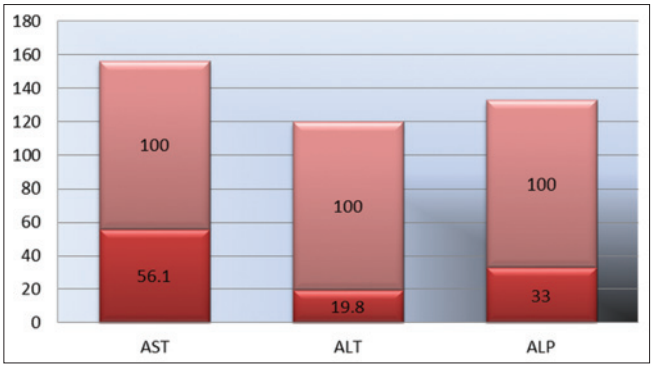

Figure 4: Prevalence of aspartate aminotransferase, alanine aminotransferase and alkaline phosphatase in diabetic patients

Table 1: Comparison of serum ALT, serum AST, and serum ALP activity, in non-diabetic and T2DM patients

Parameters	Mean±SD		*t* value	*P* value
	Diabetic	Control		
AST (IU/L)	49.7±23.22	33.36±20.9	2.37	0.021
ALT (IU/L)	47.86±33.59	30.76±20.8	2.84	0.006
ALP (IU/L)	115.9±42.65	95.6±23.1	2.29	0.026

SD: Standard deviation, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, ALP: Alkaline phosphatase, T2DM: Type-2 diabetes mellitus

Table 2: Prevalence of increased AST, ALT, and ALP activity in T2DM patients

Parameters	AST	ALT	ALP
Increased %	56.1	19.8	33

AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, ALP: Alkaline phosphatase, T2DM: Type-2 diabetes mellitus

DISCUSSION

DM is often simply considered as a syndrome of disordered metabolism with abnormally high blood glucose levels (hyperglycemia). Besides the microvascular and macrovascular complications in DM a compromised immune state is also a condition that increases the susceptibility of a diabetic patient to different infections. In Harris *et al.*, studies, it was shown that individuals with T2DM have a higher incidence of liver function test abnormalities than individuals who do not suffer from DM.[16] Aminotransferase such as ALT and AST, activities are sensitive indicators of liver cell injury and are helpful in recognizing hepatocellular diseases. Chronic mild elevation of liver enzymes is frequently found in Type-2 diabetic patients. However, though all these reports suggest that the liver function is involved in the development of diabetes but no, study so far have been known to show which of these enzymes is the best markers for the development of DM.[17] This study was conducted on 30 diabetic patients and 30 healthy persons. There was no significant difference between the age and sex of the subjects from the two groups. The diabetic state of the patients was confirmed by recording their detailed medical history and finally by estimating the FPG concentration by GOD-POD method, FPG concentration > 126 mg/dl on two occasions was considered as confirmation of DM FPG recorded for diabetic patients was 257.93 ± 110.004 mg/dl. The outcomes from the present study are as follows:

Assessment of ALT Activity

The mean level of serum ALT in Type-2 diabetic patients group was 47.86 ± 33.66 IU/L in normal controls was 30.66 ± 20.81 IU/L. The ALT in fasting serum sample in diabetic patients group was found to be significantly higher in comparison to the normal control group with $P = 0.026$. Raised level of ALT was noted in 19.8% diabetic patients. These findings are consistent with the results obtained from several other studies by various researchers. According to Gonem *et al.*, it was identified that the prevalence of ALT enzyme activity in diabetic patients (n = 959) was 15.7% (151).[18] ALT catalyzes the reversible transamination between L-alanine and α-ketoglutarate to form pyruvate and L-glutamate as such having an important role in gluconeogenesis and amino acid metabolism. The reaction is reversible, but the equilibrium of the ALT reaction favors the formation of L-alanine. ALT enzyme activity is primarily found in liver but its activity although much lower. Another explanation might be up-regulation of ALT enzyme activity. Among the amino acids, Alanine is the most effective precursor for gluconeogenesis. Gluconeogenesis is increased in subjects with T2DM due to increase substrate delivery (e.g., alanine) and an increased conversion of alanine to glucose. ALT might thus be up-regulated as a compensatory response to the impaired hepatic insulin signaling or, alternatively, may leak more easily out of the hepatocytes as a consequent of fatty infiltration and subsequent damage.[19]

Assessment of AST Activity

The mean of serum AST in T2DM group was 49.7 ± 23.22 IU/L in normal control group 33.36 ± 20.9. The AST in fasting serum sample in diabetic patients was found to be

significantly higher in comparison with the normal control group with *P* value 0.021. Raised level of AST was noted in 56.1% diabetic patients. These findings are consistent with the results obtained from several other studies done by various researches. According to Goldberg *et al.*, (2007), it was identified that the prevalence of AST enzyme activity in diabetic patients was (101 patients) 15% diabetic patients.[20] The activity of transaminase enzymes AST is often measured; these enzymes function normally to transfer the amino group from an amino acid, Aspartate in the case of AST to a keto acid, producing pyruvate and oxaloacetate, respectively. It is located in the cytoplasm of the hepatocyte; an alternative form of AST is also located in the hepatocyte mitochondria. Although, both transaminase enzymes are widely distributed in other tissues of the body, the activities of ALT outside the liver are low and, therefore, this enzyme is considered more specific for hepatocellular damage.[21]

Assessment of ALP Activity

The mean of serum ALP in T2DM group was 115.9 ± 42.65 IU/L and in the normal control group was 95.6 ± 23.1 IU/L. The ALP in fasting serum sample in diabetic patients was found to be significantly higher in comparison with the normal control group with p value 0.026. Raised level of ALP (30 patients) was noted 33% (10) diabetic patients. In a study by Han *et al.*, it was found that the level of ALP in Type-2 diabetic patients was 10.20 ± 22.82 IU/L and the prevalence of ALP (n = 81) was 6.2% diabetic patients.[22] ALP is a hydrolytic enzyme serine protease acting optimally at pH 10. It has been reported in few earlier studies that many diabetics may also exhibit elevated ALP.[23] T2DM being a metabolic syndrome in which the fat metabolism is dysregulated, there is consequent elevation of FFA leading to subsequent fatty liver. ALP in the liver is found to be associated with cell membrane which adjoins the biliary canaliculus, and so high plasma concentration of the liver isoenzyme indicates cholestasis rather than simply damage to the liver cells. According to a study by Southampton university hospitals, 60 diabetics stabilized on insulin or oral hypoglycemic agents, routine liver function tests particularly ALP was elevated occasionally but rarely to more than twice the upper limit of normal. It can be concluded that functionally significant liver disease is uncommon amongst stabilized diabetic patients.[24] According to Vozarova *et al.*, it was estimated that the liver enzymes AST, ALT, and ALP were significantly higher in diabetic patients as compared to non-diabetic control.[25]

CONCLUSION

The outcomes from this study suggested that the liver enzymes (ALT, AST, and ALP) have shown higher activity with T2DM patients than individuals who do not have DM. The most common abnormality seen among these liver enzymes is elevated AST activity. The prevalence of increased activity of AST was 56.1%, ALT was 19.8% and ALP was 33%. The reason behind the elevation of these enzymes could be due to direct hepatotoxic effect of fatty acid on the liver when it is produced in excess. Mechanisms for this may include cell membrane disruption at high concentration, mitochondrial dysfunction, toxin formation, and activation and inhibition of key steps in the regulation of metabolism. Other potential explanations for elevated transaminases in insulin-resistant states include oxidative stress from reactive lipid peroxidation, peroxisomal beta-oxidation, and recruited inflammatory cells. The insulin resistant state is also characterized by an increase in pro-inflammatory cytokines such as tumor necrosis factor-α, which may also contribute to hepatocellular injury.

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Original Article

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Evaluation of Serum Procalcitonin Levels and Sequential Organ Failure Assessment Score in Assessing the Severity and Outcome of Sepsis

Vamseedhar Annam[1], Priyanka Maleedhu[2], M Vijaya Bhaskar[3], L Venugopal[4]

[1]Professor, Department of Pathology, Mamata Medical College, Khammam, Telangana, India, [2]Assistant Professor, Department of Biochemistry, Mamata Medical College, Khammam, Telangana, India, [3]Professor, Department of Biochemistry, Mamata Medical College, Khammam, Telangana, India, [4]Associate Professor, Department of General Medicine, Mamata Medical College, Khammam, Telangana, India

Abstract

Introduction: Sepsis is a systemic condition with high mortality and morbidity in emergency medicine. The septic response is a complex chain of events involving inflammatory and anti-inflammatory processes. The diagnosis and assessing the severity of sepsis is complicated by non-specific nature of signs and symptoms.

Purpose: Early diagnosis and initiation of goal-directed therapies can prevent complications of sepsis. Furthermore, assessing the severity and outcome of sepsis can reduce mortality. The present study of evaluating procalcitonin (PCT) levels and sequential organ failure assessment (SOFA) score in various categories of sepsis was conducted.

Materials and Methods: The present cross-sectional study included 100 patients based on the defined inclusion and exclusion criteria's. The study subjects were divided into three groups: Sepsis, severe sepsis, and septic shock based on the American College of Chest Physicians/Society of Critical Care Medicine guidelines. Serum PCT levels were estimated, and SOFA score was calculated for all the patients. The statistical analyzes were done using one-way ANOVA.

Results: Of 100 patients studied, there were 30 patients in sepsis group, 40 in severe sepsis group, and remaining 30 in septic shock group. The serum PCT levels were positive in 84% of the total study population. Among the groups, PCT levels were 100% positive in both severe sepsis group and septic shock group. The SOFA score was significantly increased in severe sepsis and septic shock. The mortality was 60% in severe sepsis and 83.3% in septic shock group.

Conclusion: We conclude that PCT with SOFA score can be considered as indicators in assessing the severity and outcome of sepsis.

Key words: Inflammatory, Morbidity, Mortality, Procalcitonin, Sepsis, Shock

INTRODUCTION

Sepsis is one of the leading causes of death in emergency medicine despite the use of new antibiotics and advanced resuscitation therapies. Recent data have suggested that 18 million of new sepsis occurs each year with a mortality rate of 30%.[1] Hence, early diagnosis in assessing the severity of sepsis increases the possibility of initiating timely and specific treatment.[2]

The clinical diagnosis of sepsis and also assessing its severity is complicated due to non-specific and highly variable signs and symptoms. There are various biomarkers for assessing severity of sepsis, prognostication, guiding antibiotic therapy, evaluating response to therapy, and predicting sepsis complication like organ dysfunction.[3]

Procalcitonin [PCT] has been considered as a better biomarker of systemic inflammatory response to infection.[4] It is elevated in various severe infections and inflammations. However, the exact role of PCT in various stages of sepsis remains undefined.[5] Moreover, the sequential organ failure

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Corresponding Author: Dr. Vamseedhar Annam, Department of Pathology, Mamata Medical College, Khammam, Telangana, India. Phone: +91-9701500592. E-mail: vamseedhar_a@yahoo.com

assessment (SOFA) score can assess the severity of sepsis and multi-organ failure at the beginning of sepsis and after 48 h.[6] Hence, the present study was conducted including both serum PCT levels and SOFA score in assessing the severity of sepsis.

MATERIALS AND METHODS

The present cross-sectional observational study was carried out in a tertiary health care center at Telangana, India. A total of 100 patients were included in the study.

Inclusion Criteria

- The patients with age above 18 years
- Clinical diagnosis of sepsis.

Exclusion Criteria

- Patients with acute inflammatory lesions, severe burns, heat stroke, and mesenteric embolism
- Patients on treatment with antibiotics and tumor necrosis factor-α inhibitors
- History of recent surgeries, cardiac surgery, recent trauma
- Patients with malignant neoplasm.

Informed consent and ethical clearance were taken from the patient attendants. A detailed clinical history, general physical examination, and systemic examination of the patients were carried out.

The study subjects were divided into three groups: (1) Sepsis, (2) severe sepsis, and (3) septic shock based on the American College of Chest Physicians/Society of Critical Care Medicine (ACCP/SCCM) consensus guidelines.[5] The presence of organ dysfunctions (cardiovascular, neurological, respiratory, renal, hepatic, and coagulation) was assessed using a SOFA score (Table 1).[7]

Peripheral blood sample were collected from all the patients in sterile vacutainer and transported at room temperature to the central laboratory within 24 h of collection (as per the laboratory directions). Serum PCT levels were estimated, and SOFA score was calculated for all the patients.

Serum PCT was measured by semi-quantitative rapid assay (BRAHMS PCT-Q). It is an immunochromatographic test using monoclonal mouse anti-calcitonin antibody conjugated with colloidal gold (tracer) and a polyclonal sheep anti-calcitonin antibody (solid phase).[8]

Statistical Analysis

The statistical analysis was done using mean, standard deviation, and ANOVA.

RESULTS

Of the 100 patients studied, there were 30 patients in sepsis group, 40 in severe sepsis group, and remaining 30 belonged to septic shock group. The most common age group involved was 41-50 years (35.3%), 51-60 years (30%), and 31-40 years (34.6%) in sepsis, severe sepsis, and in septic shock groups, respectively. Males were more frequently affected than females with male:female ratio being 1.7:1%.

In the present study, serum PCT was positive in 84% and negative in 16% of the total study population (mean value 20.38 ± 35.49 ng/ml). Among the groups, PCT was positive in 46.7% of sepsis group, 100% in both the severe sepsis group and septic shock group ($P < 0.001$) (Table 2).

The SOFA score in the present study was analyzed between severe sepsis group and septic shock group based on SOFA score. The mean value of SOFA score among the total group was 2.03 ± 2.97. In severe sepsis group, SOFA score was 1.23 ± 1.29 while in septic shock group, the SOFA score was 5.92 ± 3.96. The mean levels of SOFA score were statistically significant for the diagnosis of severe sepsis and septic shock ($P < 0.001$*) (Table 3).

In our study among the three groups, the overall mortality was 50%. It was 3.3% in sepsis, 60% in severe sepsis, and 83.3% in septic shock group (Table 4). Mean serum

Table 1: SOFA score

SOFA score	0	1	2	3	4
Respiratory: PaO_2/FiO_2	> 400	≤400 221-300	≤300 142-220	≤200 67-141	≤100 <67
Hematology: Platelet count [10^3/mcL]	>150	≤150	≤100	≤50	≤20
Hepatic: Bilirubin (mg/dL)	<1.2	1.2-1.9	2.0-5.9	6.0-11.9	>12.0
Cardiovascular: Hypotension	No Hypotension	MAP<70 mmHg	Dopamine ≤5[a] or dobutamine (any dose)	Dopamine >5[a] or epinephrine ≤0.1[a] or norepinephrine ≤0.1[a]	Dopamine >15[a] or epinephrine >0.1[a] or norepinephrine >0.1[a]
Renal: Creatinine (mg/dL)	<1.2	1.2-1.9	2.0-3.4	3.5-5.9; urine output ≤500 mL/day	>5; urine output <200 mL/day
Neurologic: Glasgow coma scale score	15	13-14	10-12	6-9	<6

SOFA: Sequential organ failure assessment, PaO_2: Arterial oxygen tension, FiO_2: Fractional inspired oxygen, MAP: Mean arterial pressure, [a]Adrenergic agents administered for at least 1h (doses given are in μg/kg/min)

Table 2: Association of PCT with Diagnosis in patients studied

Procalcitonin	Sepsis	Severe sepsis	Septic shock	Total
≤1	16 (53.3%)	0 (0%)	0 (0%)	16 (16%)
1-10	14 (46.7%)	19 (47.5%)	0 (0%)	33 (33%)
10.1-50	0 (0%)	21 (52.5%)	23 (76.7%)	44 (44%)
50.1-100	0 (0%)	0 (0%)	3 (10%)	3 (3%)
>100	0 (0%)	0 (0%)	4 (13.3%)	4 (4%)
Total	30	40	30	100
Mean±SD	1.50±1.95	13.49±9.69	55.66±54.61	20.38±35.49

Variation between groups: *F* statistics: 26.57, df: 2, *P* value: 0.001*, SD: Standard deviation, PCT: Procalcitonin

Table 3: Association of SOFA score with diagnosis in patients studied

SOFA score	Sepsis	Severe sepsis	Septic shock	Total
0	30 (100%)	19 (47.5%)	0 (0%)	49 (49%)
1-5	0 (0%)	21 (52.5%)	15 (50%)	36 (36%)
6-10	0 (0%)	0 (0%)	12 (40%)	12 (12%)
>10	0 (0%)	0 (0%)	3 (10%)	3 (3%)
Total	30	40	30	100
Mean±SD	0	1.23±1.29	5.92±3.96	2.03±2.97

Variation between groups: *F* statistics: 81.75, df: 2, *P* value: 0.001*, SOFA: Sequential organ failure assessment, SD: Standard deviation

Table 4: Association of outcome with diagnosis in patients studied

Outcome	Sepsis	Severe sepsis	Septic shock	Total
Death	1 (3.3%)	24 (60%)	25 (83.3%)	50 (50%)
Recovery	29 (96.7%)	16 (40%)	5 (16.7%)	50 (50%)
Total	30	40	30	100

PCT levels in patients who succumbed to death were 43.78 ng/ml and patients who survived had 6.22 ng/ml.

DISCUSSION

Sepsis is a complex chain of events involving cell-mediated and humoral immunity, inflammatory and anti-inflammatory reactions, and also circulatory disturbances.[9] It has become a common problem in intensive care units of healthcare and also responsible for mortality and morbidity of the elderly population. Martin *et al.*[10] reported that sepsis more frequently occurred in men, which was similar with our study. The probable reason could be that men have more exposure to various environmental conditions and stress factors.

The diagnosis of sepsis remains a challenge, as both clinical and standard laboratory tests are not very much helpful. Based on ACCP/SCCM criteria, the most common observed group was severe sepsis group with 40% followed by sepsis group and septic shock group (30% each). Furthermore, the microbiological assessment appears unreliable because of many negative culture results. However, a multitude of potential biomarkers has been used in clinical studies.[11] Indeed, a few biomarkers have been assessed for their ability to distinguish septic patients from non-septic patients. Among the various biomarkers, PCT has been extensively used for diagnosis of sepsis but not for the severity of sepsis.[4] Hence, the present study was conducted to know the role of serum PCT in assessing the severity of sepsis. Previous documented reports suggest that raised PCT levels can be observed in trauma[12] and major surgery[13] and cardiac surgery.[14] Therefore, we excluded these patients in our study.

Harbarth *et al.*[15] and Brunkhorst *et al.*[16] reported high levels of PCT among severe sepsis and septic shock group. In the present study, we observed increased serum PCT levels in 84% of the total study population. There was a significant statistical association for PCT between the severe sepsis and septic shock groups ($P < 0.001$).

Although, a small amount of PCT is found in the peripheral circulation of healthy subjects, they are increased in infectious, non-infectious, and inflammatory conditions.[17] These various conditions release pro-inflammatory mediators (e.g., interleukin-1β, interleukin-6, and tumor necrosis factor-α) either by direct pathway (induced by lipopolysaccharides or toxins released by microbes) or indirect pathway (cell-mediated response). The pro-inflammatory mediators further may stimulate monocytes and can induce calcitonin mRNA expression in the non-neuroendocrine cells to release unprocessed PCT. Since, there are no specific storage secretory granules for PCT; the unprocessed PCT is released into the plasma resulting in increased PCT levels.[18] Thus, PCT appears to possibly aid in assessing the severity of sepsis, and also can support in predicting the prognosis of sepsis.

In the present study, SOFA score was increased among severe sepsis and septic shock groups ($P < 0.001$). Similar results were also observed by studies conducted by Bale *et al.*[7] and Moreno *et al.*[19] Among the three groups, mortality was high in septic shock group (83.3%) followed by severe sepsis group (60%). Thus, increased SOFA scores reflect the poor functioning of the organ systems during the course of severe sepsis and septic shock groups, mostly in non-surviving patients. Therefore, SOFA score can be a better predictor of mortality and also assess the severity of sepsis.

CONCLUSION

Serum PCT levels and SOFA score were significantly elevated in patients with severe sepsis and septic shock indicating their utility in predicting the severity of sepsis. Moreover, early identification of severity can prevent the fatal outcome of

sepsis. Therefore, Serum PCT levels with SOFA score can be considered as helpful indicators in assessing the severity of sepsis and outcome of sepsis complications.

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Original Article

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Breast Carcinoma, Receptor Status, and Her2 neu Overexpression Revisited

R D Puvitha[1], S Shifa[2]

[1]Senior Assistant Professor, Department of Pathology, Coimbatore Medical College, Coimbatore, Tamil Nadu, India, [2]Assistant Professor, Department of Pathology, Madurai Medical College, Madurai, Tamil Nadu, India

Abstract

Background: A study conducted by the WHO revealed that Chennai has the highest incidence of breast carcinoma among all leading centers in India. For every two newly diagnosed case, one is dying. Early detection and treatment are the only way to prevent such deaths. Estrogen receptor (ER) progesterone receptor (PR) status, and Her2 neu (human epidermal growth factor receptor 2) overexpression study aid in deciding the treatment strategies. Study design: Cross-sectional descriptive study.

Aim: To statistically evaluate the occurrence of breast lesions in patients attending Coimbatore Medical College hospital and compare it with the global census. In addition to compare ER, PRs, and Her2 neu status with the possible variables we encounter.

Materials and Methods: The 368 breast specimens that were sent to the pathology department for the period of 3-year were analyzed. Both H&E stained sections and ER, PR, and Her2 neu status were reviewed by a team of experienced pathologists in our post-graduate teaching institute.

Results: Totally 368 breast tumor cases were analyzed in our study. Out of that, 63.35% were malignant breast cases. Invasive ductal carcinoma (not otherwise specified [NOS]) [79%] was most commonly encountered, and most of them were grade two tumors (88.5%). The ER/PR expression was more in carcinoma in stage 1 and II and in tumors without nodal metastasis (P = 0.001). Her2 neu expression was seen more in high-grade tumors and in those with nodal metastasis (P = 0.001). There was an inverse relationship between ER/PR status and Her2 neu expression (P = 0.001).

Conclusion: When compared with the western studies the ER, PR expression was low in our study group. Moreover, there was an inverse relationship between the ER, PR expression, and Her2 neu status.

Key words: Ductal carcinoma, Estrogen receptor, Progesterone receptor, Node

INTRODUCTION

For the past 4 years, breast cancer (BRCA) in overtaking all other cancers that affect women with an alarming number (1, 55,000 new cases/year) causing more than 6 million deaths per year.[1,2] The mean age of occurrence is 42 years.[2,3] Racial difference was also noted, black women were affected at a relatively younger age (45 years).[4] Prognosis and management of breast carcinoma are influenced by variables such as histological type and grade, tumor size, lymph node status, lymphovascular invasion, proliferating rate, DNA content, estrogen receptor (ER), progesterone receptor (PR) status, and Her2 neu overexpression and fluorescence *in situ* hybridization studies using centromere enumeration probe 17.[5] Of all these factors, the receptor and molecular studies had made a sea of change in the diagnosis and the treatment of breast carcinoma. While molecular tests are expensive and are not easily available, immunohistochemical (IHC) analysis is comparatively cheaper, useful for targeted therapy and a good prognostic factor.

The interrelationship of ER, PR status, and Her2 neu overexpression has an important role in the management of breast carcinoma. ER/PR status is inversely related to Her2 neu status. Survival and response to hormone therapy (tamoxifen) are more favorable among women who are receptor positive, intermediate for tumors discordant

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Corresponding Author: Dr. S Shifa, Department of Pathology, 82, J. N. Nagar, Old Natham Road, Madurai - 17, Tamil Nadu, India. Phone: +91-9486669274. E-mail: shifafrin@gmail.com

on receptor status and less favorable for receptor negative patients. However, if there is an amplification of both ER and Her2 neu, then the patient would not respond to tamoxifen.[6] Tamoxifen acts as an agonist if there are both ER expression and Her2 expression and cause proliferation of the tumor tissue, leading on to the resistance of tamoxifen.[7] In such cases, it has been shown that trastuzumab therapy is more effective. Patients with lone Her2 neu overexpression are also candidates for trastuzumab.[5,8,9] Thus, IHC studies have a role as a decision maker in the targeted therapy. This study is done to evaluate the ER, PR, and Her2 neu status and to compare it with the various variables we encounter as we analyze the cases.

MATERIALS AND METHODS

This is a cross-sectional study spanning over a three year period. 368 breast specimens were received during the study period. A detailed history regarding age, parity, socioeconomic status, family history, menstrual history, lactation history, and previous biopsy reports was reviewed in all the cases.

Inclusion Criteria

Newly diagnosed cases were included in our study.

Exclusion Criteria

Patients who had the neoadjuvant therapy were excluded from our study.

Patients with other associated malignancies were excluded from our study.

Macroscopy

Detailed gross examination pertaining to the overall size of the specimen, appearance of skin with measurements of scars or incisions, the appearance of the nipple and areola, tumor size, consistency, margins, and nodal status was noted from the records.

Microscopy

Slides from all the cases stained with hematoxylin and eosin were assessed. The histological assessment of tumor grade was done by modified Bloom–Richardson scoring system. Nodal status and margin involvement were recorded in each case. The WHO classification was used to classify the tumors.

Immunohistochemistry

Both ER/PR assay and Her2 neu assay were done in our study because of the following reasons: Hormone receptors are well-established biomarkers in breast carcinoma and their assessment helps in predicting the response to endocrine therapy.[10-12] Her2 neu is a prognostic marker as overexpression of Her2 neu in breast carcinoma leads to recurrence and worst prognosis.[13,14] IHC analysis of hormone receptor assay and Her2 neu status was done on the paraffin-embedded tissue blocks by the supersensitive polymer HRP system based on non-biotin polymeric technology.

Scoring System

IHC stained slides were evaluated for the presence of reaction, cellular localization (nuclear or cytoplasm), pattern of staining (focal or diffuse), and intensity of reaction in the individual tumor cells (strong or weak). Scoring for ERs and PRs was done using Quick score system and for Her2 neu, the scoring was done according to the guideline published by Ellis *et al.*[15,16] Quick score system uses two principles, intensity and proportion.[15] The quick score system based on intensity is as follows: When there are no staining - score 0. Weak stain- score 1, moderate stain - score 2, and strong stain - score 3. The staining system based on the proportion of stain is as follows: 1% nuclear stain - score 0, 1-10% stain-score 2, 11-33% - score 3, 34-66% - score 4, and 67-100% - score 5. This comes with a maximum score of eight. Score of more than two is considered as positive.[17] The advantage of this score is that it correlates with the probability of response to endocrine therapy.[18]

For Her2 neu scoring the following rule was followed: No staining or incomplete membrane staining and faint/barely perceptible in ≤10% of the tumor cells - Her2 neu negative. Incomplete and faint membrane staining in >10% of the invasive tumor cells are taken as Her2 neu 1+. A weak to moderate complete membrane staining in >10% tumor cells are graded as Her2 neu 2+. A strong complete membrane staining in> 10% tumor cells are graded as Her2 neu 3+.

Statistics

The statistical analysis was performed with Statistical Package for Social Science (SPSS) software version 11. The Pearson Chi-square test was used to compare the possible correlation between ERs, PRs, and Her2 neu with tumor size, nodal status, histological variants, and grades.

RESULTS

A total of 27,638 specimens were received. The distribution of benign breast disease (36.65%) and malignant breast tumors (63.35%) are depicted in (Table 1). Benign tumors had a peak incidence in the age group 21-30 years, whereas the malignant tumors had a peak incidence in the age group 41-50 years (Table 2).

Table 3 shows the distribution of histological variants in breast carcinoma. 79% were invasive ductal carcinoma (IDC), NOS type (Table 3), 88% of cases were Grade II tumors, and 46% of the cases had metastatic deposits in the lymph nodes. Dixon *et al.* and Omar Hameed in their studies had mentioned that IDC was the predominant histological variant.[19,20] In our study, the incidence of invasive lobular carcinoma was 3%, and it correlated with Foote and Stewart *et al.*'s study.[21]

When ER/PR status was analysed, both were positive in 24.24% of the cases and both were negative in 48.48% (Table 4). In Wilbur and Barrows study, ER positivity was observed in 73% of the cases and PR positivity was observed in 63% of the cases.[22] 70% of the BRCA were ER positive, and 60-65% were PR positive, according to Mohsin.[12] ER/PR expression increases as the age of the patient advances (Table 5). Her2 neu expression and inverse relationship between ER/PR and Her2 neu is depicted in (Tables 6 and 7). When ER/PR status was correlated with tumor grade, it was strongly expressed in low-grade tumors (Table 8). Most of the ER/PR positive cases were 2-3 cm in size (Table 9). When it was statistically analyzed, the $P = 0.003$ which highlight the significance of this correlation. When the nodal status was correlated with ER/PR expression, high ER/PR expression was seen in those without nodal metastasis (Table 10). Statistical analysis was done between these variables and was found to be significant ($P = 0.001$). In Huang *et al.*'s study, ER positivity was less in nodal positive tumors.[23]

Table 1: Distribution of cases

Total number of specimens	Total number of breast specimens	
	Benign	Malignant
27,638	135	233

Table 2: Age distribution

Age group (in years)	Benign tumors	Malignant tumors
<20	24	-
21-30	58 (57%)	12
31-40	30	32
41-50	14	105 (63.33%)
51-60	7	46
60 and above	2	38

Table 3: Distribution of the histopathological variants

Histological variants	Number of cases	Percentage
IDC-NOS type	184	79
Invasive lobular carcinoma	7	3
Mucinous carcinoma	14	6
Papillary carcinoma	7	3
Metaplastic carcinoma	7	3
Neuroendocrine carcinoma	7	3
Medullary carcinoma	7	3

NOS: Not otherwise specified, IDC: Invasive ductal carcinoma

Table 4: Distribution and correlation of ER/PR status

Group	Percentage
ER+/PR+	24.24
ER−/PR+	18.18
ER+/PR−	9.10
ER−/PR−	48.48

ER: Estrogen receptor, PR: Progesterone receptor

Table 5: Correlation of age and receptor status

Age group (years)	ER/PR positive (%)
21-30	-
31-40	50
41-50	27.3
51-60	77.77
61-70	80
>70	-

ER: Estrogen receptor, PR: Progesterone receptor

Table 6: Expression of Her2 neu in breast carcinoma

Her2 neu positive	Her2 neu negative (%)
42.42	57.58

Table 7: Correlation of receptors with protein expression

ER/PR status	Her2 neu (%)	
	Positive	Negative
Positive	6	45
Negative	36	12

ER: Estrogen receptor, PR: Progesterone receptor

Table 8: Correlation of grade, receptor status and Her2/neu expression

Histological grade	Number of cases (%)	ER/PR positive (%)	Her2 neu positive (%)
Grade I	4	4	-
Grade II	88	54	50
Grade III	8	-	8

ER: Estrogen receptor, PR: Progesterone receptor

Table 9: Correlation of tumor size with hormone receptors and Her2 neu expression

Tumor size (cm)	ER/PR positive (%)	Her2 neu positivity (%)
T1 - <2	66	14
T2-2-5	75	29
T3 - >5	33	57

ER: Estrogen receptor, PR: Progesterone receptor

42% of the cases were Her2 neu positive in our study (Table 6). Kumar *et al.* in their study had mentioned that Her2 neu oncogene overexpression was much higher among Indian BRCA patients 46.3% compared to 25-30% in the western literature.[24] Her2 neu positivity was seen more when the tumor size was >5 cm (Table 9). When the tumor grade was correlated with Her2 neu expression, all higher grade tumors expressed Her2 neu. When it was statistically analyzed, the significant *P* value was obtained (0.001). Her2 neu expression was seen more in those who had metastasis in the node and was analyzed statistically (Table 10). Significant *P* value was obtained ($P = 0.001$).

Table 7 shows an inverse relationship of ER, PR expression, and Her2 neu status. Statistical analysis was performed with the SPSS version 11 and found to be significant ($P = 0.001$). In Huang *et al.*'s study, an inverse relationship with receptor and oncoprotein expression was observed, which correlated with our study.[23]

Table 10: Correlation of receptor status and Her2 neu expression with nodal status

Nodal status	Number of cases (%)	ER/PR positive (%)	Her2 neu positivity
Positive	46	33	67
Negative	54	56	11

ER: Estrogen receptor, PR: Progesterone receptor

Table 11: Comparative analysis of distribution of histological variants of our study with others

Histological types	Dixon *et al.*[19] (%)	Hameed[20] (%)	Current study (%)
IDC-NOS type (Figure 1)	79	>70	79
Lobular carcinoma	10	5-15	3
Mucinous carcinoma (Figure 2)	2	1-5	6
Medullary carcinoma	2	1-7	3
Papillary carcinoma (Figure 3)	1	2	3
Solid neuroendocrine carcinoma	<1	Rare	3
Metaplastic carcinoma	-	2-5	3

NOS: Not otherwise specified, IDC: Invasive ductal carcinoma

DISCUSSION

In the Indian scenario, breast carcinoma and cervical carcinoma account for about 60% of malignancies in women, the incidence of BRCA alone being 10.4%.[2] It has been proposed that the common denominator of risk factors such as menarche, nulliparity, age at first birth and late menopause that lead on to the breast carcinoma is a strong and prolonged estrogen stimulation operating in a genetically susceptible background.[3,25,26] Breast carcinoma can occur sporadically or in a hereditary background. About 25% familial cancers can be attributed to two highly penetrant autosomal dominant genes BRCA 1, early onset and BRCA 2, early onset located in 17q21 and 13q12.3, respectively. BRCA 1 associated BRCA are medullary carcinoma (67%) and mucinous carcinoma (55%). BRCA 2 mutation does not have a distinct morphologic appearance.[8]

The peak age incidence of malignant breast tumors in our study was 41-50 years. Ejam and Farhood in his study had observed the peak age incidence as 30-50 years, which correlated with our study.[27] Onitilo *et al.* in their study had mentioned the peak incidence as 62.7 years.[28] The mean age incidence in Ghosh *et al.*'s study was 49 years, which correlated with our study.[29]

The incidence of various histological variants encountered by Dixon *et al.* and Hameed were comparable to our study (Table 11).[19,20] In Nikhra *et al.*'s study, 95.34% of the tumor was infiltrating ductal carcinoma.[30] Foote and Stewart had recorded that the incidence of lobular carcinoma was 4.9-12% in a post-menopausal age group in their study.[21] In our study, the incidence of lobular carcinoma was 3%, which correlated with their study, but the age incidence in our study was 35 years in contrast to theirs.

Both ER/PR and Her2 neu were employed in our study. A brief introduction of both: ERs and PRs are nuclear transcription factors that are involved in breast development, growth, differentiation, and tumorigenesis.[18,31] ER regulates the expression of other genes such as progesterone and bcl2.[31] There are two forms of ER referred to as ER alpha and ER beta encoded by 6p25.1 and 14q, respectively.[32] ER alpha is found in endometrium, BRCA cells, ovarian stroma, and hypothalamus. ER beta distribution is seen in kidney, brain, bone, heart, and lungs.[33] ER and PR positive tumors tend to have a significantly longer disease-free survival than with receptor negative tumors.[10-12]

Her2 neu [c-erb B -2] belongs to epidermal growth factor receptor family. It is an oncogene that encodes a transmembrane glycoprotein with tyrosine kinase activity located in 17q 11.2 –q12.[13] Her-2 neu overexpression in breast carcinoma leads to recurrence and worst prognosis.[13,14]

In our study, ER and PR were positive in 51.6% cases, and both the receptors were negative in 48.4% cases (Table 7). Her2 neu overexpression was observed in 42.7% cases. This is in correlation with Kumar *et al.*'s study [Her2 neu-46.3%], Shet *et al.*'s study (receptor expression range from 52 to 57%), and Mudduwa study (ER - 45.7%, PR -48.3%).[17,24,34] In our study, ER/PR positivity and Her2 neu negativity were observed in mucinous carcinomas, papillary carcinoma, and neuroendocrine carcinoma. Lee *et al.* in their study had observed ER and PR positivity and Her2 neu negativity in the neuroendocrine tumor of the breast.[35]

Reiner *et al.* and Rosen *et al.* had observed that papillary carcinoma of the breast was ER/PR positive and Her2 neu negative.[9,36] Diab *et al.* and Shousha *et al.* had observed ER/PR positivity and Her2 neu negativity in mucinous carcinoma of the breast.[37,38] All these studies correlated with our study. In our study, medullary carcinoma and metaplastic carcinoma were triple-negative (ER, PR, and Her2 neu). Oberman *et al.*, Rosen *et al.*, and Soomro *et al.* in their studies had encountered similar results.[9,39,40]

Young patients tend to have a high level of circulating estrogen and correspondingly low expression of receptors. Accordingly, in our study, there was increased immune reactivity to ER/PR as the age advances. Dutta *et al.* and Almasri and Al Hamad studies showed similar results.[41,42]

In our study, there was an inverse relationship between hormone receptors and oncoprotein expression (Table 7). Huang, *et al.*'s study showed similar results.[23]

In our study, ERs/PRs were 100% positive in Grade I tumors, and Her2 neu overexpression was 100% positive in Grade III tumors (Table 8). Rosen *et al.* and Jovicic-Milentijevic *et al.*'s studies correlated with ours in this aspect.[9,43]

For the practical purpose, we had categorized the tumor size based on TNM stage as follows: T1- <2 cm, T2 = 2-5 cm, and T3 - >5 cm. As depicted in Table 9, 75% of T2 showed receptor positivity and Her2 neu overexpression was seen in T2 and T3 tumors. Rosen *et al.* and Dutta *et al.*'s study also showed an inverse relationship between tumor size and Her2 neu overexpression and ER/PR status respectively.[9,41]

In our study, receptor positivity was found to be higher among the nodal metastasis negative patients 55.55% and Her2 neu overexpression was seen more in node positive cases than the node-negative patients (Table 10). Dutta *et al.* in their study had observed Her2 neu overexpression in node-positive patients.[41] Huang *et al.* in their study had mentioned that ER/PR expression was less in node-positive patients.[23] The results of these two studies were similar to our study.

Two cases in our study showed positivity for ER/PR and Her2 neu (Table 7). Francis *et al.* and Bhargava *et al.* in their studies had observed hybrid ER/PR and Her2 neu expressions.[44,45]

CONCLUSION

ERs and PRs positive tumors were common in post-menopausal women, tumors of more than 2 cm size, histological Grade-I, and in nodal negative patients.

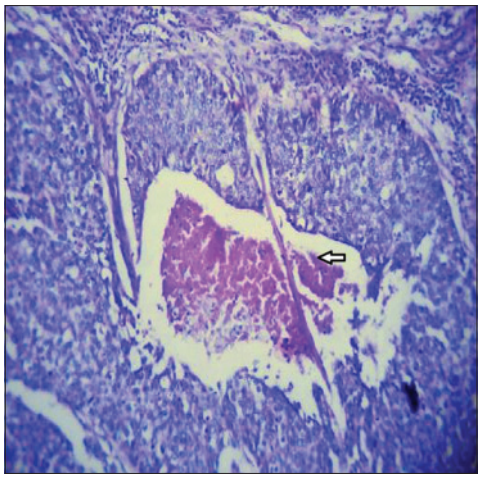

Figure 1: Tumor cells arranged in ductular pattern with central comedo necrosis (arrow) - Invasive ductal carcinoma (H and E, ×40)

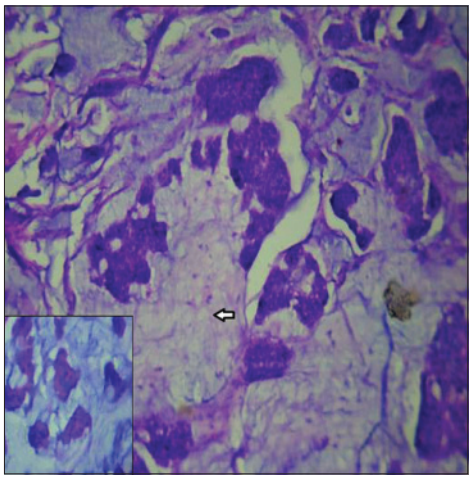

Figure 2: Tumor cells floating in a mucinous pool (arrow). Inset shows the tumor cells (H and E, ×10)

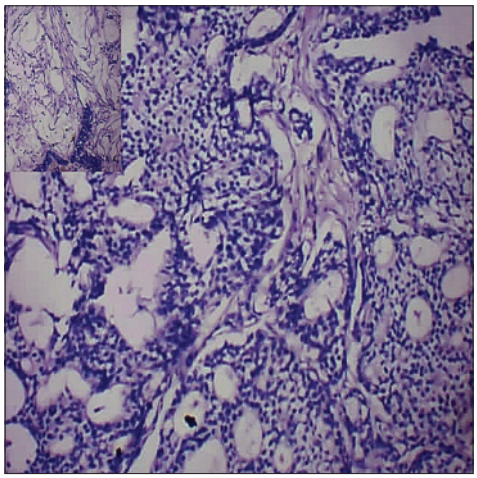

Figure 3: Solid papillary carcinoma showing a cribriform pattern. Inset show focal mucinous areas (H and E, ×10)

Oncoprotein overexpression was common among the tumors of more than 2 cm size, Grade III tumors and in

nodal positive patients. Hormone receptor and oncoprotein expression showed inverse relationship. Compared to the studies from the western world, ER/PR positive tumors were found to be low, while Her2 neu overexpression was higher in our study group.

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Original Article

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Role of Ultrasound in the Assessment of Dengue Fever

K S Vedaraju[1], K R Vijay Kumar[1], T V Vijayaraghavachari[2]

[1]Associate Professor, Department of Radio-Diagnosis, Bangalore Medical College and Research Institute, Bengaluru, Karnataka, India, [2]Post-graduate Student, Department of Radio-Diagnosis, Bangalore Medical College and Research Institute, Bengaluru, Karnataka, India

Abstract

Background: Dengue fever (DF) is caused by a single-stranded RNA virus of Flaviviridae transmitted by mosquitoes. The incidence of DF has increased 30-fold in the last four decades, and more than half the world's population are now threatened with infection from dengue virus.

Objective: The purpose of our study was to describe sonographic findings and the role of ultrasonography (USG) in the assessment of patients with DF, and its complications and to find out whether ultrasound is an adjunct to clinical and lab profile in the diagnosis of DF.

Materials and Methods: 102 patients who were serologically diagnosed as having DF between July and September 2015 were referred for ultrasound scanning of the abdomen and thorax, and the findings were analyzed. The various ultrasound features were expressed as percentages. Association of various sonological findings with different age groups or platelet count was assessed through Chi-square test of statistical significance. $P \leq 0.05$ was considered for statistical significance.

Results: Out of the 102 patients, 85 had gall bladder (GB) wall thickening (83.3%), 55 had ascites (53.9%), 28 had bilateral pleural effusion (27.4%), 21 had only right pleural effusion (20.6%), 12 had only left pleural effusion (11.7%), 34 had hepatomegaly (33.3%), 30 had splenomegaly (29.4%), 2 had pericardial effusion (1.9%), and 3 had no abnormal ultrasound findings (2.9%). The sonographic abnormalities, including GB wall thickening, ascites, pleural effusion, hepatomegaly, and splenomegaly, were significantly higher in patients with significantly decreased platelet count ($P < 0.05$).

Conclusion: USG is an important accessory tool for the early diagnosis of plasma leakage signs and for prediction of the disease severity, identifying mild and severe cases of dengue hemorrhagic fever, besides contributing in the differential diagnosis with other causes of febrile disease.

Key words: Complications, Dengue, Ultrasonography

INTRODUCTION

Dengue fever (DF) is caused by a single-stranded RNA virus of flaviviridae transmitted by mosquitoes.[1] DF is widely distributed in many countries in Southeast Asia, Central and South America, and the Western Pacific regions.[2] The incidence of DF has increased 30-fold in the last four decades, and more than half the world's population are now threatened with infection from dengue virus (DEN).[3]

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The purpose of our study was to describe sonographic findings and the role of ultrasonography (USG) in the assessment of patients with DF, and its complications and to find out whether ultrasound is an adjunct to clinical and lab profile in the diagnosis of DF.

MATERIALS AND METHODS

All ultrasound examinations were performed with Siemens Antares and Philips IU 22 machines, using 3.5-5 MHz probes. Abdominal scanning is done after 6 h of fasting to allow better distension of gall bladder (GB). GB wall thickening is measured by placing the calipers between the two layers of the anterior wall. Thoracic scanning is done in either sitting or supine posture. Both the pleural spaces are evaluated through an intercostal approach. Pericardial space is also evaluated for

Corresponding Author: Dr. T V Vijayaraghavachari, No 42/1, I Floor, K. No 4th Street, Narayana Pillai Street Cross, Shivaji Nagar, Bengaluru - 560 072, Karnataka, India. Phone: +91-8861125627. E-mail: chari.vijay89@gmail.com

effusion subcostally. In all the patients, serological tests for dengue will be performed. The serological investigations for dengue including non-structural protein-1 Ag test and dengue immunoglobulin M/immunoglobulin G test were performed to confirm the diagnosis.

102 patients (54 males and 48 females) who were serologically diagnosed as having DF between July and September 2015 were referred for ultrasound scanning of the abdomen and thorax, and the findings were analyzed.

RESULTS (TABLES 1-3)

Out of the 102 patients, 85 had GB wall thickening (83.3%) (Figures 1 and 2), 55 had ascites (53.9%) (Figure 3), 28 had bilateral pleural effusion (27.4%), 21 had only right pleural effusion (20.6%) (Figure 4), 12 had only left pleural effusion (11.7%), 55 had ascites (53.9%) (Figure 5), 34 had hepatomegaly (33.3%), 30 had splenomegaly (29.4%), 2 had pericardial effusion (1.9%), and 3 had no abnormal ultrasound findings (2.9%).

In our study, DF was most commonly seen in the age group of 20-39 years (48.0%).

GB wall thickening was the most common finding noted in 85 patients (83.3%), followed by pleural effusion in 61 patients (59.8%), and ascites in 55 patients (53.9%). The least common sonological finding was pericardial effusion (1.9%).

In patients with pleural effusion, bilateral (27.4%) and right (20.6%) pleural effusion were more common than left sided pleural effusion (11.7%).

Ascites was more common in 0-19 years age group (90.3%), while GB wall thickening was more common in the 20-39 years age group (87.7 %) and >40 years age group (86.4%).

Table 1: Incidence of different sonographic findings in DF

USG findings	Number of patients	Percentage
Gall bladder wall thickening	85	83.3
Ascites	55	53.9
Pleural effusion		
Bilateral	28	27.4
Right	21	20.6
Left	12	11.7
Hepatomegaly	34	33.3
Splenomegaly	30	29.4
Pericardial effusion	2	1.9
Normal	3	2.9

Total number of cases=102. DF: Dengue fever, USG: Ultrasonography

Table 2: Incidence of USG findings in relation to different age groups

USG findings	0-19 years	20-39 years	>40 years
Total	31	49	22
Gall bladder wall thickening	23	43	19
Ascites	28	19	8
Pleural effusion	24	28	9
Hepatomegaly	6	23	5
Splenomegaly	6	16	8
Pericardial effusion	2	0	0
Normal	1	2	0

USG: Ultrasonography

Table 3: Correlation of USG findings with platelet count

USG findings	<40,000	40,000-80,000	80,000-150,000	>150,000
Total	54	33	12	1
Gall bladder wall thickening	53	29	3	0
Ascites	34	18	3	0
Pleural effusion	34	20	7	0
Hepatomegaly	18	10	6	0
Splenomegaly	20	5	5	0
Pericardial effusion	2	0	0	0
Normal	0	0	0	3

USG: Ultrasonography

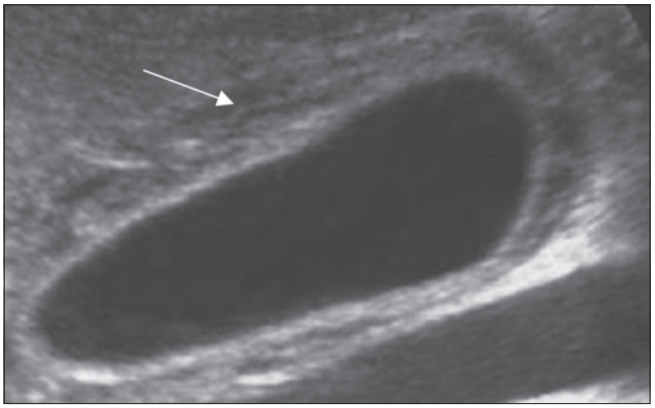

Figure 1: A 22 years male patient with dengue fever, ultrasound shows thickened and edematous gall bladder wall (arrow)

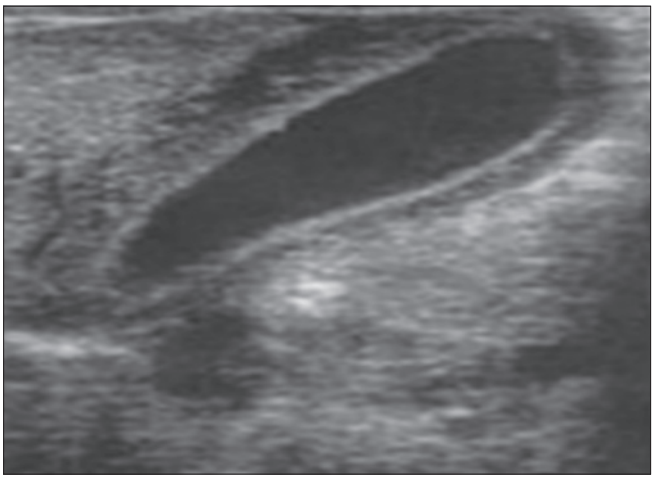

Figure 2: A 47 years female patient with dengue fever, ultrasound shows thickened and edematous gall bladder wall (arrow)

GB wall thickening was seen in most of the patients whose platelet count was <40,000 (98.1%). Ascites (62.9%) and pleural effusion (62.9%) were the other common findings seen in patients whose platelet count was <40,000.

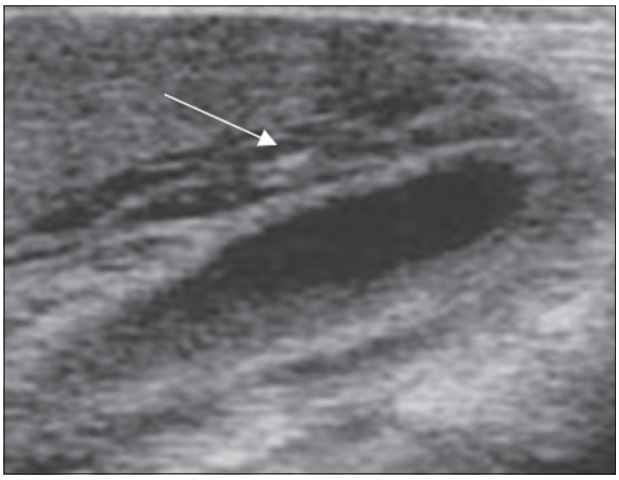

Figure 3: An 11-year-old male child, with dengue fever showing thickened and edematous gall bladder wall (arrow)

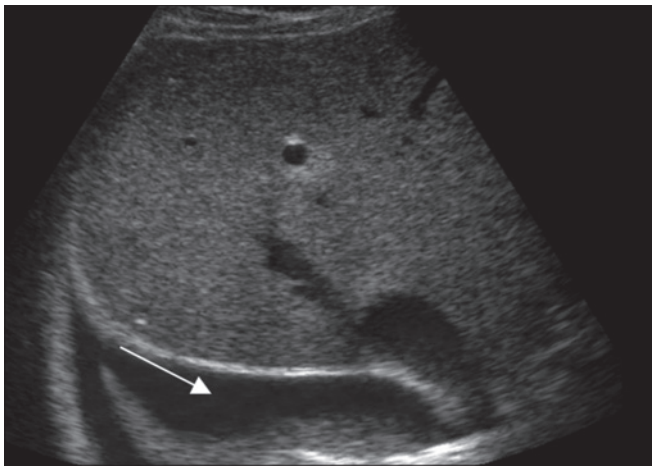

Figure 4: A 42-year-old male patient with dengue fever, ultrasound shows moderate right pleural effusion (arrow)

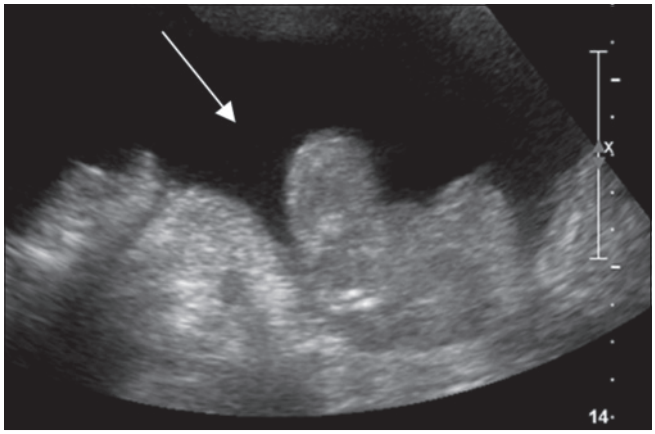

Figure 5: A 17-year-old female patient with dengue fever, ultrasound shows minimal to moderate free fluid (arrow) in the peritoneal cavity with surrounding bowel loops

In patients with platelet count of 40,000-80,000, GB thickening is most common finding (87.8%), followed by pleural effusion (60.6%).

In patients whose platelet count was 80,000-150,000, pleural effusion (58.3%) was more common than GB wall thickening (25%).

In three patients with platelet count more than 150,000, no sonological abnormality was detected.

DISCUSSION

Dengue is the most rapidly spreading mosquito-borne viral disease in the world. In the last 50 years, incidence has increased 30-fold with increasing expansion to new countries and in the present decade, from urban to the population.

An estimated 50 million dengue infections occur annually, and approximately 2.5 billion people live in dengue-endemic countries.[4]

DEN is a single-stranded RNA virus with four distinct serotypes (DEN-1 to -4). These serotypes of the DEN belong to the genus Flavivirus, family Flaviviridae. Among them, genotypes of DEN-2 and DEN-3 are frequently associated with severe disease accompanying secondary dengue infections.[5-7]

The various serotypes of the DEN are transmitted to humans through the infected *Aedes* mosquitoes, principally *Aedes aegypti*, widely distributed throughout tropical and sub-tropical countries. Dengue transmission also occurs through *Aedes* albopictus, *Aedes polynesiensis,* and several species of the *Aedes scutellaris* complex. Each species has a particular ecology and geographical distribution.[8]

After an incubation period of 4-10 days, the infection can produce a wide spectrum of illness, although most infections are asymptomatic or subclinical infections. Primary infection is thought to induce lifelong immunity to the infecting serotype.[9] Individuals suffering an infection are protected from illness with a different serotype within 2-3 months of the primary infection but with no long-term cross-protective immunity.

Clinically dengue manifests with sudden onset of high fever with chills, muscle and joint pain, intense headache, retro-orbital pain, and backache. Fever usually lasts for about 5 days, but rarely for more than 7 days.[10] Recovery is usually complete by 7-10 days. A small proportion of persons who have previously been infected by one dengue serotype develop bleeding on infection with another dengue serotype. This is termed dengue hemorrhagic fever (DHF).

DHF causes endothelial leakage which results in hemoconcentration and serous effusions and can lead to circulatory collapse. This can lead to dengue shock syndrome, which poses a greater fatality risk than bleeding alone.[11,12]

Leukopenia is observed near the end of the febrile phase of illness. Lymphocytosis, with atypical lymphocytes, usually develops before defervescence or shock. Patients with dengue have significantly lower total white blood cell and platelet counts than patients with other febrile illnesses in dengue-endemic populations.[13]

The ultrasound findings in DF include GB wall thickening, pericholecystic fluid, minimal ascites, pleural effusion, pericardial effusion, and hepatosplenomegaly.[14]

In a similar study conducted by Venkata Sai *et al.*, GB wall thickening was the most common finding (100%), followed by pleural effusion (93.1%) and ascites (53.2%).[14]

In a study conducted by Santhosh *et al.* (2014), out of 96 sero-positive dengue cases, 66.7% patients showed edematous GB wall thickening, 64.5% patients showed ascites and 50% patients had pleural effusion.[15]

In our study, GB wall thickening was the most common finding (83.3%), followed by pleural effusion (59.8%), and ascites (53.9%). Furthermore, GB wall thickening, ascites, and pleural effusion were more common in patients with platelet count less 80,000. Thus, severity of the disease, which is usually assessed by clinical features and platelet count, can also be assessed by sonography.

DF is typically a self-limiting illness with a mortality rate of <1%. With treatment, DHF has a mortality rate of 2-5%. Dengue hemorrhagic fever has a mortality rate as high as 50% without treatment. Survivors usually recover without sequelae and develop immunity to the infecting serotype.

CONCLUSION

USG is a relevant and important ancillary tool for the early diagnosis of plasma leakage signs and for prediction of the disease severity, identifying mild and severe cases of DHF, and contributing in the differential diagnosis with other causes of febrile disease.

Furthermore, diagnosis can be made early in the course of disease compared with other modes of diagnosis. During an epidemic of dengue, ultrasound findings of GB wall thickening with or without polyserositis in a febrile patient should suggest the possibility of DF/DHF.

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Original Article

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Detection of Extrapulmonary Tuberculosis from Various Samples in Sputum Smear Negative Patients

K Rama Lakshmi[1], V Surya Kumari[2], N Vasundhara[3], K Suresh[4]

[1]Assistant Professor, Department of Microbiology, Culture & Drug Susceptibility Testing Laboratory, RNTCP, Andhra Medical College, Visakhapatnam, Andhra Pradesh, India, [2]Assistant Professor, Department of Pulmonology, Andhra Medical College, Visakhapatnam, Andhra Pradesh, India, [3]District Tuberculosis Control Officer, Visakhapatnam, Andhra Pradesh, India, [4]Senior Lab Technician, Culture & Drug Susceptibility Testing Laboratory, RNTCP, Andhra Medical College, Visakhapatnam, Andhra Pradesh, India

Abstract

Background: Extra pulmonary tuberculosis (EPTB) can occur in isolation or along with PTB in immune-competent patients. EPTB accounts for 15-20% of all cases of TB. EPTB remains a challenging diagnosis for both clinicians and microbiologists. This study is conducted to detect EPTB from various samples in sputum smear negative patients.

Materials and Methods: 100 samples from clinically suspected patients of EPTB received at culture and drug susceptibility testing lab under RNTCP, Andhra Medical College, Visakhapatnam were included in the study. All samples were processed for Ziehl-Neelsen (ZN) stain and culture for *Mycobacterium* TB was done on Lowenstein-Jensen (LJ) medium as per the guidelines of National TB Research Institute, Chennai. The positive cultures were processed for line probe assay-polymerase chain reaction (LPA-PCR) with MTBDR kit as per the guidelines.

Results: Out of the 100 extra-pulmonary samples, processed 9% were positive by ZN staining and 12% were positive by LJ culture. Those samples positive by ZN smear and LJ culture were all positive by LPA (100%). Out of 12 LPA performed samples, 9 (75%) were both rifampcin and isoniazid (INH) sensitive, 1 (8.3%) was rifampcin and INH resistant, 1 (8.3%) was rifampcin resistant and INH sensitive, and another sample was rifampcin sensitive and INH resistant. Out of 12 LPA tests performed two samples (16.7%) were rifampcin resistant indicating multidrug-resistant TB.

Conclusion: EPTB is not given priority earlier in TB control programs in developing countries as the proportion is low and less infectious than PTB. As the incidence of MDRTB is increasing in PTB, an attempt has been made in this study to detect resistance pattern of isolated cultures by LPA and found that it was 16.7% in EPTB.

Key words: Cultures, Extra pulmonary tuberculosis, Program, Sensitive

INTRODUCTION

Tuberculosis (TB) can involve any organ system in the body. While pulmonary TB (PTB) is the most common presentation, extra PTB (EPTB) is also an important clinical problem.[1,2] The term EPTB describes isolated occurrence of TB at body sites other than the lung. However, when an extra pulmonary focus is evident in a patient with PTB, such patients have been categorized under PTB as per the guidelines of WHO.[3]

EPTB constitutes about 15-20% of all cases of TB.[4,5] In HIV-positive patients, EPTB accounts for more than 50% of all cases of TB.[6,7]

In India and other developing countries, lymph node (LN) TB constitutes to be the most common form of EPTB followed by pleural effusion, bone and joint TB, genitourinary TB, TB meningitis, and others.[8-10]

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Corresponding Author: Dr. K Rama Lakshmi, Department of Microbiology, Andhra Medical College, Visakhapatnam, Andhra Pradesh, India. Phone: +91-9440677787. E-mail: ramakoripella@yahoo.com

An accurate diagnosis of TB is desirable before the start of anti-TB treatment. The sensitivity and specificity are low for Ziehl-Neelsen (ZN) stain in EPTB. The turnaround time (4-8 weeks) is long for the gold standard culture in Lowenstein-Jensen (LJ) medium though sensitive and should be followed by identification tests.[11] Though there are limitations an attempt has been made to detect the EPTB in this study by these two methods and culture positive samples were processed for line probe assay to detect *Mycobacterium tuberculosis* (MTB) and the sensitivity pattern of rifampicin and isoniazid (INH).

MATERIALS AND METHODS

The present study was conducted in the culture and drug susceptibility testing (C and DST) Lab under RNTCP, Andhra Medical College, Visakhapatnam during the period of 2012-2013. 100 samples from clinically suspected EPTB patients received at C and DST lab were included in the study.

All cases already on anti-TB treatment or had been confirmed as having PTB were excluded from the study. The sputum smear negative by ZN stain cases which were clinically diagnosed as EPTB were included in the study.

The processing of samples for ZN staining was done as per the guidelines of RNTCP,[12] and the processing for culture was done as per the guidelines of National TB Research Institute (NIRT), Chennai.[13] The processing for line probe assay (LPA) from positive growths was done with MTBDR kit (Hain life sciences).

All the samples were collected under strict aseptic conditions. Sample transportation, processing, and inoculation were done as per the Guidelines of NIRT Chennai. The samples were processed for LPA as per the kit literature.

Inoculated LJ medium slopes were incubated at 37°C.

Culture reading was done:

1. All the cultures were read every week for up to 8 weeks using the same methodology used for pulmonary samples as per the NIRT guidelines.
2. Typical MTB growths on LJ medium were subjected for biochemical tests and LPA.

Biochemical Tests

The mycobacterial isolates obtained in culture were subjected to biochemical testing for species characterization by carrying out nitrate reduction tests and absence of growth on LJ medium with paranitrobenzoic acid.

Quality control was carried out using the MTB H37RV strain as a positive control and a reagent control without organism as a negative control.

LPA-polymerase chain reaction (PCR) was performed as per the kit literature (MTBDR kit Hain life sciences).

RESULTS

In our study, the majority of the patients (48%) were between the age group of 21 and 40 years, followed by 11-20 years (17%) and 41-50 years (15%) (Table 1), with a male:female ratio of 1.8:1 (64:36) (Table 2). Most of the samples received were of LNs (30) followed by pleural fluid (28), cerebrospinal fluid (18), bone and synovial fluid (10), ascetic fluid (6), pericardial fluid (4), and endometrial tissue (1) (Table 3). Out of the 100 samples, 9 (9%) were positive for acid-fast bacilli (AFB) by ZN staining and 12 out of 100 samples (12%) were culture positive on LJ medium. All the 12 culture-positive samples were positive for MTB by LPA. Out of 12 LPA results, 9 (75%) were both rifampicin and INH sensitive, 1 (8.3%) sample was both rifampicin and INH resistant, 1 (8.3%) was

Table 1: Age wise distribution (*n*=100)

Age (years)	Number
1-10	2
11-20	17
21-30	26
31-40	22
41-50	15
51-60	6
>61	12
Total	100

Table 2: Gender wise distribution (*n*=100)

Gender wise distribution
Males=64
Females=36

Total=100

Table 3: Sample wise distribution

Nature of clinical samples	Number of samples	Number of TB detected positive and percentage
LN	30	7 (23.3)
Pleural fluid and pus	28	3 (10.7)
CSF	18	0 (0)
Bone and synovial fluid	10	1 (1)
Ascitic fluid	6	1 (16.6)
Urine	4	0 (0)
Pericardial fluid	3	0 (0)
Endometrial tissue	1	0 (0)
Total	100	12

LN: Lymph node, CSF: Cerebrospinal fluid, TB: Tuberculosis

Table 4: Distribution of LPA results

Biochemical Tests	*n*=12	Percentage
Rifampicin and INH sensitive	9	75
Rifampicin resistant and INH sensitive	1	8.3
Rifampicin sensitive and INH resistant	1	8.3
Rifampicin and INH resistant	1	8.3

INH: Isoniazid, LPA: Line probe assay

rifampicin resistant and INH sensitive, and 1 (8.3%) was rifampicin sensitive and INH resistant (Table 4). Out of the 12 samples, 2 samples (16.7%) were rifampicin resistant indicating MDR-TB. Out of 30 LN samples, 7 (23.3%) were MTB positive; out of 28 pleural fluid samples, 3 (10.7%) were positive; out of 10 bone and synovial fluid samples, 1 (10%) was positive; and out of 6 ascitic fluid samples, 1 (16.6%) was positive. Samples from other sites were negative for MTB (Table 4).

DISCUSSION

TB remains a major global public health problem. It is estimated that about one-third of the world's population is infected with MTB.[14] Extra pulmonary forms have been increasingly reported, accounting for 20-50% of all cases of TB in recent studies.[15-17] ETB remains a challenging diagnosis for both clinicians and microbiologists.[18] Signs and symptoms are most often non-specific, and obtaining material for culture often requires an invasive procedure that cannot be easily repeated.

The early diagnosis of EPTB is challenging because of the paucibacillary nature of these infections, resulting in a very rarely positive smear microscopy finding and a long incubation time required for growth. Hence, procedures such as nucleic acid amplification tests (NAATS) with enhanced sensitivity is required and to be available for diagnosis of EPTB.

In the present study, most of the clinically suspected patients were between the age groups of 21 and 40 years, with male:female ratio of 1.8:1 which correlates with the study of Siddiqui *et al.*,[11] who reported 2.03:1 and Chakravorty *et al.*[19]

In the present study, 9% of the samples were positive for AFB by ZN staining, whereas Siddiqui *et al.*,[11] reported 5% positivity.

MTB growth on LJ medium was positive in 12% of samples which correlates with Siddiqui *et al.*,[11] who reported 15% positivity. Of 9 cases which were positive by microscopy, all 9 (100%) showed growth on LJ medium. In addition, the LJ medium could detect 3 out of 91 (3.3%) cases which were negative by microscopic examination in our study, which correlates with Siddiqui *et al.*[11]

Out of the 9 samples that showed presence of AFB on microscopy all 9 (100%) were positive by LPA (PCR) and out of 12 cases which showed growth on LJ media all 12 (100%) were positive by LPA (PCR) in our study which correlates with Siddiqui *et al.*[11]

In the present study, LNs were the most common site of EPTB, 7 (23.3%) out of 30 cases were positive followed by pleural fluid 3 (10.7%) out of 28 cases and 1 (10%) case out of 10 cases from bone and synovial fluid and 1 (16.6%) case out of 6 cases from ascetic fluid which correlates with Sreeramareddy *et al.*,[20] who reported 16.4% positivity for LN samples, Sharma and Mohan[21] reported 35% for LNs, pleural fluid 20%, bone and joint 10%, and Siddiqui *et al.*[11] reported 17.4% for ascitic fluid.

Out of 12 LPA positive samples 9 (75%) were both rifampicin and INH sensitive 1 (8.3%) sample was both rifampicin and INH resistant, 1 (8.3%) was rifampicin resistant, and INH sensitive, 1 (8.3%) was rifampicin sensitive and INH resistant.

CONCLUSION

EPTB is not given priority earlier in TB control programs in developing countries as the proportion is low and less infectious than PTB.

As the incidence of MDRTB is increasing in PTB, an attempt has been made in this study to detect resistance pattern of isolated cultures by LPA and found that it was 16.7% in extra PTB.

As early diagnosis of EPTB is challenging because of the paucibacillary nature of the infections, procedures such as NAATS with enhanced sensitivity is required and to be available for diagnosis of EPTB.

As the incidence of EPTB is increasing because of HIV and in view of multidrug-resistance, the EPTB in RNTCP programme is enhanced for early diagnosis and treatment to decrease morbidity and mortality.

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Original Article

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Validity of 6-min Walk Test in Assessment of Severity among Patients with Chronic Obstructive Pulmonary Disease

Lokendra Dave[1], Vivek Rajoriya[2], T N Dube[3], B S Yadav[4], Nishant Shrivastava[5], V K Sharma[6]

[1]Professor and Head, Department of Tuberculosis Chest, Gandhi Medical College, Bhopal, Madhya Pradesh, India, [2]Post-graduate Student, Department of Medicine, Gandhi Medical College, Bhopal, Madhya Pradesh, India, [3]Professor and Head, Department of Medicine, Gandhi Medical College, Bhopal, Madhya Pradesh, India, [4]Professor, Department of Cardiology, Gandhi Medical College, Bhopal, Madhya Pradesh, India, [5]Assistant Professor, Department of TB Chest, Gandhi Medical College, Bhopal, Madhya Pradesh, India, [6]Ex-Professor and Head, Department of Medicine, Gandhi Medical College, Bhopal, Madhya Pradesh, India

Abstract

Background: The 6-min walk test (6-MWT) is commonly used for evaluation of patients with cardiac or pulmonary diseases and prognostic relevance. Accordingly, the 6-MWT has been used as a primary endpoint in most randomized controlled trials of newly developed therapies in pulmonary arterial hypertension, which is the most common and progressive extrapulmonary manifestation observed among patients with chronic obstructive pulmonary disease (COPD).

Materials and Methods: Total 100 male patients who attended the chest medicine out-patient department, with the symptoms suggestive of COPD were included in this study, and the study was done to evaluate the 6-min walking distance (6-MWD) and correlated with echocardiographic findings suggestive of pulmonary hypertension as a predictor of severe COPD in these patients.

Result: All the COPD cases enrolled in the study were males, with mean age 59.5 ± 2.5 years. These patients were grouped under mild (21%), moderate (23%), and severe (56%) groups according to GOLD criteria's. The study results showed that as the COPD severity increases, the incidence of pulmonary hypertension also increases as identified by echocardiographic right ventricular systolic pressure (RVSP) and when correlated with 6-MWD, it substantially decreases as pulmonary pressures increases. The average RVSP was 59.6 ± 4.4 mmHg in severe COPD patients with mean 6-MWD 134.8 ± 4.8 m, whereas it was 47.2 ± 6.8 in moderately severe COPD with 6-MWD of 196.6 ± 5.7 m while it was 39.3 ± 5.1 in mild groups with 6-MWD of 316.4 ± 6.9 m. These values were found to be significant when they were compared to each other in different groups ($P < 0.001$).

Conclusion: 6-MWD may offer a reliable alternative method to assess the severity of COPD as it is well-correlated with the severity of pulmonary hypertension in COPD patients and may help in the follow-up of these patients.

Key words: Chronic obstructive pulmonary disease, Validity, Walk

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a major cause of morbidity and mortality throughout the world. The prevalence and burden of COPD are expected to increase in the future, due to continued exposure to the risk factors and changing age structure of the world's population.[1,2] The severity of COPD is usually assessed on the basis of a single parameter - forced expiratory volume in 1 s (FEV1). However, the patients with COPD have systemic manifestations that are not reflected by this. Hence, a multidimensional grading system, which may assess the respiratory and systemic expressions of COPD, has to be designed to predict outcome in these patients.[3] BODE index has been proposed to serve this purpose in patients with COPD.[4] The four factors that can predict the severity are the body-mass index (B), the degree of airflow obstruction (O) and dyspnea (D), and exercise capacity (E), measured by the 6-min walk test (6-MWT). These variables are used to construct the BODE index,

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Corresponding Author: Dr. Lokendra Dave, Department of Tuberculosis Chest, Gandhi Medical College, Bhopal - 462 001, Madhya Pradesh, India. Phone: +91-9893155531. E-mail: drlokendradave@yahoo.com

a multidimensional 10-point scale in which higher scores indicate a worse prognosis. Accordingly, 6-MWT is one of the components for assessment of COPD patients.

COPD is associated with significant extrapulmonary (systemic) effects, among which cardiac manifestations are most common. If FEV1 <50% of predicted, cardiovascular disease accounts for approximately 50% of all hospitalization and nearly one-third of all deaths. One of these manifestations is pulmonary arterial hypertension (PAH), which adversely affects survival and exercise capacity and is associated with an increased risk of severe acute exacerbations.

The 6-MWT is commonly used for the evaluation of patients with cardiac or pulmonary diseases, as a form of submaximal exercise testing that is simple, reproducible, safe, inexpensive, applicable to everyday activities, sensitive to therapeutic interventions, and also of prognostic relevance.[5,6]

Accordingly, the 6-MWT has been used as a primary endpoint in most randomized controlled trials of newly developed therapies in PAH.[7,8]

The present study was done to evaluate patients of COPD with 6-MWT, and its correlation with pulmonary hypertension: Echocardiographic findings.

MATERIALS AND METHODS

After clearance and permission of the Institutional Ethical Committee, total 100 COPD patients who attended our outpatient clinic as well as indoor (from January 2013 to June 2015), at Chest Medicine Department, Gandhi Medical College, Bhopal were enrolled. The present analysis was restricted to male patients only, to improve the accuracy, as sex may be a confounding factor in many of the parameters assessed. During selection, patients with chronic lung disease other than COPD, hypertension, any known primary cardiac disease, any systemic disease that can cause pulmonary hypertension, and patients who were unable to perform spirometry, all were excluded from the study. Informed consent was obtained from all patients.

For each enrolled subject, a detailed history of dyspnea was taken, and patients were subjected to routine investigations, including complete blood count, lipid profile, blood sugar, blood urea, serum creatinine, Electrocardiogram, arterial blood gas, and chest X-ray. On the day of enrollment, height and weight were measured twice during the examination. Body mass index (BMI) was calculated by the formula - BMI = weight in kg/(height in ms).[2] Spirometry was performed with spirometer equipment - RMS Helios 401 that met the American Thoracic Society performance criteria, in each of the cases on enrollment into the study and then, 20 min following the administration of 2.5 mg salbutamol nebulization. The procedure was repeated on 3 occasions every time, and the best value was taken. FEV1 (% predicted) was also noted.

Transthoracic echocardiographic assessment of pulmonary pressures was done for all the patients, on ultrasound systems (Phillips Healthcare HD7-XE Classic model) and reported according to the guidelines of the American Society of Echocardiography. The comprehensive examination included standard two-dimensional echocardiography for anatomic imaging and Doppler echocardiography for assessment of velocities. Doppler measurements were carried out over 3 heart cycles during passive expiration. Non-invasive assessment of systolic pulmonary artery pressures (sPAP) was achieved by measurement of right ventricular systolic pressure (RVSP). PAH was defined in this study as sPAP ≥25 mmHg, according to the definition of pulmonary hypertension.[9,10] PAH was classified into the mild, moderate, and severe category as sPAP 25-50, 50-70, and >70 mmHg, respectively.

6-MWT was performed twice with a rest of 30 min, and the average distance was taken according to ATS guidelines.[11] Patients were asked to walk on a level ground for maximum possible distance within the duration of 6 min. This 6-min walking distance (6-MWD) was measured and compared with RVSP/sPAP value, and any correlation, if statistically significant, was noted.

Observation

Total 100 COPD patients as cases were enrolled in the study. All the cases were males, with mean age 59.5 ± 2.5 years. These patients were grouped under mild, moderate, and severe groups according to FEV1 % of predicted and as per GOLD criteria's. There were (21%) patients, who had mild COPD, Moderate were (23%) while 56% patients had severe COPD.

The study results showed that as the COPD severity increases, the incidence of pulmonary hypertension also increases, as identified by echocardiography RVSP findings and when it was compared to 6-MWD, in same groups, the walking distance substantially decreases with increase in pulmonary pressures. The average RVSP was 59.6 ± 4.4 in severe copd patients with mean 6-MWD 134.8 ± 4.8 m, and 47.2 ± 6.8 in moderate COPD with 6-MWD of 196.6 ± 5.7 m, while it was 39.3 ± 5.1 in mild groups with 6-MWD of 316.4 ± 6.9 m. These values were found to be significantly different, when they were compared to each other, in all different three groups ($P < 0.001$) (Figure 1).

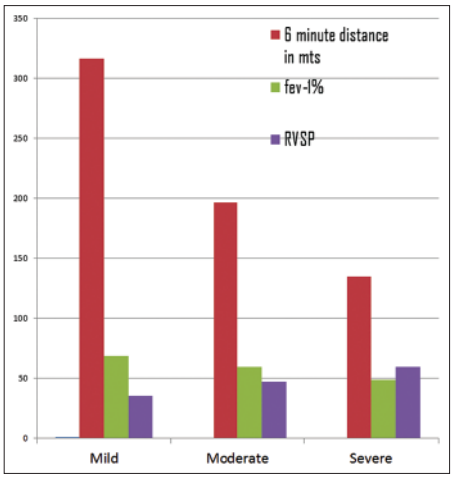

Figure 1: Mean 6 min walking distance, forced expiratory volume in 1 s % of predicted, and right ventricular systolic pressure: Comparison among groups

DISCUSSION

The natural history of COPD, being one of a progressive downhill course, PAH has generally been viewed as a late stage development occurring in patients with severe airways obstruction and a chronic hypoxemic state. The actual incidence of pulmonary hypertension in COPD is not known because it has not been screened systematically using reliable diagnostic tools (right-heart catheterization) in the wide clinical spectrum of COPD. However, indirect data suggests that the incidence of pulmonary hypertension in COPD is high.

Direct measurements of pulmonary artery pressure (P_{pa}) obtained at right-heart catheterization have been conducted only in small series of patients. In 1972, Burrows *et al.*[12] reported the hemodynamic findings in a group of 50 patients with severe COPD (FEV1/forced vital capacity [VC], 37%). The average value of mean P_{pa} was 3.46 kPa (26 mmHg), with 20% of these patients showing P_{pa} above this average value. In a series of 175 patients with severe COPD (FEV1/VC, 40%) and mild hypoxemia (arterial oxygen tension (P_{aO2}) 8.38 kPa (63 mmHg)), reported by Weitzenblum *et al.*,[13] the number of patients with pulmonary hypertension (mean P_{pa}>2.66 kPa (20 mmHg)) was 62 (35% of the group). The same group of investigators reported again, a similar incidence of pulmonary hypertension in a subsequent study carried out in 93 patients, 32 of them (34%) had a mean P_{pa} (20 mmHg).[14]

Recently, increased understanding of the pulmonary vascular pathology in PAH associated with COPD as well as the recognition that it is an important determinant of exercise limitation, dyspnea, and survival have led to renewed interest in the pathogenesis and therapeutics of this facet of COPD. Furthermore, identification of a subset of patients of COPD who have an unusually severe form of PAH as well as the observation that pulmonary vascular changes may occur in smokers even without hypoxemia has provided additional impetus into research in PAH associated with COPD. Recently, 6-MWT has been used to evaluate and stratify performance and prognosis in pulmonary hypertension patients.[9] Mathai *et al.*,[15] retrospectively analyzed data from pulmonary hypertension: Response to tadalafil trial, in which PAH subjects were randomized to tadalafil, a phosphodiesterase type-5 inhibitor, or placebo. And found that an improvement in 6-MWT of approximately 33 m is associated with improvement in quality-of-life and hence advocated 6-MWT for assessment. More recent data do strongly suggest that the baseline 6-MWD is predictive of outcome in PAH.[16,17]

In our study, while comparing 6-MWD and pulmonary hypertension values indirectly measured on transthoracic echocardiography (RVSP) in COPD patients, it was found that as the severity of pulmonary hypertension increases, the distance covered in 6 min decreases. This walking test proved highly acceptable to the patients, and stable, as well as reproducible results, was achieved after the two walks.

Data from the registry to evaluate early and long-term PAH disease management (REVEAL) and the French registry also demonstrate that the baseline 6-MWD is predictive of outcome in PAH.[7] In the REVEAL registry, a baseline 6MW ≥440 m was associated with longer survival, whereas a 6MW of <165 m was associated with increased mortality at 1 year. In addition, multivariable analysis indicated that a greater 6 MW, among other factors, was significantly associated with improved survival and was a strong predictor of death in PAH. Same results were also cited in study by Guyatt *et al.*,[18] where, they investigated the potential value of the 6-min walk as an objective measure of exercise capacity in patients with chronic heart failure, the test was administered six times over 12 weeks among 18 patients with chronic heart failure and 25 with chronic lung disease. The authors concluded that the 6 min walk is a useful measure of functional exercise capacity and a suitable measure of outcome for clinical trials in patients with chronic heart failure.

Similarly, a study done by Miyamoto *et al.*,[19] where the 6-MWT was performed by 43 patients with PPH, together with echocardiography, right-heart catheterization, and measurement of plasma epinephrine and norepinephrine. Distance walked in 6 min was significantly shorter in patients with PPH than in age- and sex-matched healthy subjects (297 ± 188 versus 655 ± 91 m, $P < 0.001$).

During a mean follow-up period of 21 ± 16 months, 12 patients died of cardiopulmonary causes. Among non-invasive parameters including clinical, echocardiographic, and neurohumoral parameters, only the distance walked in 6 min was independently related to mortality in PPH by multivariate analysis. These results suggest that the 6-MWT, a submaximal exercise test, reflects exercise capacity determined by maximal cardiopulmonary exercise testing in patients with PPH, and the distance walked in 6 min also has a strong, independent association with mortality.

In our study too, it has been observed that 6-MWD can also be used to predict the severity of COPD, in terms of an indirect indicator of pulmonary hypertension. Hence, presumably, these patients can also be followed-up after using medications and oxygen therapy, whether it could be improved or not. This 6-MWT can be used to predict severity in COPD patient, in remote areas where health resources are scarce.

Limitations of the Study

1. A relatively small number of patients were studied, and this is a hospital based study and may not be representative of the general COPD patient's population. Furthermore, only male patients were included in this study, since COPD is more common among male patients. This was aimed so as to make the study group as uniform as possible. By eliminating the gender-related differences, such selection would negate the differences in 6-MWD among various patients studied, as well as in FEV1 and the patient's perception of dyspnea. Hence, perhaps the results of this study cannot be projected for female patients with COPD without further confirmation.
2. Accurate measurements of pulmonary hypertension are done by right-heart catheterization, and there may be some pitfalls in echocardiographic measurements, however, being a non-invasive method, it was preferred.
3. Patients who were not able to perform tests (pulmonary function test, 6-MWT) could not be evaluated.
4. As a cross-sectional and short study, the present study is limited in its ability to elucidate, whether improvement in 6-MWD after treatment, also reverses or improvise the other parameters analyzed?

CONCLUSION

6-MWD may offer a reliable alternative method to assess the severity of COPD, as it is well-correlated with the severity of pulmonary hypertension in COPD patients and may probably offer help in following up of therapeutic benefits.

Since the assessment of 6-MWD requires no special instrument, It could be of great practical value in a primary health care setup, to identify individuals who need further evaluation and referral at higher center for further workup.

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Original Article

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Clinico-pathological Study of Bladder Cancer in a Tertiary Care Center of South India and Impact of Age, Gender, and Tobacco in Causing Bladder Cancer: A Single Center Experience

Ramesh Chinnasamy[1], Sriram Krishnamoorthy[2], Leena Joseph[3], Natarajan Kumaresan[2], Venkat Ramanan[2]

[1]Post-graduate Student, Department of Urology, Sri Ramachandra Medical College & Research Institute, Chennai, Tamil Nadu, India, [2]Professor, Department of Urology, Sri Ramachandra Medical College & Research Institute, Chennai, Tamil Nadu, India, [3]Professor, Department of Pathology, Sri Ramachandra Medical College & Research Institute, Chennai, Tamil Nadu, India

Abstract

Introduction: Bladder cancer (BC) is one of the most common urological malignancies. It is the fourth most common cancer in men and eighth most common malignancy in women of the western world. As per the Indian cancer registry, BC constitutes the ninth most common malignancy and accounts for an overall 3.9% of all cancer cases.

Purpose: The purpose of this manuscript is to do a clinico-pathological study on the BCs and to assess the impact of smoking, age, gender, and adequacy of treatment on the final outcome of the disease.

Materials and Methods: This was a retrospective audit on patients with BCs. All patients with BCs, diagnosed and treated in our institution between 2011 and 2015 were included in our study.

Results: A total of 156 patients were diagnosed and treated over a period of 4½-year from January 2011 to June 2015. Painless total hematuria was the most common presentation seen in 111 patients. BC has been predominantly a disease of elderly age group. High-grade cancers were found predominantly in patients above 60 years of age (n = 70), with a P = 0.04, while in patients <60 years of age, both high and low-grade cancers were of almost same incidence. The risk of tumor recurrence is considerably less in those who receive adjuvant Bacille Calmette-Guerin or mitomycin C therapy, and the difference between the two groups is statistically significant, with a P < 0.0001.

Conclusion: The overall incidence of BC in India is on the rise. Tobacco has been a very strong predisposing factor for BC occurrence. A high index of clinical suspicion, as well as a thorough exploration of all possible epidemiological factors, will help the clinicians and epidemiologists in formulating a definitive disease control program.

Key words: Bacille Calmette-Guerin therapy, Bladder cancer, Hematuria, Smoking, Tobacco, Urothelial malignancy

INTRODUCTION

Bladder cancer (BC) is one of the most common urological malignancies. It is the fourth most common cancer in men and eighth most common malignancy in women of the western world.[1] As per the Indian cancer registry, BC constitutes the ninth most common malignancy and accounts for an overall 3.9% of all cancer cases.[2] With increasing use of tobacco in various forms and with an ever increasing risk of exposure to occupational hazards, more and more of these BCs are being diagnosed nowadays. In spite of various stringent measures taken by various authorities with respect to manufacturing and legislative changes to workplace hygiene, many BCs still do rise through a risk of exposure to occupational carcinogens.[3]

Smoking has been recognized as a very strong independent risk factor for bladder tumor occurrence and recurrence.

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Corresponding Author: Dr. Sriram Krishnamoorthy, Department of Urology, Sri Ramachandra Medical College, Chennai - 600 116, Tamil Nadu, India. Phone: +91-9444174743, +91-8056139257. E-mail: sriramuro@gmail.com

Refraining from smoking for more than 15 years has been identified to reduce the risk of tumor recurrence as well.[4] In general, the risk increases as the frequency and duration of smoking levels increase and the risk typically decreases in former smokers than in current smokers.[5]

Gender has been found to affect the overall survival prognosis of patients with BC. Men have a three-fold greater risk of developing BC than women, but female gender is identified as an independent adverse prognostic factor in terms of both recurrence and progression of the disease. Women with BC are more often diagnosed with a higher tumor stage than men.[6]

Traditionally, BC is usually seen as a disease of advanced age. Nowadays, with an increased use of various diagnostic techniques and increased health awareness among the common public, many new cases of BCs are being diagnosed at a relatively younger age.[7]

Herein, we have analyzed the clinico-pathological characteristics of BC and explored the impact of various factors such as age, gender, and tobacco smoking on tumor characteristics and cellular biology.

MATERIALS AND METHODS

Patient Information

Data of patients with BC, diagnosed and treated in our hospital from January 2011 to June 2015 were traced from our Medical Records Department case files and studied. The available information regarding patients' age, gender, symptoms and mode of presentation, history of tobacco smoking, and use of smokeless tobacco in various forms such as paan masala, tobacco leaves with betel nuts, chewing rolled dried leaves of tobacco were all collected and analyzed.

Treatment Protocol

All patients diagnosed with BC underwent an initial cystoscopic evaluation to identify the type of lesion, its number, and the location. Our hospital being a tertiary referral center, most of the patients already have had an initial urine cytology and cystoscopic evaluation done elsewhere. Transurethral resection of bladder tumor was performed in all patients. Deep muscle biopsy was sent in a separate container, and the uropathologist was requested to specifically look for the presence of detrusor muscle in the specimen and document presence or absence of muscle invasiveness. Those patients, in whom deep muscle invasion could not be commented on, were subjected for re-resection after 3 weeks. Otherwise, re-resection for high-grade non-muscle invasive BCs (HGNMIBC) was not done as a routine. All patients with NMIBC were subjected for adjuvant therapy. 80 mg of intra vesical Bacille Calmette-Guerin (BCG) was our first choice. In those patients who could not tolerate BCG or in whom BCG administration was contraindicated, 40 mg of mitomycin C was administered.

Diagnostic Protocol

All pathological staging and grading were done using the International Society of Urological Pathology classification. Papillary lesions were reported as Ta, non-muscle invasive lesions as T1 and deep detrusor muscle invasive lesions as T2. Grade 1 and 2 were clubbed together as low grade, and Grade 3 lesions were categorized as high-grade lesions. In those specimens where muscle invasiveness could not be commented were subjected for re-resection.

Statistical Analysis

All collected information were analyzed using SPSS software, version 18. The categorical data (variables) such as age, gender, smoking history, smokeless tobacco usage were compared using Chi-square test and Fisher's exact test.

RESULTS

Demographic Incidence

A total of 156 patients were diagnosed and treated over a period of 4½-year from January 2011 to June 2015.

Of these patients, isolated painless total hematuria was the most common presenting symptom, seen in 111 patients. Loin pain associated with hematuria was seen in 18 and irritative urinary symptoms with hematuria in 17 patients. 10 patients had an incidentally detected bladder lesion. Table 1 summarizes the clinical and pathological characteristics of all the 156 patients in our study.

Transitional cell carcinoma (TCC) and its variants constituted the most common histological type, seen in 153 patients (98%). Figure 1 and Table 2 summarizes the spectrum of various histological types noted in our patients.

Impact of Age

BC has been predominantly a disease of elderly age group. The youngest reported patient in our study was 26 years old, who had presented with a solitary polypoidal growth and painless total hematuria, and the oldest reported was an 84-year-old male, with a mean age of 61.5 years and a median age of 60. Figure 2 describes the age distribution of BC in our study. Table 3 describes the age wise pathological distribution of all BCs. High-grade cancers were found predominantly in patients above 60 years of age ($n = 70$), while in patients <60 years of age, both high and low-grade

cancers were of almost same incidence. With regards to the stage of the tumor, T1 tumors accounted for 87% of all BCs.

Table 1: Summary of the clinical and pathological characteristics of all 156 patients in our study

Characteristics	Number (%)
Total number of patients	156
Stage	
T1G1, T1G2	57 (36.6)
T1G3	78 (50)
T2	5 (3.1)
Others**	16 (10.3)
Grade	
Low	57 (36.6)
High	99 (63.4)
Tumor size (cm)	
<3	115 (73.71)
>3	41 (26.28)
Type of growth	
Polypoidal	117 (75)
Sessile	39 (25)
Number of tumors	
Single	121 (77.6)
Multiple	35 (22.4)
Symptoms	
Hematuria alone	111 (71.2)
Irritative symptoms with hematuria	17 (10.9)
Loin pain with hematuria	18 (11.5)
Incidentally detected	10 (6.4)

**Others include squamoid, sarcomatoid, undifferentiated, and glandular variants of TCC, TCC: Transitional cell carcinoma

Table 2: Spectrum of various histological types of bladder cancers observed in our study

Pathology	Number (%)
T1G1, T1G2	57 (36.6)
T1G3	78 (50)
T2	5 (3.2)
Sarcomatoid	2 (1.3)
Squamoid	5 (3.2)
Plasmacytoid	1 (0.6)
Undifferentiated	3 (1.9)
Glandular variant	4 (2.6)
Angiomyxoma	1 (0.6)
Total	156 (100)

Table 3: Impact of age on tumor grade and stage

Characteristics	<60 years	>60 years	*P* value
Number of patients	55	101	
Smokers	41	70	0.58
Non-smokers	14	31	
Tumor grade (TCC)			
Low (*n*=57)	26	31	0.039 (without
High (*n*=99)	29	70	yates correction)
Tumor stage			
T1 (*n*=135)	46	89	0.08
T2, others (*n*=21)	3	18	

TCC: Transitional cell carcinoma

Impact of Gender

Table 4 describes the gender wise distribution of BCs. More than 80% of patients were males, with the male to

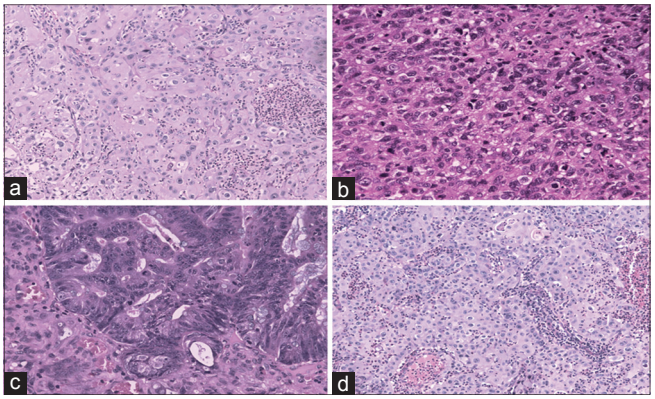

Figure 1: Spectrum of various histological types of TCC bladder. (a) urothelial carcinoma with squamoid differentiation (H and E ×100), (b) urothelial carcinoma with sarcomatoid differentiation (H and E ×100), (c) urothelial carcinoma with glandular differentiation (H and E ×100), (d) high-grade tumor with dense inflammatory response (H and E ×100)

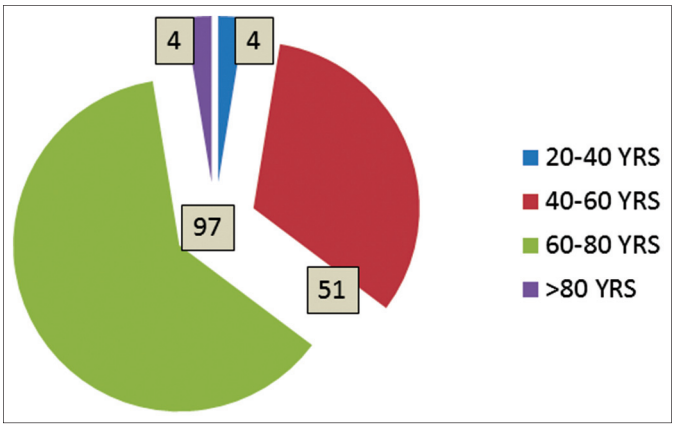

Figure 2: Age distribution of bladder cancer

Table 4: Impact of gender on tumor grade and stage

Characteristics	Male	Female	*P* value
Number of patients	127	29	
Smokers	109	2	<0.0001
Non-smokers	18	27	
Grade			
Low (*n*=57)	47	10	0.8346
High (*n*=99)	80	19	
Stage			
T1	121	14	0.1411
T2 and others	16	5	
Exposure to risk factors			
Tobacco smokers	109	2	
Non-smokers	18	27	
Paan chewers	90	26	
Agricultural pesticides	80	24	

female ratio being 4.4:1. Smoking was the predominant predisposing factor in a majority of males. Only two females gave a history of tobacco smoking. On the other hand, there was a greater incidence of smokeless tobacco usage among the female group, which could have been one of the causative factors for tumor occurrence. Exposure to fertilizers and pesticides were common in both the genders. In such patients, it is evident that either smokeless tobacco or exposure to pesticides and fertilizers may be a stronger predisposing factor, even in those who are never smokers, suggesting that such possible risk factors may be more readily detectable in those unexposed to potent risk factors such as tobacco smoke.

Impact of Treatment

Of the 156 patients, 135 were of NMIBC type. Adjuvant treatment was offered for 125 patients. 10 of them refused any further treatment. Table 5 describes the impact of treatment on the final outcome of the disease. From Table 5, it is well-evident that the risk of tumor recurrence is considerably less in those who receive adjuvant BCG or mitomycin C therapy, and the difference between the two groups is statistically significant, with a $P < 0.0001$. Of the 125 patients, 86 received intra vesical BCG therapy. From the Table 5, Figure 3 gives an overview of the details of treatment given.

Table 5: Impact of adequate treatment on final outcome in T1 patients (*n*=135)

???	Adjuvant treatment given (6 cycles) (*n*=99)	Adjuvant treatment not given/incomplete [*n*=36 (26+10)]	Two-tailed *P* value
Recurrence	1	12	<0.0001
No recurrence	98	21	
Total	99	36	

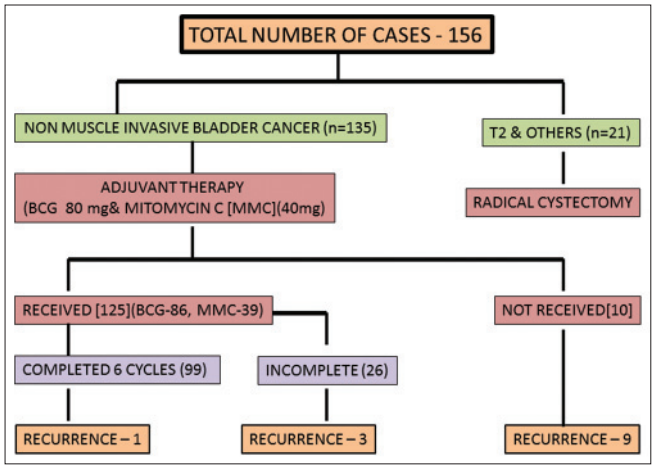

Figure 3: An overview of details of treatment given

DISCUSSION

Urothelial cancers account for 5.6% of all male and 1.8% of female cancers in India, with an actual crude rate incidence of about 1 in 174 men and 1 I 561 women.[8]

BC is one of the most common urothelial malignancies. The most common presentation is total painless hematuria, which is seen in more than 90% of all patients with BCs. However, almost all patients will have microscopic hematuria.[9] In our study, 83% of them had painless hematuria as the initial presenting symptom and 93% of them had hematuria at some point of time or the other before a diagnosis is made.

TCC is the most common histological variety, seen in 90% of patients with BC.[10] Various variants of TCC such as squamoid, sarcomatoid, and glandular differentiation are reported, which are very rarely seen. Most of the TCCs are NMIBC and are treated by transurethral resection. More than half of these patients experience recurrence with time.[11]

Furthermore, the epidemiology shows a strong association of BC with various environmental factors such as tobacco smoking, use of smokeless tobacco, exposure to aromatic amines, pesticides, and fertilizers.[12] Furthermore, it exhibits a field change potential, where the entire urothelium is exposed to the effects of such elements with carcinogenic potential.[13]

Cigarette smoking has been a major independent risk factor for BC. Smokers have four-fold increased incidence of developing BC compared to non-smokers.[14] The risk increases as the frequency and duration of smoking levels increase and typically decreases in former smokers compared to current smokers.[15] In our study, overall, 111 patients (71%) were smokers. This less number of overall incidences may probably be due to a majority of female patients being non-smokers. It is also possible that many of the smoking women may not have actually revealed the history of smoking when asked. However, when male patients alone were looked into, 86% of them were found to be chronic smokers.

Tobacco in other forms is also identified to be one of the major predisposing factors. In one of the largest studies conducted by University of Delhi, India, Dwivedhi *et al.*, observed that smokeless tobacco in various forms predisposes to the development of BC.[16] In their study, they observed that paan masala, gutka, khaini or surti, which are various forms of smokeless tobacco, contain procarcinogens such as tobacco, betel

nut, sugar coated fennel, saccharin, and heavy metals such as silver in unknown quantities, which leads to an increased occurrence of BC in this subset of population. Rafique observed that Pakistani women with strong exposure to such smokeless tobacco are more prone to develop BC.[17]

Such BCs usually are of NMIBC type. DeMarco *et al.* observed that at the time of initial diagnosis, 75-85% of all BCs are non-muscle invasive. However, 20-40% of them progress to invasive type within 5 years of primary treatment.[18] This stresses the fact that urothelial malignancies are an ongoing phenomenon, and one needs a more regular and systematic follow-up with appropriate adjuvant therapy.[19]

Optimal treatment of HGNMIBC has always been a challenging task. Such tumors have a variable and unpredictable biological behavior.[20,21] Such patients should be advised to undergo regular adjuvant intravesical BCG therapy and a close follow-up.

Shahin noted that approximately 30% of patients remain recurrence free after BCG therapy, an additional 30% recur after BCG therapy and another 30% progress to muscle invasive stage.[22] Based on such data, some authors have justified the role of radical cystectomy for patients with HGNMIBC.[23]

Limitations

Our study has a few limitations. First of all, it is a study of all patients operated in the last 4½ years, where the follow-up period in a majority of patients is <2 years. There is also a possibility of selection bias, as only patients with documentation of muscle in the specimen were included in our study. The lack of control comparison group also hampers the assessment of the actual efficacy of adjuvant therapy.

CONCLUSION

The overall incidence of BC in India is on the rise. HGNMIBC is a potentially lethal disease. In such cases, transurethral resection alone may not be sufficient, and patients must be subjected for adjuvant therapy and a long-term follow-up. There is a definite male preponderance, owing largely to a greater risk of exposure to risk factors. With advanced age, BCs tend to be of a higher grade with a more lethal outcome. Tobacco in any form has been a very strong predisposing factor for BC occurrence. A high index of clinical suspicion, as well as a thorough exploration of all possible epidemiological factors, will help the clinicians and epidemiologists in formulating a definitive disease control program. Awareness among the public should also be emphasized to make them realize the deleterious consequences of exposure to such risk factors and also to report themselves to the treating physician on the development of any signs and symptoms of BC.

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Original Article

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Autonomic Variation of Blood Pressure in Middle-Aged Diabetics: A Prospective Study

M Usharani[1], K Chandini[2]

[1]Professor and Head, Department of Physiology, Rajiv Gandhi Institute of Medical Sciences, Srikakulam, Andhra Pradesh, India, [2]Assistant Professor, Department of Physiology, Rangaraya Medical College, Kakinada, Andhra Pradesh, India

Abstract

Introduction: Cardiovascular disease is one of the leading causes of mortality and morbidity in patients having diabetes.

Materials and Methods: 100 middle-aged patients having diabetics attending diabetic outpatient department, King George Hospital, Visakhapatnam were considered for this study. On the basis of age, patients were divided into two groups Group 1 - 36-45 years and Group 2 - 46-55 years. Parameters such as resting blood pressure (BP), body temperature, BP response to standing (orthostatic test), BP response to sustained handgrip were measured.

Results: The mean ± standard deviation of all the parameters above are determined, and results were analyzed. Changes within the groups before and after the tests were analyzed by paired *t*-test. Inter group changes were analyzed by unpaired "*t*" test.

Conclusion: Sympathetic tests have shown significant abnormal responses in diabetics as compared to parasympathetic tests.

Key words: Autonomic, Diabetics, Middle-aged

INTRODUCTION

Diabetes mellitus (DM) refers to a group of common metabolic disorders that share the phenotype of hyperglycemia.[1] Non-insulin-dependent DM occurs mainly in middle-aged and elderly and is much more common than insulin-dependent DM.[2] DM is a global epidemic affecting at least 8.3% of the global population and 371 million people worldwide with a significant proportion (50%) remaining undiagnosed. The number of patients with diabetes in India is currently around 40.9 million and is expected to rise to 101 million by 2030. Cardiovascular disease (CVD) is the leading cause of mortality and morbidity in patients with diabetes, and subsequently, the primary goal of diabetes treatment is to reduce the burden of CVD as well as the vascular complications associated with diabetes.[3]

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Autonomic neuropathies affecting the cardiovascular system cause a resting tachycardia and orthostatic hypotension.[1]

Quantitative autonomic function tests consist of a series of simple non-invasive tests for detecting cardiovascular autonomic neuropathy (CAN).

Autonomic function tests are considered reliable, reproducible, simple, and quick to carry out, and all of them are non-invasive. The present study is undertaken to assess the severity of adverse effects of diabetes on autonomic functions of the cardiovascular system which helps in early detection of CAN in asymptomatic diabetic and there by promotes timely diagnostic and therapeutic intervention.

MATERIALS AND METHODS

Selection of Subjects

100 diabetic patients who belong to the middle-age group of 35-55 years attending the diabetic Outpatient Department in King George Hospital, Visakhapatnam were selected.

Corresponding Author: Dr. M Usharani, Department of Physiology, RIMS, Srikakulam, Andra Pradesh, India. E-mail: ushaprasad6@gmail.com

Inclusion Criteria

- Cases of already diagnosed Type II diabetes
- Cases who are in the age group of 35-55 years
- Cases who are attending the diabetic outpatient department in King George Hospital, Visakhapatnam.

Exclusion Criteria

- Patients suffering from cardiac, neuronal, and other endocrinal disorders
- Patients under medications other than oral hypoglycemic.

Methods to Collect the Data

The protocol was explained to the subjects and patients, who volunteered for the present study and informed consent was obtained from each of the participants. The subjects were asked to have light breakfast 2 h before the tests and were instructed not to have coffee, tea, or cola 12 h prior to the tests. The subject was asked to relax in the supine position for 30 min. Blood pressure (BP) was measured with sphygmomanometer by the standard auscultatory Riva-Rocci method.

Materials

Autonomic function tests can be carried out using:

1. Sphygmomanometer
2. Hand grip dynamometer.

Physiological parameters

Resting BP

The resting BP was recorded in the supine position using mercury sphygmomanometer and expressed in mmHg.

Body temperature

The body temperature of the subjects was measured by a mercury thermometer.

Procedure of Autonomic Evaluation

In the early 1970's, two simple non-invasive cardiovascular reflex tests were proposed such as BP response to standing up and BP response to the sustained handgrip. These tests have been widely used in a variety of studies.[4]

BP response to standing (orthostatic test)

The subject was asked to rest in a supine position for 5 min. The resting BP was recorded. The subject was then asked to stand unaided and remain standing unsupported for 3 min. The BP was recorded at 30 s and 3 min after standing up. The difference between the resting and standing BP levels was calculated. The fall in systolic BP (SBP) at 30 s on standing noted. A fall of 30 mmHg or more was defined as abnormal, fall between 11 and 29 mmHg as borderline and fall of 10 mmHg or less was considered normal.

BP response to sustained handgrip

In this test, sustained muscle contraction is measured by a handgrip dynamometer, causes a rise in SBP diastolic BP (DBP) and heart rate. The dynamometer is first squeezed to isometric maximum and then held at 30% maximum for 5 min. BP was recorded in the non-exercising arm five times at 1 min interval during the procedure. The maximum reading of the DBP was taken as the final value. Then, the rise in DBP was calculated by subtracting resting DBP from this value. A rise in DBP of <10 mmHg was defined as abnormal, 11-15 mmHg as borderline and 16 mmHg or more as normal.

Heart rate response to deep breathing, valsalva maneuver, and standing are known as tests to evaluate parasympathetic nervous system pathway, whereas BP response to standing and to sustained handgrip allow the assessment of sympathetic nervous system activity.

Observation and Results

The mean ± standard deviation (SD) of the age of the groups 36-45 years and 46-55 years were found to be 41.125 ± 2.95 and 51.51 ± 2.78, respectively.

The mean ± SD of body temperature of the groups 36-45 years and 46-55 years were found to be 96.74 ± 1.01 and 96.64 ± 2.48, respectively

The mean ± SD of resting SBP and DBP, of the age group 36-45 years is found to be 116.25 ± 13.45 and 76.67 ± 10.90 and of the age group 46-55 years is found to be 123.95 ± 14.43 and 81.18 ± 11.54, respectively.

Tables 1 and 2 are showing BP response to standing (orthostatic test-fall in SBP).

BP response to sustained handgrip has been depicted in Tables 3 and 4.

Age and SBP and DBP in the age group 36-45 years has been shown in Table 5.

BP response to standing and sustained hand grip in the age group 36-45 years has been shown in Table 6.

Table 1: Mean±SD of BP response to standing in the age groups 36-45 years and *t* value and *P* value

BP response to standing in age group 36-45 years			
SBP	**Mean±SD**	***t***	***P***
Resting	116.25±13.45	11.09	0.0001
Standing	104.08±15.82		
Difference	12.17±5.37		

In the age group of 36-45 years, the mean±SD of resting SBP is found to be 116.25±13.45, SBP after standing is 104.08±15.82, and fall in SBP is 12.17±5.37, the difference is statistically significant (*P*=0.0001). SD: Standard deviation, BP: Blood pressure, SBP: Systolic blood pressure

BP response to standing and sustained handgrip before and after the maneuver in the age group of 36-45 years is been shown and reading is given in Table 7.

Age, sex, resting BP of age Group 36-45 years and 46-55 years subjects have been given in Table 8.

BP response to standing and sustained hand grip in the age group 46-55 years is shown in Table 9.

Table 2: Mean±SD of BP response to standing in the age groups 46-55 years and *t* value and *P* value

BP response to standing in age group 46-55 years			
SBP	**Mean±SD**	***t***	***P***
Resting	123.95±14.43	16	0.0001
Standing	109.61±16.49		
Difference	14.34±7.81		

In the age group of 46-55 years, the mean±SD of resting SBP is found to be 123.95±14.43, SBP after standing is 109.61±16.49, and the fall in SBP is 14.34±7.81, the difference is statistically significant (*P*=0.0001). SD: Standard deviation, BP: Blood pressure, SBP: Systolic blood pressure

Table 3: Mean±SD of BP response to sustained handgrip in the age groups 36-45 years and *t* and *P* value

BP response to sustained handgrip in age group 36-45 years			
DBP	**Mean±SD**	***t***	***P***
Resting	76.67±10.90	110.13	0.0001
Handgrip	89.75±12.06		
Difference	13.08±6.32		

In the age group of 36-45 years, the mean±SD of resting DBP is found to be 76.67±10.90 DBP after sustained handgrip is 89.75±12.06 and the rise in DBP is 13.08±6.32, the difference is statistically significant (*P*=0.0001). SD: Standard deviation, BP: Blood pressure, DBP: Diastolic blood pressure

Table 4: Mean±SD of BP response to sustained handgrip in the age groups 46-55 years and *t* and *P* value

DBP	Mean±SD	*t*	*P*
Resting	81.18±11.54	17.82	0.0001
Handgrip	94.70±14.12		
Difference	13.51±6.61		

In the age group of 46-55 years, the mean±SD of resting DBP is found to be 81.18±11.54 DBP after sustained handgrip is 94.70±14.12 and the rise in DBP is 13.51±6.61. The difference is statistically significant (*P*=0.0001). SD: Standard deviation, BP: Blood pressure, DBP: Diastolic blood pressure

Table 5: Age and SBP and DBP in the age group 36-45 years

	Age (in years)	SBP (mmHg)	DBP (mmHg)
Mean	41.125	116.25	76.67
SD	2.95	13.45	10.90
SEM	0.60	2.75	2.23

SBP: Systolic blood pressure, DBP: Diastolic blood pressure, SD: Standard deviation, SEM: Standard error of mean

BP response to standing and sustained handgrip before and after the maneuver in the age group of 46-55 years (Table 10).

Table 6: BP response to standing and sustained hand grip in the age group 36-45 years

	Fall in SBP (mm Hg)	Rise in DBP (mmHg)
Mean	12.17	13.08
SD	5.37	6.32
SEM	1.10	1.29

SBP: Systolic blood pressure, DBP: Diastolic blood pressure, SD: Standard deviation, BP: Blood pressure

Table 7: BP response to standing and sustained handgrip before and after the maneuver in the age group of 36-45 years

	SBP (mmHg)	SBP to standing (mmHg)	Fall in SBP (mmHg)	DBP (mmHg)	DBP to handgrip (mmHg)	Rise in DBP (mmHg)
Mean	116.25	104.08	12.17	76.67	89.75	13.08
SD	13.45	15.82	5.37	10.90	12.06	6.32
SEM	2.75	3.23	1.10	2.23	2.46	1.29

SBP: Systolic blood pressure, DBP: Diastolic blood pressure, SD: Standard deviation, BP: Blood pressure

Table 8: Age and resting BP in the age group 46-55 years

	Age (in years)	SBP (mmHg)	DBP (mmHg)
Mean	51.51	123.95	81.18
SD	2.78	14.43	11.54
SEM	0.32	1.66	1.32

SBP: Systolic blood pressure, DBP: Diastolic blood pressure, SD: Standard deviation, BP: Blood pressure

Table 9: BP response to standing and sustained hand grip in the age group 46-55 years

	Fall in SBP (mm Hg)	Rise in DBP (mmHg)
Mean	14.34	13.51
SD	7.81	6.61
SEM	0.90	0.76

SBP: Systolic blood pressure, DBP: Diastolic blood pressure, SD: Standard deviation, BP: Blood pressure

Table 10: BP response to standing and sustained handgrip before and after the maneuver in the age group 46-55 years

	SBP (mmHg)	SBP to standing (mmHg)	Fall in SBP	DBP (mmHg)	DBP to handgrip (mmHg)	Rise in DBP
Mean	123.95	109.61	14.34	81.18	94.70	13.51
SD	14.43	16.49	7.81	11.54	14.12	6.61
SEM	1.66	1.89	0.90	1.32	1.62	0.76

SBP: Systolic blood pressure, DBP: Diastolic blood pressure, SD: Standard deviation, BP: Blood pressure

The abnormal BP response to standing in the subjects may be due to vagal damage as a part of diabetic autonomic neuropathy (Table 11).

DISCUSSION

BP Response to Standing

- In the present study, the mean SBP was found to be decreased in all the groups from lying down to one minute after standing which was statistically significant. The fall was due to decrease venous return and decreased cardiac output on standing affected by gravity.[4]

In their study on 50 diagnosed cases of DM Chugh *et al.*, in 2011, titled "QT dispersion in patients of DM without manifest cardiac dysautonomia," they found that 2 subjects showed an abnormal response, and 10 subjects were found to have a borderline response of BP to standing.

In 2014, Prakash *et al.* studied 100 diabetic patients matched against 50 normal healthy controls in their study titled "A cross-sectional study for the evaluation of autonomic nervous system functioning in Type 2 DM patients." When the BP response to supine to standing was evaluated, there was a significant decrease in SBP among controls and cases ($P < 0.05$).[5,6]

Chavan *et al.*, in 2009, in their study titled "determination of sensitivity among various cardiovascular autonomic function tests in diabetic patients of Bijapur" recruited 11 diagnosed diabetic patients and 15 healthy age-matched controls. Subjects were subjected to six standardized cardiovascular autonomic reflex function tests. Only one diabetic subject has shown abnormal response, and four subjects have shown borderline response of BP to standing.[7]

Caird *et al.*, in 494 people of aged 65 years or more living at home, have found drop of 20 mmHg or more in systolic pressure occurred on standing in 24%, 30 mmHg or more in 9% and of 40 mmHg or more in 5 % in their study on "Effect of posture on BP in the elderly.[8]

Table 11: Percentage distribution of cases according to age groups in normal, borderline, and abnormal patterns in BP response to standing

	Fall in SBP			
Age group (years)	Total (%)	Normal (%)	Borderline (%)	Abnormal (%)
36-45	24 (100)	14 (58.3)	10 (41.7)	0 (0)
46-55	76 (100)	39 (51.3)	32 (42.1)	5 (6.6)

SBP: Systolic blood pressure, BP: Blood pressure

In a study on "effect of posture on BP in elderly patients" by Spalding J.M.K, Johnson R.H, Smith A.C, and Wollner L. have observed a fall in SBP of more than 20 mmHg in 11 patients after they had sat 5 min and in 17 patients after they had stood for 2 min. The maximum fall was 60 mmHg (SBP) on standing, and several patients felt dizzy on sitting as well as standing. All patients with fall in SBP of over 20 mmHg had evidence of CVD.[9]

Kempler *et al.*, have concluded that a fall of more than 20 mmHg in SBP after standing up seemed to be most reliable criterion for the assessment of orthostatic hypotension in the diagnosis of autonomic neuropathy in patients with Type-I DM in a study involving 3007 randomly selected Type-I diabetic patients on BP response to standing in diagnosis of autonomic neuropathy: The EURODIAB IDDM complications study.[10]

V. BP response to sustained handgrip.

The values of mean ± SD for both the age groups are given in Tables 3 and 4.

The statistical analysis: The values of paired "*t*" test and "*P*" value are given in Tables 3 and 4, respectively.

Chavan *et al.*, in 2009, in their study titled "Determination of sensitivity among various cardiovascular autonomic function tests in diabetic patients of Bijapur" recruited eleven diagnosed diabetic patients and fifteen healthy age-matched controls. Subjects were subjected to six standardized cardiovascular autonomic reflex function tests. Three diabetic subjects have shown abnormal response where the rise in BP was <10 mmHg and four subjects have shown borderline response of BP to standing.[7]

In their study on 50 diagnosed cases of DM Chugh *et al.*, in 2011, titled 'QT dispersion in patients of DM without manifest cardiac dysautonomia," they found that 4 subjects showed abnormal response and 9 subjects were found to have borderline response of BP to sustained handgrip.[6]

In a study on "acupuncture effects on autonomic response to cold pressor and handgrip exercise in healthy humans" by Holly R. M, Janki B.S, Jun Liang Yu Katit Hui, in 2004, found that in normal healthy human, acupuncture at P6, LIV 3, and LI 4 does not attenuate the BP or heart rate response during handgrip exercise or cold pressor test.[11]

CONCLUSION

Involvement of nervous system is a well-known complication of diabetes. Neuropathy is one of the most common complications of diabetes. At an early

stage, autonomic dysfunction may be asymptomatic or mildly symptomatic. Symptomatic autonomic neuropathy carry worst prognosis, so early diagnosis is essential for maximum benefit. More sympathetic tests have shown significant abnormal responses in diabetics compared to parasympathetic tests. Probably no single test suffices indicating normality or autonomic neuropathy in diabetics, and a battery of tests reflecting both parasympathetic and sympathetic functions is preferable.

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Original Article

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Knowledge, Attitude and Practice of General Practitioners Regarding Typhoid Fever

Uttam Kumar Paul[1], Kanai Lal Barik[2], Keshab Sinharay[3], Smarajit Banik[4], Arup Bandyopadhyay[5]

[1]Associate Professor, Department of Medicine, Mata Gujri Memorial Medical College, Kishanganj, Bihar, India, [2]Professor, Department of Pediatrics, Burdwan Medical College, Bardhaman, West Bengal, India, [3]Professor, Department of Medicine, Nil Ratan Sircar Medical College, Kolkata, West Bengal, India, [4]Assistant Professor, Department of Medicine, North Bengal Medical College, Siliguri, West Bengal, India, [5]Professor and Head, Department of Physiology, Mata Gujri Memorial Medical College, Kishanganj, Bihar, India

Abstract

Background: Typhoid fever is a very common infectious disease in the tropics, particularly in India with a hugely devastating mortality and morbidity figures. It is expected that a better understanding of the knowledge, attitude and practice of the primary care physicians should be there, in general, practitioners toward typhoid fever.

Materials and Methods: The study was a non-parametric prospective non-interventional research work carried out in five places in Bihar and West Bengal, *viz*, Kishanganj, Raiganj, Bardhaman, Siliguri, and Kolkata. The study was performed for a period of 6-month from January 2015 to July 2015. The participants for the study are medical graduates mostly as full-time general practitioners mostly working in slum urban and rural set ups, and having no medical postgraduate qualification whatsoever. The whole study was divided into three phases - Phase 1, Phase 2, and Phase 3.

Results: About 81% of the general practitioners diagnose typhoid most of the time by clinical examination alone, without taking any support from any laboratory investigation. 83% of our general practitioners give supportive care most of the time. 65% of the general practitioners most of the time and 26% always, that is 91% highly prefer to apply empirical antibiotic. 93% of general practitioners always 5% most of the time order for Widal test. Again only 3% of general practitioners order for blood culture and that also occasionally, while 97% never do so. Some often noteworthy findings in our study include 92% of general practitioners do not use thermometer, 69% do not count pulse rate, 88% do not even think of brady/tachycardia, 86% do not inspect tongue, 98% do not inspect rose spots, 77% do not palpate abdomen and 65% do not look for hepatosplenomegaly.

Conclusion: The diagnosis and treatment of our general practitioners do tally with the expected norms of a general practitioner in the Indian subcontinent. However, they should improve attitude and give more importance to clinical skills.

Key words: Attitude, General practitioner, Infectious disease, Knowledge, Practice, Typhoid

INTRODUCTION

Typhoid fever is a very common infectious disease in the tropics.[1] As we all know infecting organisms are emerging day by day through various adaptations and changes which lead to a burden on global socio-economic, environmental and ecological factors let alone on community medicine.[2] In the UK, there is per 100,000 population a year. Each year, the world over, there are at least 13-17 million cases of typhoid fever, resulting in 600,000 deaths per annum. 80% of these cases and deaths occur in Asia alone.[3] Knowledge toward emerging patterns of infectious organisms, ways of their transmission, particularly among baseline doctors is essential to prevent the spreading of typhoid fever. Lack of knowledge about the principles of clinical examination including history taking in relation to typhoid fever, diagnosis, treatment and counseling of this disease, leads to increased spreading, morbidity, complications and mortality of this globally endemic and serious disease. This study was, therefore, undertaken to evaluate the knowledge, attitude and practices of primary care physicians, that is, general practitioners in regard to typhoid fever, its presentation, factors raising suspicion of typhoid fever, way of handling of these cases, diagnosis, treatment and counseling by

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Corresponding Author: Dr. Arup Bandyopadhyay, Department of Physiology, Mata Gujri Memorial Medical College, Kishanganj - 855 107, Bihar, India. E-mail: arupbanerjee1953@gmail.com

these family physicians, in Bihar and West Bengal, mostly in slum urban and rural areas. It is expected that a better understanding of the knowledge, attitude and practices of baseline primary care physicians toward typhoid fever would help us to take proper steps by the leaders of the medical community to anticipate, to take actions, and hopefully ameliorate current and future scenario.

MATERIALS AND METHODS

The study was a nonparametric prospective non-interventional research work carried out in five places in Bihar and West Bengal, *viz*, Kishanganj, Raiganj, Bardhaman, Siliguri, and Kolkata. The study was performed for a period of 6-month from January 2015 to July 2015. The participants for the study are medical graduates mostly as full-time general practitioners mostly working in slum urban and rural set ups, and having no medical postgraduate qualification whatsoever. Only willing doctors who declare that they come across a good enough number of patients and take full charge for their diagnosis and treatment and also counsel these patients for quicker relief, complete cure and also further prevention of re-infection, relapse, and community spreading of disease.

The whole study was divided into three phases, *viz*., Phase 1: Designing and validation of total 18 questions to be distributed among the selected general practitioners in the form of leaflets. Of these, the first 7 questions were in a four-point Likert scale, the points being always, most of the times, occasionally and never. The second set also consists of 7 questions which was all of the objective type with only yes/no response. Out of the last 4 questions, the first two were of multiple choice type and the third question was again of yes/no response and the last question was related to third, that is, should be filled up in words if the answer to the question was "yes."

Phase 2: Teaching, explaining and monitoring of the general practitioners regarding how to do the study and fill up the question paper given to them. Interviewing with the general practitioners on one is to one basis was done by any one of our authors with questions prepared and structured, and presented to the interviewee in an identical way using a strict predetermined order. It is ensured that no influence is made over them to express their free opinions and true findings

Phase 3: Evaluation and statistical analysis of the filled up question papers.

About 20-30 general practitioners were selected from each of the five earmarked areas, and a total of 122 general practitioners opinions and findings could be actually collected. An informed written consent was taken from each participant of the study and permission from our institutional ethical committee was also obtained.

To ensure the quality of the data, each completed questionnaire was annually checked before computerized analysis. The results of the data were reported as percentages.

RESULTS

Table 1 is depicts the response obtained from general practitioners taken by Likert Scale.

Table 2 depicts the results for the questions giving responses by general practitioners exhibiting their knowledge for typhoid fever

Table 3 depicts the results for the questions giving responses by general practitioners exhibiting their attitude and practice for typhoid fever.

DISCUSSION

The clinical manifestations and severity of typhoid fever vary both ethically and geographically. Most of the patients with typhoid fever are children or young adults from 5 to 25 years of age.[4-6] Again, studies in typhoid endemic areas have shown that many patients of typhoid (particularly children) are marked as suffering from "non-specific fever" only to be proved wrong at the end often landing up to fatal or extremely serious outcomes.[7-9]

The following ingestion of the bacteria *Salmonella enterica* (serotype typhi), an asymptomatic period follows that usually lasts 7-day and in extreme cases may range from 3 to 60 days. The onset of bacteremia is marked by fever and malaise. Patients typically present to the hospital toward the end of the 1st week after the onset of symptoms with fever often with chills (bur rarely rigor), a dull frontal headache, malaise, anorexia, nauses, poorly localized abdominal discomfort, a dry cough, generalized whole body myalgia, but the physical signs are comparatively new.[4-6,10,11] A coated tongue, tender abdomen, hepatomegaly and splenomegaly, are common. A relative bradycardia is considered common in typhoid, although in many geographical region this has not been a constant feature. Adults often have constipation, but in children and in young adults and in all age groups with compromised immunity like diabetes, HIV (AIDS), etc. diarrhea is a more common.

Table 1: Responses (percentage) of the general practitioners against Likert chart questions

Questions	Always (%)	Most of the time (%)	Occasionally (%)	Never
You diagnose typhoid fever only by clinical examination	(2)	(81)	(17)	
Give supportive care	(13)	(83)	(4)	
Apply empirical antibiotic	(26)	(65)	(6)	(3)
Order for Widal test	(93)	(5)	(2)	
Order for blood culture			(3)	(97)
Order for newer diagnostic test i.e., typhidot test			(12)	(88)
Repeat Widal test in positive cases after 7 days			(11)	(89)

Table 2: Responses (%) of the general practitioners exhibiting their knowledge related to typhoid fever

1. Which antibiotic usually you apply empirically in a suspected typhoid fever patient?
   (a) Fluoroquinolones (32%), (b) Azithromycin (42%),
   (c) Amoxycillin (6%), (d) Chloramphenicol (4%),
   (e) Cefixime16%, (f) Others
2. In which indication you use parenteral antibiotic in typhoid fever?
   (a) Persistent vomiting (56%), (b) Severe diarrhea (8%),
   (c) Abdominal distension (4%), (d) All of the above (32%)
3. Do you prefer to use combination of antibiotic in typhoid fever?
   Yes (38%)/No (62%)
4. If yes, which combination?
   (a) Cefixime+Azithromycin (26%), (b) Cipro+Azithromycin (12%)

Table 3: Attitude and practices related questionnaire showing responses (%) of the general practitioners

Do you measure temperature with thermometer during exam of fever patient	Yes (8)	No (92)
Do you count pulse rate of fever patient routinely	Yes (31)	No (69)
Do you think of relative brady/tachycardia in a fever patient	Yes (12)	No (88)
Do you inspect tongue for coating in a suspected typhoid patient	Yes (14)	No (86)
Do you inspect abdomen to find rose spots in a suspected typhoid patient	Yes (2)	No (98)
Do you palpate abdomen to note caecal gurgling in a suspected typhoid patient	Yes (23)	No (77)
Do you palpate abdomen for hepato/splenomegaly in a suspected typhoid patient	Yes (35)	No (65)

In our study, we have found that 81% of the general practitioners diagnose typhoid most of the time by clinical examination alone, without taking any support from any laboratory investigation. Parry *et al.*, in New England Journal of Medicine also states that in areas of endemic disease, fever without any evident cause that lasts for more than one week should be considered typhoid until proved otherwise.[12]

83% of our general practitioners give supportive care most of the time. As it is told that effective antibiotics, good nursing care, adequate nutrition, careful attention to fluid and electrolyte balance, and prompt recognition and treatment of complications are necessary to avert death. 65% of the general practitioners most of the time and 26% always, that is 91% highly prefer to apply empirical antibiotic. It is, however, suggested that fluoroquinolones, azithromycin, and third generation cephalosporin are mainly used to treat typhoid, the former two when the patient is unable to take the drug orally due to excessive vomiting or symptoms state.[13]

It is told that the "Widal test" for diagnosis of typhoid fever is unreliable,[14] but in our study 93% of general practitioners always 5% most of the time order for Widal test. However, another authority has mentioned that (according to the WHO) Widal test, the most widely available in India, is acceptable for typhoid diagnosis provided it is done after 1 week of onset of fever.[15] In our study repeat, Widal test after 7 days is done never by 89% of general practitioners. Again only 3% of general practitioners order for blood culture and that also occasionally, while 97% never do so, whereas recent evidence strongly suggests that diagnosis of typhoid fever is largely dependent on blood culture or polymerase chain reaction.[16] Associations of Physicians of India guidelines say, the limitations of use of blood culture: Lack of facilities of blood culture in rural even in many urban areas, about 20 ml (a large volume) of blood is needed for best cultures, sensitivity test is difficult to do and not reliable, and lastly even it is done it is positive only in 40-60% of cases.[15] Furthermore, typhidot test is ordered never in 88% cases and only occasionally in 12%. It has also not proved to be reliable.[13,17-22]

Some often noteworthy findings in our study include 92% of general practitioners do not use thermometer, 69% do not count pulse rate, 88% do not even think of brady/tachycardia, 86% do not inspect tongue, 98% do not inspect rose spots, 77% don't palpate abdomen and 65% do not look for hepatosplenomegaly. Among antibiotics, azithromycin and fluoroquinolones are most preferred. Persistent vomiting is the principal cause of using parental antibiotic (56%). 62% prefer not to use any combination antibiotics when they use a (cefixime plus azithromycin) combination is the preferred one.

CONCLUSION

Finally, it can be concluded from our study that the diagnosis and treatment of our general practitioners do

tally with the expected norms of a general practitioner in the Indian subcontinent, but they are to some extent quite unable to work out some basic clinical activities, probably because of the heavy load of patients in this high populous country. Yet, they should improve attitude and give more importance to clinical skills, because high standard laboratory facilities are not available here. Therefore, their attitude and practice are in paradox with their contexts that typhoid should be clinically diagnosed and empirically treated in India.

It is, therefore, strongly suggested that training programs for the general practitioners on behalf of the authorities, is the need of hour to manage and control the devastating effects of typhoid which is both a common and serious disease.

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Original Article

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Role of Infection and Inflammation as Possible Causative Factors for Raised Serum Creatinine in Patients with Unilateral Ureteral Calculus Obstruction: A Prospective Case-Control Study

Suresh Kumar Reddy[1], Sriram Krishnamoorthy[2], Natarajan Kumaresan[2], Venkat Ramanan[3]

[1]Consultant Urologist, Department of Urology, KIMS Hospital, Nellore, Andhra Pradesh, India, [2]Professor of Urology, Department of Urology, Sri Ramachandra Medical College & Research Institute, Chennai, India, [3]Professor & Head of Urology, Department of Urology, Sri Ramachandra Medical College & Research Institute, Chennai, India

Abstract

Introduction: Patients with the stone disease on many occasions present with obstructive uropathy. The reasons may be multi-factorial. One of the major postulated mechanisms is the role of infection and inflammation being the causative factors.

Purpose: With this aim in mind, we prospectively evaluated the role of infection and inflammation as possible causes of raised serum creatinine in patients with unilateral ureteral calculus disease.

Materials and Methods: A prospective case-control study of all patients who presented to the Urological Department with unilateral ureteric calculi was performed. 50 patients who presented with raised serum creatinine (>1.3 mg%), with structurally normal contralateral kidneys were included in the study group (SG), and another randomly selected 50 patients without raised serum creatinine were included in the control group (CG).

Results: Patients in SG had a mean age of 39.86 and those in the CG aged had a mean age of 38.26. Males clearly predominated, with the male:female overall ratio of 3:1. Of the co-morbid conditions, diabetes and hypertension were found to be more in the SG (16% and 22%, respectively), as compared to CG (8 and 10%, respectively). The mean serum creatinine levels at a presentation in the SG and CGs were 1.9 mg% and 1.0 mg%, respectively and the two-tailed $P < 0.0001$. The majority of patients in the SG had a glomerular filtration rate of <60 ml/min, while a majority of those in the CG were of more than 60 ml/min. Among the laboratory parameters, absolute leukocyte count, C-reactive protein, and erythrocyte sedimentation rate were found to be statistically significant difference between the study and CGs.

Conclusion: This study evaluates the factors that might cause an abnormal renal function in patients with unilateral ureteral obstruction. Further, well-designed studies are needed to substantiate the hypothesis drawn from this study.

Key words: C-reactive protein, Glomerular filtration rate, Obstructive uropathy, Serum creatinine, Ureteric calculus, Ureteral obstruction

INTRODUCTION

The lifetime prevalence of kidney stone disease is estimated at 10% in men and 6% in women, with the probability of having a stone varying according to age, gender, race, and geographic location.[1] Its overall prevalence is still on the rise.[2] Stone disease typically affects adult men more commonly than adult women. By a variety of indicators, including inpatient admissions, outpatient office visits, and emergency department visits, men are affected two to three times more frequently than women, but the ratio in the recent past has narrowed down considerably from 3.4 to 1.3 males per female.[3] Most stones become symptomatic when they fall into the ureter causing pain or obstruction.

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Corresponding Author: Sriram Krishnamoorthy, Department of Urology, Sri Ramachandra Medical College, Chennai - 600 116, India. Phone: +919444174743/8056139257. E-mail: sriramuro@gmail.com

Infected hydronephrosis is a common complication of ureteral obstruction produced by urolithiasis and can be lethal if it progresses to septicemia.[4] Prompt and effective diagnosis and treatment are necessary to avoid urosepsis, a systemic inflammatory response syndrome whose diagnosis is based on physical examination (fever, increased heart rate, and tachypnea) and laboratory data (leukocytosis, leukopenia, and marked neutrophilia).[5]

The emergency intervention of the obstructed urinary tract is required together with antibiotic therapy and sometimes intensive management.[6] Despite these measures, Stone formers had a significantly higher risk for all-cause mortality with a hazard ratio of 1.95.[7]

Bilateral ureteral calculus obstruction due to calculus disease causing elevated serum creatinine and a decline in renal function is well-established. Many time, we come across situations where, unilateral ureteral calculus obstruction causes a decline in renal function even though they have a structurally normal kidney on ultrasound and patients not having any preexisting disease. We have tried to study this group of patients to find out the reasons for raised serum creatinine. With this particular aim in mind, we prospectively evaluated the role of infection and inflammation as possible causes of raised serum creatinine in patients with unilateral ureteral calculus disease.

MATERIALS AND METHODS

A prospective case-control study of all patients who presented to the urology department in the period from January 2010 to March 2011 with a history of ureteric colic secondary to unilateral ureteric calculi were evaluated.

50 patients during the study who presented with raised serum creatinine (> 1.3 mg%), with structurally normal contralateral kidneys were included in the study group (SG) and another randomly selected 50 patients without raised serum creatinine were included in the control group (CG). Informed consent obtained from all the patients. All details regarding patient's demographics, clinical details, investigation findings, the outcome of management were entered in the Proforma.

Inclusion Criteria

All patients aged <60 years, with unilateral ureteral calculi obstruction and raised serum creatinine with apparently normal contralateral kidney were included in SG and those without raised creatinine as CG.

Exclusion Criteria

Those patients with long-standing diabetes mellitus and hypertension of more than 5 years, elderly age of more than 60 years, bilateral calculus ureteral obstruction, stone obstruction in a solitary functioning kidney, patients with pre-existing chronic kidney disease and those who required external diversion at the initial presentation (percutaneous nephrostomy) were all excluded from the study. The primary endpoint of the study was the time of reaching nadir value of serum creatinine after the intervention.

Initial Evaluation

All patients who presented with history suggestive of ureteric colic were evaluated with the following protocol:

1. History and physical examination.
2. Laboratory investigations
   a) Absolute leukocyte count
   b) Serum creatinine: The raised serum creatinine at presentation was confirmed by a repeat analysis prior to inclusion into the study
   c) Estimated glomerular filtration rate (GFR)
   d) Erythrocyte sedimentation rate (ESR)
   e) C-reactive protein (CRP)
   f) Urinalysis and urine culture sensitivity.
3. Radiological imaging
   Ultrasonography abdomen: To look for cortical thickness, dilatation of pelvicalyceal system, and presence of echogenic debris.
   Non-contrast computed tomography of kidney, ureter, bladder; to look for stone size, stone site, degree of dilatation, perinephric stranding if any, forniceal rupture and other evidence of stone impaction like ureteral wall edema and tortuosity of the ureter.
4. Intraoperative findings
   a. Degree of stone impaction such as presence of mucosal edema/congestion at the site of stone impaction
   b. Ease of negotiability of ureteric guide wire or catheter, beyond the site of stone impaction
   c. Evidence of infection/inflammation in the system, proximal to the stone such as turbid urine
   d. Urine specimen from the corresponding kidney was sent for culture, after relief of obstruction.
5. Follow-up: All patients were subjected to a daily serum creatinine monitoring until a nadir level was reached. Those who did not reach normal serum creatinine levels by 2 weeks were considered as having associated nephropathy. Apart from serum creatinine, the other parameters considered and compared with CG were CRP, ESR, estimated creatinine clearance, and urine culture.

All patients were started on parenteral antibiotics Cefaperazone - Sulbactum combination preoperatively and then switched over to culture-specific antibiotic. Those who had sterile urine were continued with the same antibiotics postoperatively. All patients underwent ureteroscopy and

had a double J stent placed, which was removed in 2 weeks' time, once nadir creatinine levels were reached.

The Definition of Abnormal Lab Parameters Included the Following

1. Serum creatinine more than 1.3 mg/dl is defined as elevated
2. Absolute leukocyte count more than 12000 cells/cu mm is defined as leukocytosis
3. An ESR of more than 20 mm (Wintrobe's method) in one hour is defined as elevated ESR
4. Quantitative estimation of CRP was done by enzyme-linked immuno-assay. A value of >0.6 mg/dl is abnormal
5. GFR is calculated by Cockcroft-Gault formula
6. Estimated creatinine clearance, or GFR
   a. ([140-age] × mass [in kg])\(72 × Serum creatinine [in mg/dL])
   b. If the patient is female, multiply the above by 0.85
   c. The value of GFR <90 ml/min is considered as abnormal.
7. Statistical analysis was performed using the SPSS v.16 package (SPSS Inc. Chicago, IL). A $P < 0.05$ was considered as statistically significant.

RESULTS

A total of 100 patients were recruited in the present study. It was a prospective case-control study, with two groups, each containing 50 patients. Table 1 gives the summary of the demographic data, patient characteristics, patients' symptomatology and constitutional symptoms at presentation, blood biochemistry values, pre- and intra- operative urine culture, and associated co-morbid illnesses.

Table 1: Summary of the demographic data and characteristics in study and control groups

Characteristics	SG	CG	*P* value
Number	50	50	
Mean age	39.86	38.26	
Gender			
Male	42	33	<0.0001
Female	8	17	
Co-morbidities			
Diabetes	8	4	0.105
Hypertension	11	5	
Constitutional symptoms			
Fever	20	7	<0.0004
Vomiting	27	8	
Loin pain	50	50	
Duration of loin pain (in days)	6.3	2.64	
Clinical findings			
Loin tenderness	32	8	<0.001
Palpable tender kidney	42	1	<0.001
Blood parameters			
Leukocytosis (>17,000)	13	0	<0.0005
Elevated CRP	46	10	<0.0001
ESR	50	6	<0.0001
Urine culture			
Pre-operative urine culture positivity	1	0	
Intra operative urine culture positivity	3	2	1.000

ESR: Erythrocyte sedimentation rate, CRP: C-reactive protein, SG: Study group, CG: Control group

Patients in SG aged between 19 and 60 years, with the mean age of 39.86 and those in the CG aged between 24 and 60 years, with a mean age of 38.26. There was not much of a difference between the two groups as far as age at presentation is concerned.

The two genders showed striking differences. Males clearly predominated, with the male:female overall ratio of 3:1. There was a statistically significant difference in gender between these two groups ($P \leq 0.0001$).

The duration of pain ranged from 1 to 21 days in the SG, with a mean of 6.73, whereas the mean duration of pain was only 2.64 in the CG.

Of the co-morbid conditions, diabetes and hypertension were found to be more in the SG (16% and 22%, respectively), as compared to CG (8 and 10%, respectively). However, because in none of these patients, the co-morbid conditions were present for more than 2 years, it is unlikely that these co-morbid conditions would have had any effect on baseline renal function.

Among the constitutional symptoms, only fever, vomiting, and loin tenderness were found to be significantly different between the study and CGs. In the SG, 40% presented with fever, whereas 14% of them had the fever, in CG. This data were found to be statistically significant. 54% from the SG ($n = 27$) and 16% from the CG had vomiting as the principal bothersome constitutional symptom. Two patients each from both the groups had hematuria. Even though all patients had loin pain, tenderness was elicited in 64% of patients in the SG, but in only 16% in the other group ($P \leq 0.001$). On the other hand, a palpable tender kidney was found in 60% of patients SG and only in 2% of patients in CG. This difference was also statistically significant ($P < 0.001$).

Figure 1 presents the serum creatinine levels on admission in the both the groups. The majority of them in SG (72%) had a serum creatinine of <2 mg%. Two patients had a serum creatinine of more than 3.1 mg%. The mean serum creatinine levels in the SG and CGs were 1.91 mg% and 1.07 mg% with standard deviation (SD) of 0.169 and 0.563 and standard error of means (SEM) of 0.024 and 0.080, respectively. The two-tailed *P* value by Fischer's exact test was <0.0001.

Figure 2 depicts the overall GFR in both the groups. From the above data, one could observe that a majority of patients

in the SG had a GFR of <60 ml/min, while a majority of those in the CG were of more than 60 ml/min. It was also observed that only 11 patients (22%) in the SG and none in the SG had a GFR of more than 100 ml/min. The two-tailed *P* value by Fischer's exact test equals 0.0001; Mean GFR in the SG and CGs were 53.9 ml/min and 90.9 ml/min with an SD of 19.8 and 53.9 and SEM of 2.80 and 2.15, respectively.

Figure 3 gives an overview of the types of ureteric calculi encountered in our study. Figure 3a and c shows the ureteric stones in the SG and CG respectively. Figure 3b and d shows the radiological imaging that is suggestive of stone impaction and consequent upper urinary tract infection

Among the laboratory parameters, absolute leukocyte count, CRP, and ESR were found to be statistically significant difference between the two groups.

Tables 1 and 2 depict the details of absolute leukocyte count in both the groups. In the present study, the raised absolute count was classified as mild (12001-17000), moderate (17001-22000), and severe (>22000). From this study, it was observed about 16% in the SG had normal leukocyte levels. Moreover, moderate to severe leukocytosis was observed only in the SG ($P \leq 0.0005$).

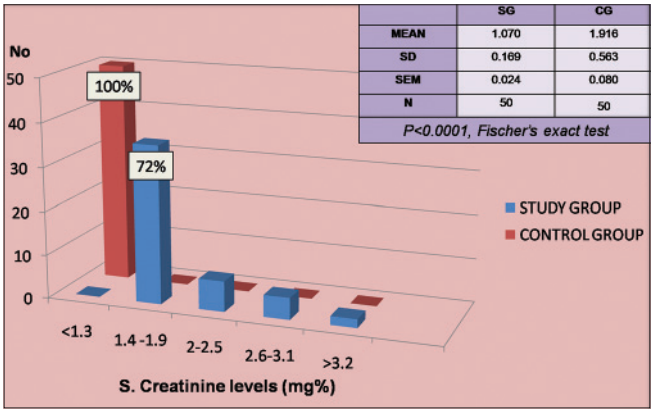

Figure 1: Serum creatinine levels at initial presentation in both the groups

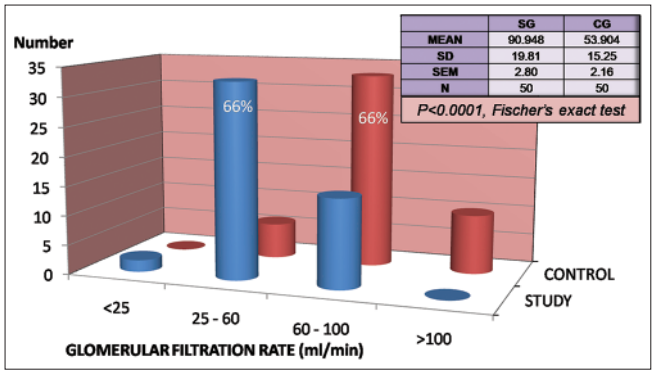

Figure 2: Glomerular filtration rate levels at initial presentation in both the groups

From Table 1, it was observed that 92% of patients ($n = 46$) in the SG had elevated CRP, whereas 80% of patients in CG had normal CRP levels ($P \leq 0.0001$). It was also observed that none from the SG had normal ESR. 12% of patients in CG had elevated ESR ($P \leq 0.0001$).

There was no statistically significant difference in the urine culture between study and CG. From the above table, it was observed that only one patient in the SG had a positive culture. This very low presence of culture positivity may be

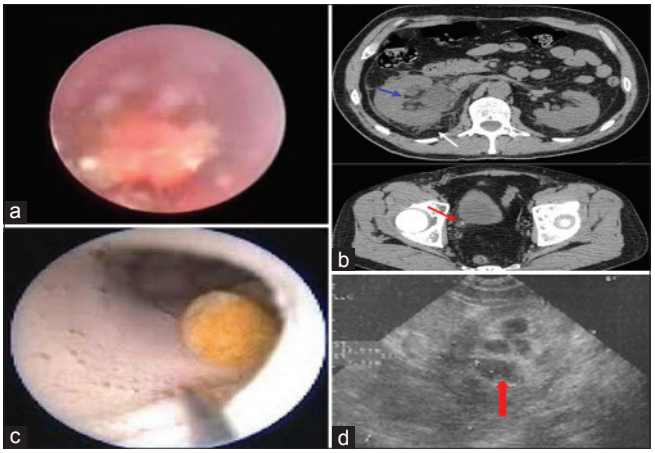

Figure 3: (a) Ureteroscopic image showing turbid infected urine after dislodging the stone, (b) Plain computed tomography kidneys, ureters, and bladder showing perinephric stranding with dilatation of right ureter with distal ureteric stone impaction, (c) Ureteroscopic image showing dislodged stone in the control group, and (d) Floating debris on ultrasonography

Table 2: Leukocyte count in SG and CG

Group	Absolute leukocyte count (%)				*P* value
	Normal	Mild	Moderate	Severe	
SG	8 (16)	30 (60)	11 (22)	2 (4)	<0.005
CG	25 (50)	25 (50)	0 (0)	0 (0)	

SG: Study group, CG: Control group

Table 3: Summary of imaging techniques and intra operative findings

Characteristics	SG	CG	*P* value
Imaging techniques			
Debris in ultrasound	31	8	<0.002
Perinephric stranding in computed tomography	31	8	<0.002
Intra operative ureteroscopic finding			
Stone impaction**	39	1	<0.0001
Ureteral edema and congestion at stone impaction site	41	18	<0.020
Purulent urine on disimpaction	37	1	<0.0001
Post-operative return of serum creatinine levels to <1.3 mg %	47	50	
Ability to negotiate the guidewire across the site of stone impaction	6	29	0.0007

**Stone impaction: Defined as either contrast not visualizing the ureter proximal to site of stone impaction or the guide wire not negotiable beyond the stone and returning back at impacted site, SG: Study group, CG: Control group

a true state of affairs or it may be a falsely negative culture secondary to impacted stone preventing urine from the obstructed site coming into the bladder.

Table 3 gives the summary of the findings of pre-operative imaging and intra operative ureteroscopic findings. Among the radiological findings, the presence of debris on ultrasound as internal echogenicity and perinephric stranding on computed tomography (CT) kidneys, ureters, bladder (KUB) were found to be significantly different between the two groups. Ultrasound screening of the kidneys showed evidence of floating debris in 62% of patients in SG, whereas 16% in the CG demonstrated debris in collecting system. The presence of debris within the collecting system is an indirect evidence of infection or inflammation in the system secondary to calculus obstruction. A statistically significant correlation ($P \leq 0.001$), further suggests that presence of debris within the pelvicalyceal system does have a significant impact on the ultimate renal function.

Non-contrast CT KUB was done in all patients in both groups. Perinephric stranding was seen in 62% of patients in the SG when compared this with CG it was only 16%. Perinephric stranding can be a feature of infection or inflammation, which may be directly or indirectly causal to raised serum creatinine. Two patients in the SG also had forniceal rupture. A 0.032 inches guide Terumo guide wire could be negotiated across the stone in only 12% in the SG, while in the CG the guide wire was negotiable in 58%, with a two-tailed *P* value that equals 0.0007. This data suggested that impaction at the stone site, strongly correlates with deterioration in renal function.

On the other hand, when urine from the kidney after disimpaction of the stone was analyzed, it was found that 2 patients from the CG and three from the SG had a positive urine culture. The low incidence of culture positivity may be a true state of affairs or it may be a falsely negative culture, because of antibiotics, received in previous 24 h.

DISCUSSION

Urinary tract obstruction is a common cause of acute and chronic renal failure. The clinical features of a kidney that is obstructed may range from being totally asymptomatic to severe acute pain. The diagnosis of an obstructed kidney is not very difficult these days, especially with the availability of high-resolution ultrasonography and computed tomography and digital intravenous urogram.[8]

During the first few hours, following acute unilateral ureteral obstruction (UUO), renal blood flow in the obstructed kidney increases secondary to preglomerular vasodilatation of renal blood vessels, which increases GFR. As the GFR increases, increased urine formation begins to gradually increase ureteral pressure.[9] After 4 h of obstruction, renal blood flow declines while ureteral pressure continues to increase along with post-glomerular vaso constriction. The increased intrarenal pressure activates the renin-angiotensin system leading to rise in the vasoconstrictors such as thromboxane A_2, which results in decreased renal blood flow and a decrease in ureteral pressure associated with preglomerular vasoconstriction.[10] The pathological changes that occur during bilateral ureteral obstruction (BUO) differ from UUO. While during UUO, the kidney passes through these three phases, in BUO the kidney passes through a phase of preglomerular vasodilatation and then a postglomerular vasoconstriction without subsequent preglomerular vasoconstriction.[11,12]

The readily available lab parameters such as absolute leukocyte count, ESR, and CRP are indirect indicators of the severity of inflammation/infection in the unilaterally obstructed renal system.[13] In our SG, these lab parameters along with few imaging parameters such as the presence of debris in the pelvicalyceal system as well as certain clinical parameters, such as fever and loin tenderness, reflecting inflammation/infection, were significantly raised.

From the present study, there is no statistical difference in age between the CG and the SGs. However, there was a statistical difference in gender. Overall, 75% of the patients, when both groups were combined, were males.

With the regard to the clinical symptoms, the presence of fever, loin tenderness, and vomiting was statistically different between both the groups. Fever is a factor, which can reflect underlying infection or inflammation. In the presence of infection, inflammatory markers such as interleukin-1, interleukin-6, should be elevated and are responsible for fever, although these markers, were not in the preview of the study. The significant difference in the presence of fever between these two groups indirectly reflects the severity and degree of infection or inflammatory process. Out of 20 patients with fever, 19 (95%) patients had elevated infective or inflammatory parameters. Out of 32 patients with loin tenderness 22 (68.75%), had elevated infective or inflammatory markers. Similarly, in the present study, there has been a strong correlation between loin tenderness and degree of obstruction ($P \leq 0.001$) Out of 32 patients with loin tenderness in the SG, 23 (74.2%) patients had perinephric stranding on CT KUB.

Rising levels of plasma creatinine in the setting of acute UUO (AUUO) often reflects acute renal failure, mandating immediate kidney drainage. It is hypothesized that re-absorption of perirenal urine extravasation, a common

result of UUO, contributes significantly to the elevation in plasma creatinine, rendering the latter an inaccurate benchmark for renal function.[14]

There has also been strong correlation between inflammatory parameters, CRP, absolute leukocyte count, ESR, and vomiting.[15-17] Out of 27 patients, who had vomiting in the SG, 23 (88.5%) patients had elevated infective or inflammatory parameters ($P \leq 0.001$). This would suggest that the presence of these factors would be an indirect evidence of inflammation and obstruction.

All the patients with perinephric stranding on CT KUB and debris on ultrasonography had elevated infective or inflammatory parameters.[18,19] Similarly, there has been a stronger correlation and statistically significant difference between these groups on radiological evidence of stone impaction and inflammation, like perinephric stranding and debris in the system.

Per-operative findings of mucosal edema or congestion at the stone site will also suggest ongoing inflammation and obstruction. Moreover, as such, in 80% of SG patients, there have been raised inflammatory or infective markers ($P \leq 0.001$). Interestingly, once the obstruction is released, the serum creatinine came down to near normal, immediately after the procedure, which reached progressively to the nadir value, within a week.

This suggests that once the obstruction is relieved, the inflammatory mediators responsible for the decrease in the renal plasma flow have improved regaining the near normal baseline GFR. This fact is once again proved by near normal return of inflammatory markers, together with this event. The mean CRP level, in the SG was 0.8 mg/dl, whereas it was 0.4 mg/dl, in CG.

This would suggest a direct or indirect correlation between inflammation/infection and rise in serum creatinine. As in 49 out of 50 patients in the SG, the raised serum creatinine came back to normal relatively rapidly after relief of obstruction and relief of possible infection. Pathological event giving rise to raised serum creatinine must be an easily and rapidly reversible process. This event most likely must be vasospasm of the afferent glomerular arteries.

In any acute unilateral ureteric obstruction, the ipsilateral afferent glomerular arteries finally undergo vasoconstriction secondary to release of thromboxane A_2. However, this normally does not lead to elevation of serum creatinine, if the contralateral kidney is normal. However, it can be hypothesized that the presence of associated inflammation/infection on top of acute obstruction, either the amount of thromboxane A_2 is secreted in larger amount or other vasoactive cytokines such as interleukin 1 and interleukin 2 are also released which then instead of acting only locally on the ipsilateral kidney by autocrine or paracrine mechanism may also affect to contralateral renal vessel by endocrine mechanism, ultimately leading to bilateral afferent renal vasoconstriction, reduction of overall GFR and eventually rise in serum creatinine.

CONCLUSION

A clinical situation of unilateral calculus ureteral obstruction with raised creatinine, in patients with structurally normal contralateral kidney, does exist. This condition is hardly ever mentioned or discussed in the urological literature. There is no ready or easy answer to explain the rise in serum creatinine in the presence of only unilateral obstruction.

This abnormal surge would probably enable the vasoactive cytokines to extend their action on the contralateral renal vessel, as well as by an endocrine mechanism and their by leading to bilateral renal vasoconstriction and reduction of GFR and thereby rise in serum creatinine. The obstructing ureteric stones in such situations are likely to be impacted and hence are not likely to respond to conservative measures. Ureteroscopic removal of stone will rapidly remove the obstruction and reverse the infective/inflammatory process on renal failure. Further, well-designed studies are needed to substantiate the hypothesis drawn from this study.

LIMITATIONS

The numbers taken for this case-control study could have been much higher. The premorbid GFR values of patients in SG are not known. The roles of vasoactive inflammatory cytokines were only hypothesized in the present study and actually were not studied. A Doppler study to document resistive index of the renal vessels, could have probably given more insight into vasospasm.

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Original Article

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Cytohistological Correlation of Thyroid Lesions with Special Emphasis on Recent Trends

Sapna Patel[1], S Harish[2]

[1]Assisstant Professor, Department of Pathology, JSS Medical College, Mysore, Karnataka, India, [2]Associate Professor, Department of Surgery, JSS Medical College, Mysore, Karnataka, India

Abstract

Background: Thyroid is a frequent site of disease in human body. Fine-needle aspiration cytology (FNAC) is a rapid, efficient, inexpensive and safe diagnostic method in these cases. FNAC has some limitations, particularly limited to representativity of samples and exact typing of neoplastic and non-neoplastic lesions.

Materials and Methods: In the present study, 130 cases of thyroid FNAC's which were subsequently followed by excision biopsy, have been analyzed, and cytohistopathological correlation has been interpreted.

Results: Of these 130 cases, 97 (75%) were non-neoplastic, 22 (17%) were benign neoplasms, and 11(8%) were malignant neoplasms. Among 97 non-neoplastic lesions, 73 cases correlated histopathologically. In the present study, sensitivity of FNAC was 78.57%, specificity was 100%, and diagnostic accuracy was 97.69% for malignant lesions.

Conclusion: FNAC is a rapid, efficient, cost-effective, relatively painless procedure and produces a speedy result with a high diagnostic accuracy. It has high rates of sensitivity and specificity in diagnosing thyroid lesions and hence is a valuable tool in the diagnosis and management of patients with thyroid lesions.

Key words: Benign, Diagnosis, Fine-needle aspiration cytology, Malignant, Non-neoplastic lesions

INTRODUCTION

Fine-needle aspiration cytology (FNAC) is now accepted as a cost-effective procedure in the initial assessment and management of thyroid enlargement. It is a valuable adjunct to preoperative screening in the diagnosis of thyroid nodules and in most cases it can distinguish between neoplastic and non-neoplastic lesions.[1] Its accuracy, when applied by experienced and well-trained practitioners, can approach that of histopathology in providing an unequivocal diagnosis. It is an extremely valuable complement to surgical histopathology. Thus, today FNAC is a well-established procedure and is a valuable tool in the diagnosis and management of a patient with thyroid lesions.[2]

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With the advent of ultrasonography (USG), guided FNAC with detailed USG findings are taken about the size and echogenicity of the lesion. The precise location of the lesion under USG offers a better yield. Under USG - solid lesions, lesions with nodular halo and punctuate calcifications are targeted. Color Doppler may be used to identify internal vascularity.[3] Apart from USG, morphometry can help in preoperative assessment and may act as an adjunct to morphological features in thyroid lesions.[4]

Hence, this study is undertaken to study the cytology of palpable thyroid lesions to minimize surgical intervention and also the need for the confirmation of the diagnosis by histopathological study for planning post-surgical management of malignant thyroid lesions.

MATERIALS AND METHODS

J.S.S. Hospital is a major tertiary referral center in South Karnataka. About 408,690 patients seek consultation as outpatients and about 51,000 are admitted as in patients a year. All the patients referred for FNAC of thyroid lesions

Corresponding Author: Dr. Sapna Patel, Assistant Professor, Department of Pathology, JSS University, Mysore, Karnataka, India.
E-mail: raxith25@gmail.com

in the cytology unit of JSS Hospital, Mysore were studied prospectively for a period of 2-year.

All the patients were clinically examined in detail, and a careful palpation of the thyroid gland was done to judge precisely the location for aspiration. Multiple passes (2-4) were done under aseptic precautions using 24-25 G needle by non-aspiration technique. A minimum of six slides were smeared with the aspirate, two for May-Grunwald Giemsa (air dried) and two each for haematoxylin eosin and papanicolaou stains (wet smears). Slides for wet smears were fixed in 95% ethyl alcohol, while the others were air dried. Stained smears were studied under light microscopy. A special stain like congored was done wherever necessary. These were correlated with histopathological examination (HPE) in 130 cases.

RESULTS

The present study deals with the FNAC of the palpable thyroid lesions and determination of the diagnostic accuracy of the aspiration cytology with histopathologic correlation. During the period of this study for 2 years, 547 cases of thyroid FNAC were done and only 130 cases were biopsied subsequently and subjected to histopathological study. Only those cases with histopathological correlation were selected for this study.

Age group of patients referred for thyroid aspirations ranged from 5 years to 70 years with mean age of 40.57 years. The majority of the patients were in the age group of 31-40 years, and most of them were females forming a female to male ratio of 6.6:1 (Table 1).

Out of 130 patients, 129 presented with a midline swelling in front of neck and one patient presented with two swellings - one in the midline in front of the neck and the other was medial to sternocliedomastoid in the submandibular region on the left side. Biochemical investigations were available in 17 cases and revealed hyperthyroidism in three cases, hypothyroidism in 2 cases and rest in euthyroid state. There were no complications following fine-needle aspiration.

The majority of the aspirates were blood mixed to frankly hemorrhagic. However, in 15 patients aspiration yielded either brown or dark brown fluid, amount ranging from 0.5 ml to 20 ml. The serous fluid was aspirated in 2 patients. Satisfactory cell sample was obtained in 127 patients while in the remaining 3 cases aspiration was unsatisfactory with satisfactory to unsatisfactory ratio of 43.3:1. For the 3 unsatisfactory aspirations USG guided FNAC was done, which yielded adequate material.

Cytohistological Findings

In the present study, the non-neoplastic lesions were more commonly encountered than the neoplastic lesions (Table 2).

Thyroglossal Duct Cyst

Patient aged 5 years presented with midline neck swelling, moving with deglutition. FNAC yielded 5 ml brown colored fluid. FNAC smears showed squamous epithelial cells, anucleate squames, foamy macrophages, occasional neutrophils and few degenerated epithelial cells. The histopathological study confirmed the cytodiagnosis of thyroglossal duct cyst.

Simple Colloid and Nodular Goitre

In the present study, the cytological diagnosis of colloid and nodular goitre was made in 72 cases out of 130. The histopathological study confirmed the cytodiagnosis in 55 cases. It differed in 17 cases of which follicular adenoma was seen in 9, Hashimoto's thyroiditis in 2, lymphocytic thyroiditis in 1, follicular adenoma with colloid goitre in 2, colloid goitre with follicular adenoma and micropapillary carcinoma in 1, colloid goitre with Hashimoto's thyroiditis in 1 and one case of medullary carcinoma. Congo red stain done was negative under polarized light.

Hyperplastic Colloid Goitre/Nodular Goitre with Hyperplasia

This was diagnosed in 3 cases and biochemical investigation was available in two cases which showed hyperthyroidism. Histopathological study confirmed the cytodiagnosis in 2 cases and differed in 1 case which was diagnosed as follicular adenoma.

Hashimoto's Thyroiditis

Cytological diagnosis of Hashimoto's thyroiditis was made in 15 cases out of 130 cases. Histopathological

Table 1: Age and sex distribution of the patients

Age group (years)	Male	Female	Total
5-10	1	0	1
11-20	0	3	3
21-30	4	27	31
31-40	5	37	42
41-50	1	24	25
51-60	5	16	21
61-70	1	6	7
Total	17	113	130

Table 2: Distribution of neoplastic and non-neoplastic lesions based on cytological study

Lesions	*n* (%)
Non neoplastic	97 (74.6)
Neoplastic	33 (25.4)
Total	130 (100)

diagnosis remained same as cytodiagnosis in 10 cases. Histopathological diagnosis differed in 5 cases of which, one was colloid goitre with cystic change, 2 follicular adenomas, one papillary carcinoma with Hashimoto's thyroiditis and one follicular adenoma with Hashimoto's thyroiditis.

Lymphocytic Thyroiditis

6 cases of lymphocytic thyroiditis were diagnosed cytologcially and all of them were females. Histopathological diagnosis remained same as cytological diagnosis in 5 cases and differed in one case which was diagnosed as follicular adenoma.

Follicular Neoplasm

Cytological diagnosis was made in 22 cases. Clinically, all these patients presented with solitary thyroid nodule. Histopathological diagnosis remained the same as the cytodiagnosis in 16 cases with a diagnostic accuracy of 72.73%. It differed in remaining 6 cases of which 4 were diagnosed as colloid goitre, 1 Hashimoto's thyroiditis and 1 colloid goitre with Hashimoto's thyroiditis. Among 16 correlated cases, one was cytologically reported as follicular neoplasm - Hurthle cell type and histopathologically diagnosed as Hurthle cell adenoma.

Papillary Carcinoma

Cytodiagnosis was made in 10 cases of which one was reported as a tall cell variant. Histopathological diagnosis remained same in all the 10 cases with an accuracy of 100%. One case had lymphnode metastasis. One case which was reported as tall cell variant in cytology correlated well with histopathology also.

Anaplastic Carcinoma

Cytodiagnosis of anaplastic carcinoma was made in 1 case. Histopathological diagnosis remained the same as the cytodiagnosis with a diagnostic accuracy of 100% (Tables 3 and 4).

The present study showed 92.86% specificity, 58.69% sensitivity and 80.77% efficacy for neoplastic lesions while for malignant lesions, it was 100%, 78.57% and 97.69%, respectively (Table 5).

Table 3: Distribution of individual thyroid lesions based on cytological study

Lesions	Number of cases	Percentage
Nodular and colloid goitre	72	55.4
Hashimoto's thyroiditis	15	11.5
Hyperplastic colloid goitre	03	2.3
Lymphocytic thyroiditis	06	4.6
Thyroglossal duct cyst	01	0.8
Follicular neoplasm	22	16.9
Papillary carcinoma	10	7.7
Anaplastic carcinoma	01	0.8
Total	130	100

DISCUSSION

FNAC is a safe, simple and inexpensive technique that has emerged as a valuable and popular adjunct in the diagnosis and management of various thyroid disorders. Nature of the disease, experience and understanding of certain limitations determine its diagnostic utility. The present study was undertaken to evaluate preoperatively with the help of FNAC, the type of thyroid lesion and to correlate the observations with the HPE to determine the usefulness of the technique.

The FNAC of the thyroid gland was performed in 547 patients of which 130 patients were selected for the study which were followed by excision biopsy. It is also one of the frequent pre-operative investigations done for thyroid diseases.

In the present study, the age of the patients ranged from 5 to 70 years with a median age of 40.57 years. Age distribution and the median age of the present study was comparable to Sekhri *et al*., study but the median age was lower when compared to Gharib *et al*., and other studies (Table 6).[5-9]

Among 130 patients, the majority were females numbering 113 and 17 males forming a male to female ratio of 1:6.6. Sex distribution was similar when compared to studies by Sekhri *et al*., but male patients were less in number when compared to studies by Burch *et al*., and others (Table 7).[5,7,8,10]

The majority (127) of the of the aspirates done by routine FNAC were satisfactory for cytological evaluation with satisfactory to unsatisfactory ratio of 43.3:1. Among the remaining 3 inconclusive aspirates, USG guided FNAC was done which yielded sufficient material for the cytological study.[11]

For considering the aspirate adequacy for the interpretation, it requires five to six groups of well-preserved cells with each group consisting of 10 or more cells. Many studies have applied the same criteria for the satisfactory aspirates. The ratio of satisfactory to unsatisfactory aspiration when compared to other studies was similar to Hsu and Boey study. It was better than Silverman *et al*., and other studies and unsatisfactory component was more than Hawkins *et al*., study (Table 8).[7,9,10,12-18]

In the present study, 97 were non-neoplastic and 33 were neoplastic lesions with non-neoplastic to neoplastic ratio of 2.9:1. Many authors have studied the cytology of thyroid lesions with ratio of non-neoplastic to neoplastic lesions

Table 4: Cytohistopathological correlation of both non-neoplastic and neoplastic lesions

Histopathological diagnosis	Cytologic diagnosis								
	Colloid/ nodular goitre	Hashimoto's thyroiditis	Thyroglossal duct cyst	Follicular neoplasm	Papillary carcinoma	Anaplastic carcinoma	Hyperplastic colloid goitre	Lymphocytic thyroiditis	
Colloid/nodular goitre	55	1	0	4	0	0	0	0	60
Hashimoto's thyroiditis	2	10	0	1	0	0	0	0	13
Thyroglossal cyst	0	0	1	0	0	0	0	0	1
Follicular neoplasm	9	2	0	16	0	0	1	1	29
Papillary carcinoma	0	0	0	0	10	0	0	0	10
Anaplastic carcinoma	0	0	0	0	0	1	0	0	1
Medullary carcinoma	1	0	0	0	0	0	0	0	1
Papillary carcinoma with Hashimoto's	0	1	0	0	0	0	0	0	1
Hashimoto's with follicular adenoma	0	1	0	0	0	0	0	0	1
Colloid goitre with follicular adenoma	2	0	0	0	0	0	0	0	2
Colloid goitre with follicular adenoma and micropapillary Ca	1	0	0	0	0	0	0	0	1
Colloid goitre with Hashimoto's	1	0	0	1	0	0	0	0	2
Lymphocytic thyroiditis	1	0	0	0	0	0	0	5	6
Hyperplastic colloid goiter	0	0	0	0	0	0	2	0	2
Total	72	15	1	22	10	1	3	6	130

Table 5: Statistical values for neoplastic and malignant lesions calculated by Galen and Gambino's method

Statistical index	For neoplasm	For malignancy
True positive	27	11
True negative	78	116
False positive	06	00
False negative	19	03
False positive error rate (%)	4.62	00
False negative error rate (%)	14.62	2.31
Sensitivity (%)	58.69	78.57
Specificity (%)	92.86	100.0
Positive predictive value (%)	81.82	100.0
Negative predictive value (%)	80.41	97.48
Efficacy (%)	80.77	97.69

Table 6: Age range and median age of different studies and present study

Authors	Age range (years)	Median age (years)
Hawkins *et al.*	9-84	43
Gharib *et al.*	11-84	52
Sekhri *et al.*	9-70	33.9±11.7
Silverman *et al.*	16-79	44.8
Burch *et al.*	15-83	51.1±14.7
Present study	5-70	40.57

Table 7: Sex distribution and male to female ratio of different studies and present study

Authors	Total cases	Male	Female	Male:female
Burch *et al.*	422	91	331	1:3.6
Silverman *et al.*	295	25	270	1:10.8
Pandit and Kinare	64	26	58	1:2
Sekhri *et al.*	300	44	256	1:6
Present study	130	17	113	1:6.6

Table 8: Satisfactory to unsatisfactory ratio of the present study and different studies

Authors	Total	Satisfactory	Unsatisfactory	Ratio
Hawkins *et al.*	1399	1377	22	63.6:1
Hsu and Boey	555	543	12	45.25:1
Silverman *et al.*	309	273	36	7.58:1
Pandit and Kinare	84	80	4	20:1
Altavilla *et al.*	2433	2041	392	5.21:1
Crile and William	135	128	7	18.28:1
Crockford and Bain	103	89	14	6.35:1
Friedman *et al.*	310	289	21	13.76:1
Gershengorn *et al.*	33	32	1	32:1
Aguilar-Diosdado *et al.* (1997)	289	252	37	6.81:1
Present study	130	127	03	43.3:1

ranging from 0.46:1 to 12.5:1. Ratio when compared to other studies, it was comparable to studies by Frable and Frable 1989 but non-neoplastic lesions were very much low when compared to Altavilla *et al*'s., study (Table 9).[8,9,13,18-21]

CONCLUSION

FNAC of thyroid lesions has been shown to be safe, simple, cost-effective and accurate method for management of palpable thyroid lesions. In the present study, it was possible to classify non-neoplastic and neoplastic lesions. Its use has decreased the number of surgeries performed.

We wish to stress the importance of doing multiple aspirations because of the fact that thyroid is affected by many lesions at a time. Cystic change can occur in both non-neoplastic and neoplastic lesions. In cystic nodules fluid should be aspirated completely, and FNAC should be done from the residual mass. If there is no palpable mass, the

Table 9: Incidence of thyroid lesions in different studies and present study

Lesions	Suen and Quenvilla		Silverman *et al.*		Present study	
Nodular and colloid goitre	133	43.75	156	50.4	72	55.4
Hashimoto's thyroiditis	41	13.48	13	4.2	15	11.5
Primary hyperplasia	-	-	5	1.6	-	-
Hyperplastic nodular goitre	-	-	-	-	3	2.3
Thyroglossal duct cyst	-	-	-	-	1	0.8
Cysts	59	19.41	19	6.1	-	-
Lymphocytic thyroiditis	-	-	-	-	6	4.6
Follicular neoplasm	41	13.49	70	22.6	21	16.1
Hurthle cell neoplasm	-	-	3	1.0	1	0.8
Carcinoma	16	5.2	-	-	-	-
Follicular carcinoma	-	-	1	0.3	-	-
Papillary carcinoma	-	-	2	0.6	10	7.7
Medullary carcinoma	-	-	2	0.6	-	-
Anaplastic carcinoma	-	-	-	-	1	0.8
Insular carcinoma	-	-	-	-	-	-
Metastatic squamous cell carcinoma	-	-	2	0.6	-	-
Metastatic sarcoma	-	-	2	0.6	-	-
Suspicious carcinoma	14	4.6	-	-	-	-
Unsatisfactory	-	-	36	11.71	-	-
Total	304		309		130	

patient should be followed up with USG examination and USG guided FNAC should be done wherever necessary.

The diagnostic accuracy can be improved when combined with advanced imaging techniques, morphometry, immunologic analysis and electron microscopy and thereby the management of thyroid diseases.

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Original Article

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Effect of Oral and Intravenous Clonidine as an Adjunct during Spinal Anesthesia

Ghosh Ishita[1], Kailash Chandra[2], Karki Geeta[3], H S Nanda[4]

[1]Post-graduate Student, Department of Anaesthesiology Critical Care and Pain Management, SRMS Institute of Medical Sciences, Bareilly, Uttar Pradesh, India, [2]Associate Professor, Department of Anaesthesiology Critical Care and Pain Management, SRMS Institute of Medical Sciences, Bareilly, Uttar Pradesh, India, [3]Assistant Professor, Department of Anaesthesiology Critical Care and Pain Management, SRMS Institute of Medical Sciences, Bareilly, Uttar Pradesh, India, [4]Professor, Department of Anaesthesiology Critical Care and Pain Management, SRMS Institute of Medical Sciences, Bareilly, Uttar Pradesh, India

Abstract

Background: There are always study going on which upsurge the onset and duration of subarachnoid block with minimal side effects.

Objective: The aim of this study was to compare the effects of oral and intravenous (IV) clonidine in spinal anesthesia in lower abdominal and lower limb surgeries.

Materials and Methods: Total 60 patients undergoing spinal anesthesia were randomly divided into three groups of 20 patients.

Group B: 0.5% bupivacaine heavy 15 mg/kg.

Group OC: 0.5% bupivacaine heavy 15 mg + oral clonidine 3 mcg/kg.

Group IC: 0.5% bupivacaine heavy 15 mg + IV clonidine 3 mcg/kg.

Result: In our study, both the drugs are α_2 agonists, but IV clonidine was found to shorten the onset and increase the duration of anesthesia compared to oral clonidine.

Conclusion: Both the drugs were found to upsurge the onset and duration of spinal anesthesia, but IV clonidine is a more effective.

Key words: Intravenous clonidine, Oral clonidine, Spinal anesthesia

INTRODUCTION

Pain is as old as mankind and may be even older. There are ample reasons to believe that it is inherent to life and so the looking for the methods of pain relief. Many techniques and drug regimen with partial or greater success have been tried from time to time by the mankind for the relief of pain.[1]

A extension of this analgesia into the post-operative period is an advantage as the need for analgesics is minimized.[2,3]

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Drugs like epinephrine and fentanyl prolong bupivacaine subarachnoid block (SAB) and analgesia but have their own limitations.[4,5]

The aim of the study was to compare motor block provided by equianalgesic concentrations of oral and intravenous (IV) clonidine in spinal anesthesia.

An imidazole was synthesized in early 1960's. Acts as an antihypertensive by virtue of its ability to decrease sympathetic nervous system output from the central nervous system.

Intrathecal clonidine when used as adjunct potentiates the effect of local anesthetics and allows a decrease in required doses.[6] A non-opioid α_2 agonist is administered sublingually, intramuscularly, IV and various other routes. It prolongs the duration of motor and sensory spinal

Corresponding Author: Dr. Ishita Ghosh, 176/59 Tagore Town, DR. A K Sur Marg, Allahabad, Uttar Pradesh, India. Phone: +91-9458701353/+91-8755664930. E-mail: ishitaghosh.25@gmail.com

blockade when used along with local anaesthetics.[6] It also acts a sedative and reduces post-operative shivering.

The dose of oral and IV clonidine is same because the bioavailability of the routes remains the same which is 3.5 mcg/kg.

MATERIALS AND METHODS

A prospective, randomized, comparative study was carried out on 60 patients of 18-60 years of age posted for elective lower abdominal and lower limb surgeries in spinal anesthesia. Detailed pre-anesthetic checkup was done on all patients and relevant hematological, biochemical and radiological investigations was done for all patients as per surgical requirements. Patients selected for the study was randomized into 3 groups of 20 patients each.

- Group B: 0.5% bupivacaine heavy 15 mg/kg.
- Group OC: 0.5% bupivacaine heavy 15 mg + oral clonidine 3 mcg/kg.
- Group IC: 0.5% bupivacaine heavy 15 mg + IV clonidine 3 mcg/kg.

Pre-anesthetic checkup of all the patients will be done 1 day prior to the surgery. All the routine hematological and biochemical investigations were done. All the patients will be preloaded with 10 ml/kg of crystalloid solution via an 18 G IV cannula. Standard anesthesia monitors were used. With the patient in the sitting position, SAB was performed at the level of L3-L4 space through midline approach using a 25G Quincke spinal needle. Thereafter, heart rate (HR), mean arterial pressure and O_2 saturation were recorded every 5 min until surgery. The sensory block was assessed using loss of sensation to pinprick. The motor block was assessed using a modified bromage scale. Sedation was assessed using a Ramsay sedation scale and visual analog scale score was recorded during the 1st h of surgery.

RESULTS

Table 1 shows age distribution of the patients of three groups.

Table 2 shows weight wise distribution of patients.

Table 3 Comparing variables sensory onset, sensory duration, motor onset, motor duration, sedation score, time of the 1st post-operative analgesia, total analgesic required post-operative (24 h).

Table 1: Age distribution of the patients of three groups

Age groups (years)	Bupivacaine (%)	Oral clonidine (%)	IV clonidine (%)
<20	1 (5.0)	3 (15.0)	4 (20.0)
20-30	9 (45.0)	12 (60.0)	5 (25.0)
31-40	5 (25.0)	4 (20.0)	4 (20.0)
>40	5 (25.0)	1 (5.0)	7 (35.0)
Total	20 (100.0)	20 (100.0)	20 (100.0)
Mean±SD	29.5±8.7	28.2±9.4	30.4±7.9

SD: Standard deviation, IV: Intravenous

Table 2: Weight wise distribution of patients

Weight in kg	Bupivacaine (%)	Oral clonidine (%)	IV clonidine (%)
40-45	3 (15.0)	2 (10.0)	4 (20.0)
46-50	6 (30.0)	7 (35.0)	9 (45.0)
51-55	7 (35.0)	6 (30.0)	4 (20.0)
>55	4 (20.0)	5 (25.0)	3 (15.0)
Total	20 (100.0)	20 (100.0)	20 (100.0)
Mean±SD	51.2±3.4	50.9±2.3	52.7±4.2

SD: Standard deviation, IV: Intravenous

DISCUSSION

Baseline Comparison of Groups

The study included the patients of age group between 20 and 60 years. In the present study, the age in Group I (control group) was 29.5 ± 8.7 years, in Group II (oral clonidine) 28.2 ± 9.4 years and in Group III (IV clonidine) 30.4 ± 7.9 years. The age was not different and thus was comparable.

The weight of patients in Group I (control group) was 51.2 ± 3.4, in Group II (oral clonidine) 50.9 ± 2.3 and in Group III (IV clonidine) 52.7 ± 4.2 kg. The weight of patients was not different and thus was comparable.

Distribution according to sex was also comparable. In our study, time of sensory onset up to T10 in Group I (control group) was 5.35 ± 0.67 min, in Group II (oral clonidine) 5.3 ± 0.73 min and in Group III (IV clonidine) 3.25 ± 0.72 min. The onset of sensory block was shortest in Group III (IV) as compared to control and oral groups.

In our study, time of motor block onset to Bromage 3 in Group I (control group) was 7.4 ± 0.75 min, in Group II (oral clonidine) 7.25 ± 0.79 min and in Group III (IV clonidine) 6.35 ± 0.75 min. The onset of motor block was earliest in Group III (IV) as compared to control and oral groups.

In our study, time of sensory regression to S1 in Group I (control group) was 163.5 ± 6.71 min, in Group II

Table 3: Comparing variables sensory onset, sensory duration, motor onset, motor duration, sedation score, time of the 1st post-operative analgesia, total analgesic required post-operative (24 h)

Variables	Mean±SD			*P* value		
	Group B	Group OC	Group IC	B versus OC	OC versus IC	B versus IC
Sensory onset (min)	5.35±0.67	5.3±0.73	3.25±0.72	0.97	<0.001	<0.001
Sensory duration (min)	163.5±6.71	165.25±7.16	175.75±7.48	0.98	<0.001	<0.001
Motor onset	7.4±0.75	7.25±0.79	6.35±0.75	0.98	<0.001	<0.001
Motor duration	136.5±5.87	140.34±22.68	148.75±22.7	0.37	0.156	0.039
Sedation score	2.85±0.88	1.9±0.72	1.3±0.47	<0.001	0.029	<0.001
Time of 1st post op analgesia	1.05±0.76	1.4±0.68	2.1±0.55	0.31	0.005	<0.001
Total analgesic required post-operative (24 h)	1.1±0.64	0.7±0.57	0.45±0.6	0.12	0.592	0.004

SD: Standard deviation

(oral clonidine) 165.25 ± 7.16 min and in Group III (IV clonidine) 175.75 ± 7.48 min. The time of sensory regression was longest in Group III (IV) as compared to control and oral group.

In our study, time of motor block onset to Bromage 0 in Group I (control group) was 136.5 ± 5.87 min, in Group II (oral clonidine) 140.34 ± 22.68 min and in Group III (IV clonidine) 148.75 ± 22.7 min. The time of motor regression was longest in Group III (IV) as companied to control and oral group.

Hemodynamic Changes

In our study, there was a statistically significant fall in HR in group oral clonidine group compared to group bupivacaine and IV clonidine ($P < 0.05$).

There was a significant fall in the systolic blood pressure in all three groups with maximum fall in Group IV clonidine, but it was not statistically significant ($P > 0.05$).

There was a significant fall in the diastolic blood pressure in all three groups with maximum fall in Group IV clonidine, but it was not statistically significant ($P > 0.05$).

Oxygen saturation was similar in all three groups.

The sedation score in Group B (bupivacaine) was 1.3 ± 0.47, (oral clonidine) OC was 1.9 ± 0.72, Group IC (IV clonidine) was 2.85 ± 0.88.

In our study, duration of analgesia in Group I (control group) was 1.05 ± 0.76 h, in group II (oral clonidine) was 1.40 ± 0.68 h and in Group III (IV clonidine) was 2.10 ± 0.55 h. The analgesia was the longest in Group IC (IV) as compared to oral and placebo groups.

In our study, total analgesic required in 1st 24 h in Group I (control group) was 1.10 ±0.64 in Group II (oral clonidine) was 0.70 ± 0.57 and in group III (IV clonidine) was 0.45 ± 0.60. Thus, the requirement of analgesic was least in IV clonidine group.

CONCLUSION

Hence, it can be concluded that IV clonidine is a more effective than oral clonidine with less incidence of side effects.

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Original Article

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Prevalence of Microvascular Complications in Newly Diagnosed Type-2 Diabetes Mellitus

Fayaz Ahmad Wani[1], Rakesh K Koul[1], Akhtar A Raina[2], Arjumand Nazir[3], Muzaffar Maqbool[1], M Hyat Bhat[4], Parvaiz A Shah[5]

[1]Assistant Professor, Department of Medicine, Government Medical College, Srinagar, Jammu and Kashmir, India, [2]Registrar, Department of Medicine, Government Medical College, Srinagar, Jammu and Kashmir, India, [3]Registrar, Department of Ophthalmology, Government Medical College, Srinagar, Jammu and Kashmir, India, [4]Consultant, Government Medical College, Srinagar, Jammu and Kashmir, India, [5]Professor and Head, Department of Medicine, Government Medical College, Srinagar, Jammu and Kashmir, India

Abstract

Background: The onset of Type-2 diabetes mellitus (T2DM) is often silent and insidious. Untreated long standing hyperglycemia is responsible for the relatively high prevalence of microvascular complications in newly diagnosed DM. Our study was aimed at assessing the prevalence of microvascular complications in newly diagnosed T2DM patients of a public tertiary care hospital in India.

Materials and Methods: A prospective, cross-sectional study was conducted in the out-patient department of medicine at a tertiary care hospital. A total of 100 consecutive patients newly diagnosed with T2DM (<6 months duration) were included in the study. Detailed history, clinical examination, and relevant investigations were done to diagnose microvascular complications.

Results: Out of the total of 100 patients in this study, 56 were males and 44 females. The age range was 30-70 years, with mean age of 53.4 ± 21.5 years. Neuropathy was present in 33% patients; retinopathy was present in 6% of patients and nephropathy was present in 50% patients. Microalbuminuria was present in 44% patients, whereas macroalbuminuria was present in 6% patients. Subjects were classified into two groups on the basis of glycated hemoglobin (HbA1C) levels. Subjects with HbA1c >7.5% had more microvascular complications than with HbA1C 6.5-7.5%, the association was not statistically significant.

Conclusion: A long phase of asymptomatic hyperglycemia in T2DM patients is responsible for microvascular complications at diagnosis. A high prevalence of microvascular complications at the time of diagnosis in our study reconfirms that assessment for these complications must be done at the time of diagnosis in all patients. Once complications develop, in addition to strict control of hyperglycemia, steps have to be taken to prevent or retard further progression of these complications and even reverse these initial phase of complications.

Key words: Diabetes mellitus, Microvascular complications, Nephropathy, Neuropathy, Retinopathy

INTRODUCTION

The onset of Type-2 diabetes mellitus (T2DM) is often silent and insidious. DM is a common disorder with an annual prevalence of 8.2%.[1] T2DM being the most common form (90%). There is usually an asymptomatic phase between the actual onset of diabetic hyperglycemia and clinical diagnosis. This asymptomatic phase is estimated to last 4-7 years, and consequently, 30-50% may remain undiagnosed. Untreated long standing hyperglycemia is responsible for the relatively high prevalence of microvascular complications in newly detected DM.[2] T2DM has significant morbidity and mortality that is attributed to the microvascular and macrovascular complications. Coronary artery disease, peripheral arterial disease, and cerebrovascular disease account for macrovascular disease, whereas retinopathy, nephropathy, and neuropathy constitute microvascular disease.[3] The "Asian Indian Phenotype" refers to certain unique clinical and biochemical abnormalities in Indians including insulin resistance, higher waist circumference despite lower body mass index (BMI), lower adiponectin and higher

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Corresponding Author: Dr. Fayaz Ahmad Wani, Department of Medicine, GMC Srinagar, Jammu and Kashmir, India. Phone:+91-9205062319. E-mail: wanifayaz.a@gmail.com

levels of highly sensitive C-reactive protein levels. This phenotype makes Asians more prone to diabetes and its complications.[4] Microvascular complications from T2DM are common, and evidence shows that early detection and identification of risk factors for retinopathy, nephropathy, and neuropathy may delay or prevent progression of microvascular complications.[5] Clinical trials have demonstrated that strict blood glucose control correlates with a reduction in the microvascular complications.[6]

Screening for microvascular complications in newly detected DM (NDDM) patients will have important implications for understanding the need of vigorous screening, effective prevention, and management of T2DM. Our study was aimed at assessing the prevalence of microvascular complications in newly detected T2DM patients of a public tertiary care hospital in India.

MATERIALS AND METHODS

We conducted a prospective, cross-sectional study in the Out-Patient Department of Medicine at Government Medical College, Srinagar, Jammu and Kashmir, India after approval from the Institute Ethical Committee. The total of 100 consecutive patients newly diagnosed with T2DM (<6 months duration) were included in the study. American Diabetic Association criteria for the diagnosis of diabetes were applied. Subjects with fasting plasma glucose of ≥126 mg/dl on two separate occasions or random plasma glucose of ≥200 mg/dl with osmotic symptoms or glycated hemoglobin (HbA1c) of ≥6.5 were considered to be diabetic. Diabetics with a co-morbid illness such as CHF, stroke, chronic liver disease, and chronic kidney disease were excluded from the study.

Detailed clinical history regarding symptoms of diabetes, microvascular complication, family and personal history was taken from the subjects. A thorough clinical examination and anthropometric measurements were done in each subject. BMI (kg/m^2) was calculated after measuring height (m^2) and weight (kg) by a stadiometer. A BMI of 18-24.9 was taken as normal, 25-29.9 as overweight and more than 30 as obese. Waist circumference was measured by inelastic and flexible tape at the midpoint between the lower margin of least palpable rib and the highest point on the iliac crest to the nearest 1 cm.

Mercury sphygmomanometer was used to check the blood pressure in sitting and standing position in right arm to the nearest 2 mmHg. BP was recorded twice 10 min apart in both arms, lying down and standing. Subjects were considered to be hypertensive if systolic blood pressure was ≥140 mmHg or diastolic blood pressure of ≥90 mmHg or subjects were taking antihypertensive medications as per records. HbA1c was measured using the variant machine. Serum cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL), and triglycerides were measured by autoanalyzer. Dyslipidemia was diagnosed if serum cholesterol was >200 mg/dl, serum LDL >100 mg/dl, and HDL <40 mg/dl or serum triglycerides >150 mg/dl. Kidney function tests included urea, creatinine, and blood urea nitrogen. Urinalysis was done for glucose, proteins, and ketone bodies.

Diabetic neuropathy was diagnosed on clinical grounds by Semmes-Weinstein 10 g monofilament pressure sensation, deep tendon reflex testing by percussion hammer and vibration sense by 128 Hz Tuning fork. Non-diabetic causes of neuropathy were excluded. Autonomic neuropathy in the form of resting tachycardia, orthostatic hypotension, gastroparesis/diarrhea, or abnormal sweating was noted. Diabetic retinopathy was assessed by direct ophthalmoscopic examination of the fundus by an ophthalmologist. Diabetic retinopathy was graded as proliferative, non-proliferative, and clinically significant macular edema. Optic disc and/or retinal neo-vascularization, or presence of vitrous or preretinal hemorrhage was graded as proliferative diabetic retinopathy. Non-proliferative diabetic retinopathy was described by the presence of microaneurysms, exudates (cotton-wool spots or lipid exudates), and/or retinal hemorrhages. Diabetic nephropathy was graded as microalbuminuric if mean urine albumin concentration was 30-300 mg/dl and macroalbuminuric if >300 mg/dl.

Data were collected over a period of 6-month from May 2015 to October 2015. Data were entered in a Microsoft excel spreadsheet. Continuous variables were summarized as mean ± standard deviation. Categorical variables as frequency and percentage. The prevalence of microvascular complications was reported as a percentage. The relationship between microvascular complications and HbA1C was analyzed using independent samples *t*-test. A $P > 0.05$ was taken as statistically significant. Analysis of data was done using SPSS version 20.0. Quantitative variables were described as mean ± 1 SD, qualitative variables were described as percentages.

RESULTS

Out of the total of 100 patients in this study, 56 were males and 44 females (Table 1). The age range was 30-70 years, with mean age of 53.4 ± 21.5 years. In this study, 30% study subjects had normal BMI (18.5-24.99 kg/m^2), 50% subjects were overweight (25-29.99 kg/m^2), and 20% subjects were obese (>30 kg/m^2). Neuropathy was present in 33% patients, 20 (35.71%) males, and 13 (29.54%)

females. Retinopathy was present in 6 (6%) of patients, 4 (7.14%) males, and 2 (4.54%) females. The majority (83.33%) of patients had non-proliferative diabetic retinopathy. Only 1 patient (16.66%) had proliferative diabetic retinopathy, and he also had clinically significant macular edema. Nephropathy was present in 50% patients including 23 (41.07%) males and 27 (61.36%) females. Microalbuminuria was present in 44% patients, 20 (35.71%) males and 24 (54.54%) females, whereas macroalbuminuria was present in 6% patients, 3 (5.35%) males, and 3 (6.81%) females. Tripathy was present in one male patient.

Subjects were classified into two groups on the basis of HbA1C levels. Group first with HbA1C in the range 6.5-7.5% and group second with HbA1C >7.5%. Although subjects in the group second with HbA1c >7.5% had more microvascular complications than the first group, the association was not statistically significant (Table 2).

DISCUSSION

T2DM is an insidious illness with a preclinical asymptomatic phase of many years during which body is exposed to ill-effects of asymptomatic hyperglycemia. This study has reconfirmed that a large proportion of patients with T2DM has developed microvascular complications of various organs even before the time of diagnosis.

Table 1: Demographic and clinical characters of study subjects

Patient characteristics	Frequency (%)
Age (mean±SD)	
53.4±21.5 years	
Sex	
Males	56
Females	44
BMI (kg/m^2)	
18.5-24.99	30
25-29.99	50
>30	20
Complications	
Neuropathy	33
Nephropathy	50
Retinopathy	6
HbA1c	
6.5-7.5	40
>7.5	60

SD: Standard deviation, HbA1C: Glycated hemoglobin, BMI: Body mass index

Table 2: Relationship between HbA1C and diabetic complications

Complication	HbA1C (%)		*P* value
	6.5-7.5 (*n*=40)	>7.5 (*n*=60)	
Neuropathy	12 (30)	21 (35)	0.761
Nephropathy	17 (42.5)	33 (55)	0.307
Retinopathy	0	6 (10)	0.102

HbA1C: Glycated hemoglobin

We evaluated microvascular complication profile of newly diagnosed T2DM patients. Mean age of our patients was 53 years which confirms that in developing countries majority of patients with diabetes are in young, productive age group (45-64 years) as compared to developed countries who develop diabetes at a higher age (>65 years).[7,8] In our 100 patients evaluated for complication profile nephropathy was more common (50%) as compared to neuropathy (33%) and retinopathy (6%), whereas other studies have shown neuropathy as the most common complication.[9-14] Microalbuminuric nephropathy was more common (88%) as compared to macroalbuminuric (12%). As the study was conducted on newly detected T2DM patients meaning patients diagnosed <6 months duration, results of nephropathy need to be reproduced after 6 months, which could have led to increased nephropathy in our study population. However, the study by Ali *et al.* have also documented nephropathy in 44.24% of subjects.[15]

Neuropathy was found to be a second most common microvascular complication in our study and was detected in 33% patients. Our results were comparable to Yash *et al.*, who found neuropathy in 36% of patients at presentation and Nambuya, who found neuropathy in 46%.[16,17] However, Karmakar *et al.*, Engelgau *et al.*, and Sosale *et al.* found neuropathy only in 9%, 14%, and 13.5% patients, respectively.[18-20]

In our study, we found that retinopathy as the least common microvascular complication (6%). Sosale *et al.* and Cathelineau *et al.* found retinopathy in 6% and 10% of patients.[20,21] Whereas Xu *et al.* and Yash *et al.* found retinopathy in 19.6% and 24% of patients, respectively.[16,22]

In our study, we found that microvascular complications were more common in patients with HbA1C more than 7.5% than in patients with HbA1C <7.5%. However, none of the values attained statistically significant difference ($P > 0.05$).

Limitations of Our Study

Our study was a tertiary care hospital-based study and not a community-based study. The sample size was relatively small. A bigger sample size and comparing the difference between the prevalence of microvascular complications in a hospital-based and community-based study in our population would be worthwhile.

CONCLUSION

Microvascular complications are a major cause of morbidity and mortality in DM. These complications can be present

even at the time of diagnosis of T2DM. A long phase of asymptomatic hyperglycemia in T2DM patients is responsible for microvascular complications at diagnosis. A high prevalence of microvascular complications at the time of diagnosis in our study reconfirms that assessment for these complications must be done at the time of diagnosis in all patients. Once complications develop, in addition to strict control of hyperglycemia, steps have to be taken to prevent or retard further progression of these complications and even reverse these initial phase of complications. Education of high-risk group regarding diabetes and its complications by electronic and print media is required so that they seek medical consultation at the earliest. We may need to screen our population for diabetes at a younger age in view of lower average age at presentation and high prevalence of microvascular complications. Primary health care providers should be sensitized to have a low threshold for screening for diabetes and encouraged to look for microvascular complications in all T2DM patients at the time of diagnosis. Screening for early detection and identification of risk factors for neuropathy, nephropathy, and retinopathy may prevent or delay the progression of microvascular complication.

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Original Article

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Comparative Functional Analysis between Titanium and Stainless Steel Proximal Femoral Nail in the Treatment of Intertrochanteric Fractures of Femur

A Prabhakaran[1], R Nandakumar[2]

[1]Post-graduate, Department of Orthopaedics, Mahatma Gandhi Medical College & Research Institute, Pillayarkuppam, Puducherry, India, [2]Professor, Department of Orthopaedics, Mahatma Gandhi Medical College & Research Institute, Pillayarkuppam, Puducherry, India

Abstract

Introduction: Intertrochanteric fractures constitute one of the most common fractures of the hip. The incidence of fractures in the trochanteric area has risen with the increasing numbers of elderly persons with osteoporosis.

Materials and Methods: The study is a prospective study done from January 2014 to July 2015 in MGMCRI, Pondicherry. The sample size was 60 with two groups of 30 each who underwent titanium and stainless steel proximal femoral nail. Patients were evaluated preoperatively and underwent closed reduction and proximal femoral nailing. Patients were mobilized immediately following surgery with full weight bearing with a walker support. Patients were assessed postoperatively with Harris hip score, radiological union, and complication related to implants and surgical site at 1, 2, 4, and 6 months.

Results: In this study, we found that majority of patients were male, with age group <60, involving mostly left side with the mode of injury being trivial fall. Type 2 Boyd and Griffin fractures were more in numbers. Harris hip score showed a significant improvement in regular follow-up in both the groups. Patients were started on early full weight bearing mobilization with walker support on the first post-operative day which helped in achieving a good outcome in Harris hip score in both the groups. Comparatively stainless steel group had three implant-related complications, and titanium groups had one implant-related complication at the end of this study. One patient in titanium group had non-union due to varus collapse. This was further treated with bipolar hemiarthroplasty. There was no surgical site infection in our study, inspite of giving only three doses of antibiotics.

Conclusion: In this study, the superiority of the properties of titanium nail did not make any significant difference with the stainless steel nail usage in relation to clinical and radiological outcome.

Key words: Intertrochanteric, Stainless steel, Titanium

INTRODUCTION

Intertrochanteric fractures constitute one of the most common fractures of the hip. The incidence of fractures in the trochanteric area has risen with the increasing numbers of elderly persons with osteoporosis.[1,2] Although a large number of different implants are available for fixation, the ideal implant for the treatment of intertrochanteric fractures is still a matter for discussion. The imperative goals of treatment are early mobilization by means of stable fixation using as minimally invasive procedure as possible. Nowadays, there is an increasing interest in intramedullary nailing, especially for unstable intertrochanteric fractures.[3-5] This study on unstable trochanteric fractures focuses primarily on the reliability of fracture determination and classification, the (biomechanical) influence of the fracture on the fixation device, and the effect of a given fixation device on the fracture (healing and outcome). As surgeons often tend to forget their own contribution and influence on successful treatment outcome, we aimed to analyze the quality of fracture handling (classification and reduction) and stabilization by the surgeon, and the subsequent impact on the treatment outcome between the groups treated with titanium proximal femoral nail and stainless steel proximal femoral nail.

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Corresponding Author: Dr. A Prabhakaran, No.564, Bharathi Street, Uppalam, Puducherry, India. E-mail: Prabhu198926@gmail.com

Aims and Objectives

Aim

- To compare and assess the functional outcome between titanium proximal femoral nail and stainless steel proximal femoral nail in the treatment of intertrochanteric fractures of the femur.

Objective

- To compare the versatile nature of titanium proximal femoral nail and stainless steel proximal femoral nail in the treatment of intertrochanteric fracture of femur
- To analyze the rate of union and surgical site complications between the two implants.

MATERIALS AND METHODS

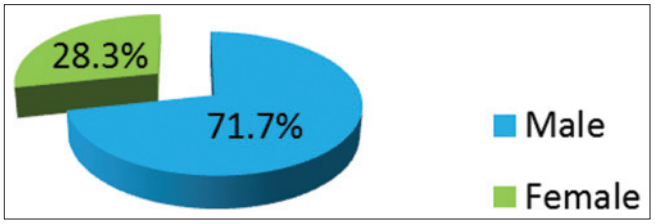
In our study, the patients who were admitted to the Mahatma Gandhi Medical College and Research Institute in the Department of Orthopedics with intertrochanteric fracture were included. The number of groups present in the study is two: Group A - those who is treated using titanium proximal femoral nail and Group B - those who are treated using stainless steel proximal femoral nail. The present study is longitudinal comparative study. The study period is from January 2014 to July 2015. Patients were treated with closed reduction and internal fixation with proximal femoral nailing by routine technique. Patients were followed up both clinically and radiologically at 1st, 2nd, 4th, and 6th month postoperatively.

RESULTS

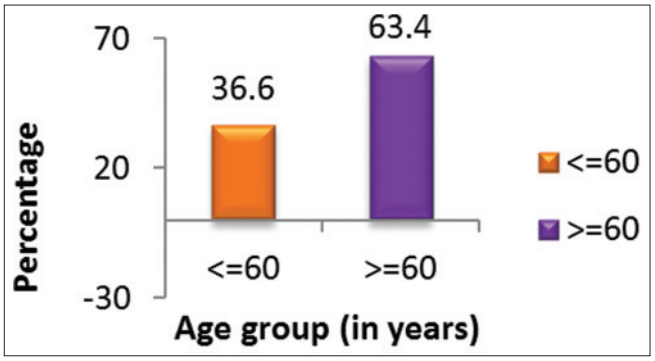
Out of 60 patients, the majority of them are male in the age group of <60 years. Their mode of injury is mostly fall alone than road traffic accident (RTA). Further injuries were observed, the majority of them had an injury at the left side and Type 2 fracture is higher than Types 3 and 4. All patients in this study received three doses of antibiotics, which was our institutional protocol. Harris hip score in the first 2 months was same showing similar results with most of the patients in both groups had fair score predominantly. During 1st month follow-up, there were less implant-related complications in titanium, but this was higher in stainless steel nail. Two patients had complications, one patient had back out of lag screw, and another patient had derotation screw tip breakage. In one patient in stainless steel nail group, we encountered stress fracture at distal locking site while fixing it intra operatively; hence, the patient was on high above knee slab postoperatively. During the 2nd month, one patient developed myositis ossificans due to massaging at native bone setting center. However, the implant-related complications were higher in stainless steel group. At the end of 4th month follow-up, Harris hip score rate was good in titanium, implant-related complications were less in titanium than stainless steel. In titanium group, one patient had non-union of intertrochanteric fracture which was then treated with bipolar hemiarthroplasty. In stainless steel group, one patient had derotation screw tip breakage. At the end of 6th month follow-up, we found that both the groups were showing improvement in Harris hip score, five patients from both the groups had excellent Harris hip, but the implant-related complications were more in stainless steel group. At the end of 6th month follow-up, when limb length discrepancy was measured, 5 patients had <10 mm shortening and 9 patients had more than 10 mm shortening of the operated limb (Graphs 1-5).

Functional Outcome at 1st Month Follow-up

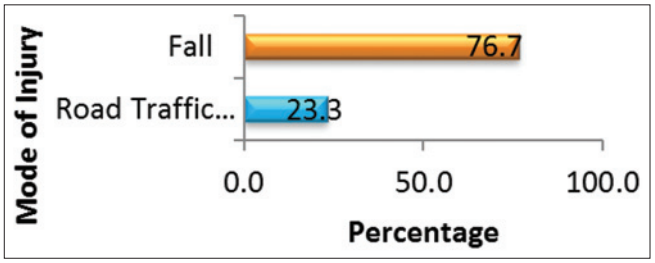
In titanium nail group, Harris hip score was poor in 6 (20.0) patients, fair in 19 (63.3%) patients and good in 5 (16.7) patients, whereas in stainless steel nail group it was fair in 17 (56.7%) patients and good in 13 (43.4) patients. There was no radiological union in both the groups. When implant-related complication is compared, titanium group did not have any complication, whereas stainless steel group had



Graph 1: Gender distribution



Graph 2: Age distribution

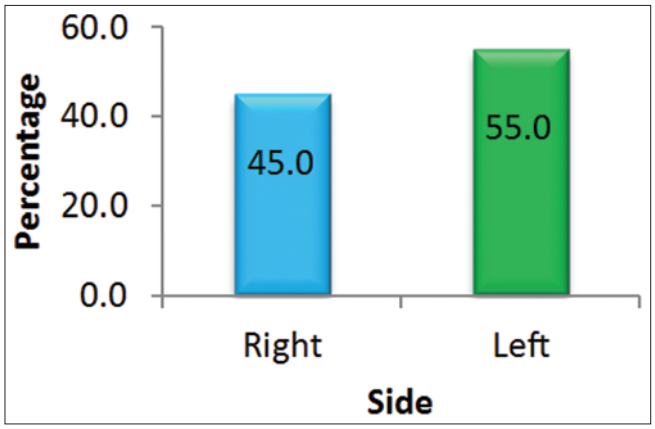


Graph 3: Mechanism of Injury

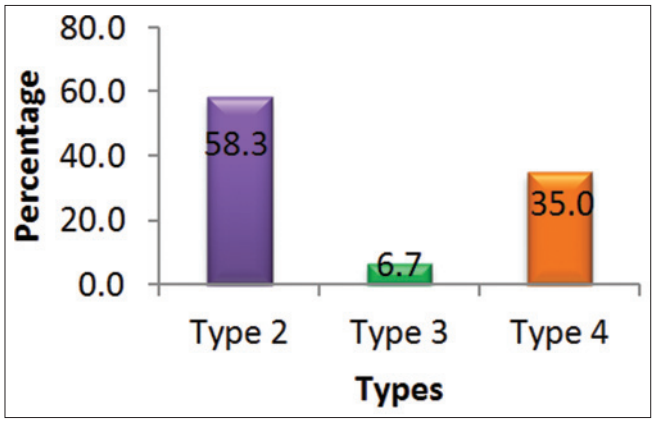
two complications, one patient had back out of lag screw, and another patient had a break of the derotation screw [Figures 1a and 2]. There was no surgical site infection in both the groups at the end of 1st month follow-up (Graph 6).

Functional Outcome at 2nd Month Follow-up

In titanium nail group, Harris hip score was poor in 6 (20.0) patients, fair in 19 (63.3%) patients, and good in 5 (16.7) patients, whereas in stainless steel nail group it was fair in 17 (56.7%) patients and good in 13 (43.4) patients. When the radiological union was compared, 27 (90.0%) patients in titanium nail group and 28 (93.3%) patients in stainless steel group did not show radiological union. In one patient, we encountered myositis ossificans at the 2nd month follow-up. There was no fresh implant-related complication in both the groups during the 2nd month follow-up. There was no surgical site related complication in both the groups at the end of the 2nd month (Graphs 7-9).



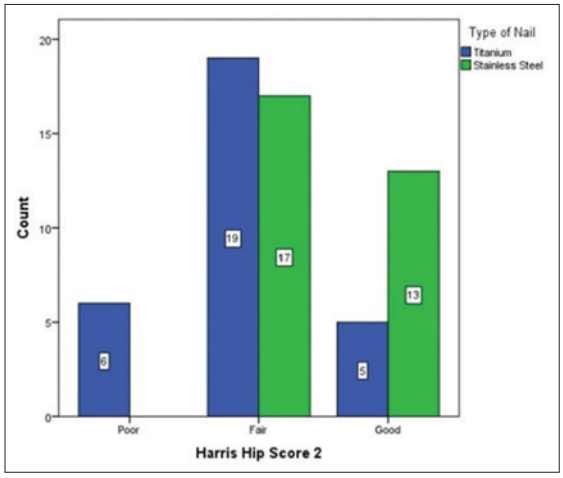
Graph 4: Distribution of side



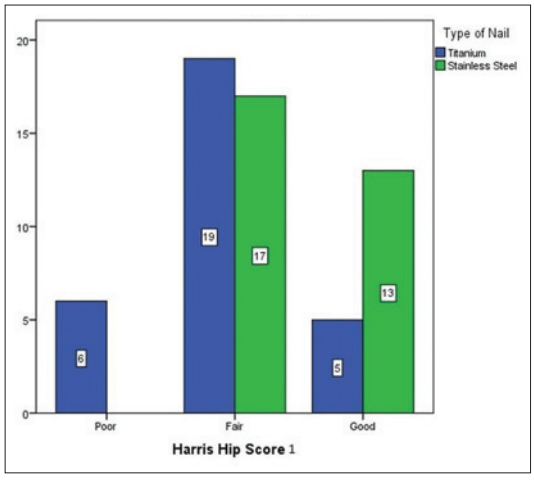
Graph 5: Distribution to Boyd and Griffin classification

Functional Outcome at 4th Month Follow-up

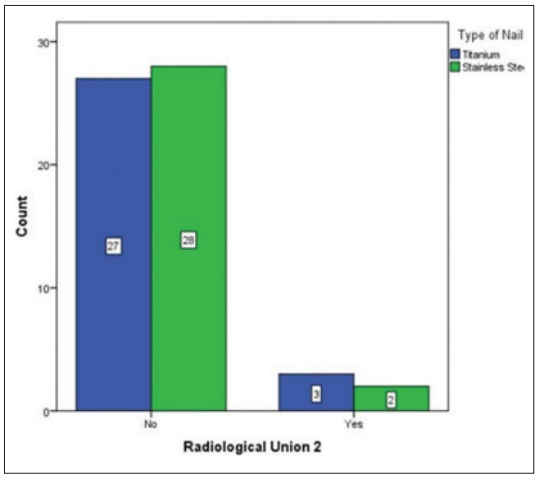
At the 4th month follow-up in titanium nail group, 2 (6.7) patients had poor, 12 (40.0) had fair, and 16 (53.3) had good Harris Hip score. In stainless steel nail group, 3 (10.0) patients had poor, 8 (26.7) patients had fair, 16 (53.3) patients had good, and 3 (10.0) patients had excellent Harris Hip score. When the radiological union was compared between both the groups, 29 (96.7%) patients in titanium group showed radiological union, while 1 patient developed non-union due to varus collapse. In



Graph 7: 2nd month Harris hip score with type of nail



Graph 6: 1st month Harris hip score with type of nail

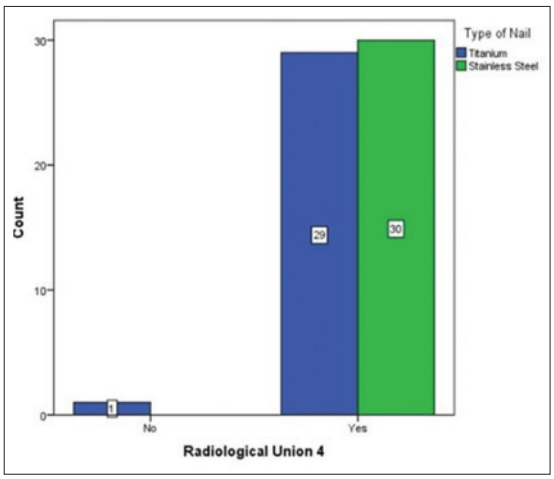


Graph 8: 2nd month radiological union with type of nail

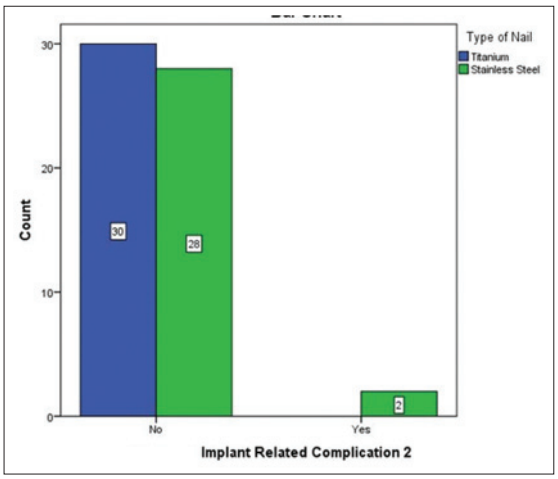
stainless steel group, all the 30 (100.0%) patients showed radiological union at the end of 4th month follow-up. When implant-related complications were compared, 29 (96.7%) patients in titanium group did not have any implant-related complication, whereas 1 patient showed nonunion of intertrochanteric fracture which was then treated with bipolar hemiarthroplasty [Figure 3]. In stainless steel nail group, 27 (90.0%) patients did not have any implant-related complication, and 1 patient had derotation screw tip breakage [Figure 1b]. There was no surgical site related complication in both the groups at the end of the 4th month follow-up (Graphs 10-13).

Functional Outcome at 6th Month Follow-up

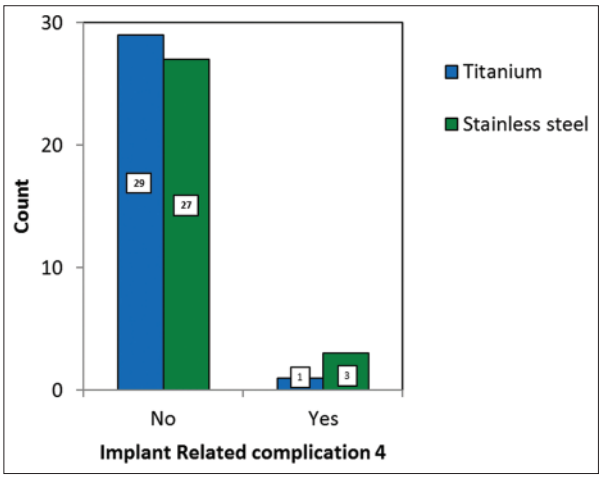
Harris Hip score at the end of the 6th month follow-up showed poor in 5 patients, fair in 2 patients, good in 18 patients, and excellent in 5 patients. In stainless steel nail group, Harris hip score showed poor in 3 patients, fair in 5 patients, good in 17 patients, and excellent in 5 patients. When the radiological union was assessed between both the groups, stainless steel group showed 100% union and titanium group showed union in 29 (96.7%) patients. There was no implant-related and surgical site related complication in both titanium and stainless steel group at the end of the 6th month follow-up (Graphs 13-16).



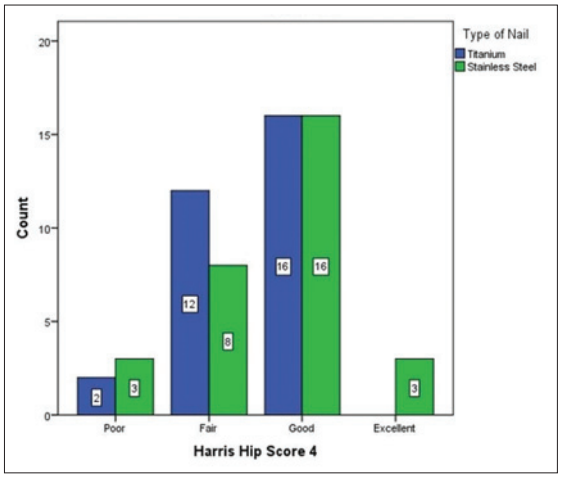
Graph 11: 4th month radiological union and type of nail



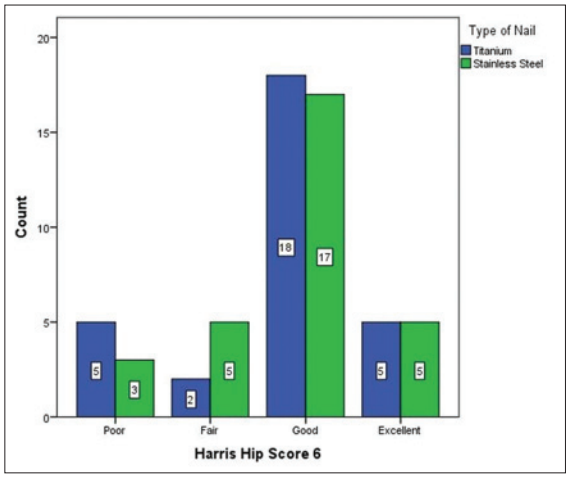
Graph 9: 2nd month implant-related complication with type of nail



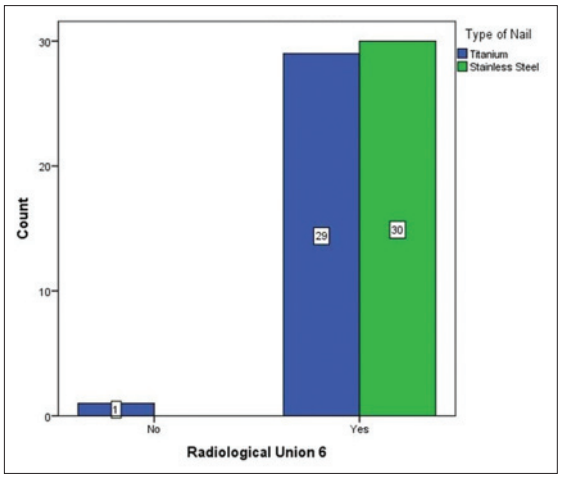
Graph 12: 4th month implant-related complication and type of nail



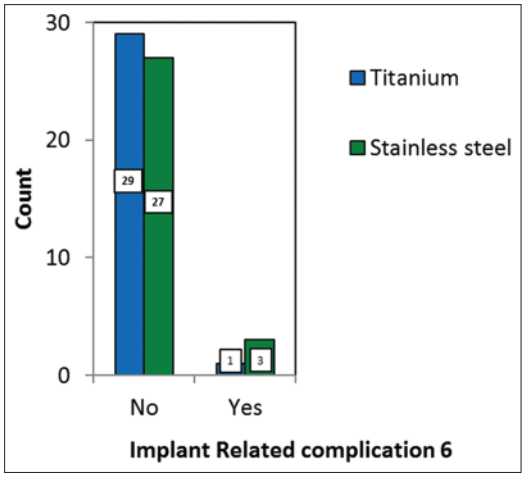
Graph 10: 4th month Harris hip score with type of nail



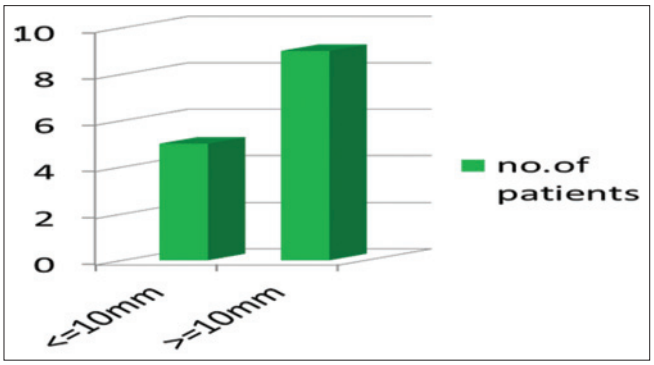
Graph 13: 6th month Harris hip score with type of nail



Graph 14: 6th month radiological union with type of nail



Graph 15: 6th implant-related complication with type of nail



Graph 16: Shortening at 6 months follow-up

DISCUSSION

The majority of them are male in the age group of <60 years were participated in this study. Age group in the study is well-supported by other studies in the field.[1,2] Their study reported that the incidence of fractures in the trochanteric area has risen with the increasing numbers of elderly persons with osteoporosis. Further, the majority of the participants in this study reported that injury occurs due to fall alone and only less number of them was involved in RTA. In line with this, the study of Huang *et al.*[6] observed the majority of the injuries occurred due to fall and RTA. With regard to the side of the injury, most of the injury reported that they had left side. In line with our study result, the studies of Ali[7] Eggensperger *et al.*[8] and Yazici *et al.*[9] showed similar results. Further, the study also observed Type 2 injury was reported higher in comparison with other types such as Types 3 and 4. Similar to this, the study of Benzel and Connoly[10] observed Type 2 injury is more complicated than other types. To attain the below objective, the present study carried out complication tests in different months are as discussed below:

In this study, 50% of the patients had titanium and remaining 50% had stainless steel nail. Most of the fractures were an unstable intertrochanteric fracture of Type 2 and Type 4. The result of the present study is supported by Baumgaertner *et al.*,[3] Adams *et al.*,[4] and Klinger *et al.*[5] where they have proved that unstable intertrochanteric fractures can be treated with intramedullary nailing. In this study, all patients were mobilized on first post-operative day which was very much supported by a study done by Mohammed *et al.*, which proves early mobilization with weight bearing improves the morbidity status of the patient and also gives a good outcome at regular follow-ups when assessed with Harris hip score.[11]

The study identifies the complications of 1st, 2nd, 4th, and 6th month, and we have found that implant-related complications were higher in terms of using stainless steel nail. In line with this, Uhthoff *et al.*[12] and Sagan *et al.*[13] showed the similar result like titanium is effective and less complications than stainless steel. In line to our study finding, the study of Wall *et al.*[14] Rios *et al.*[15] have proved that stainless steel provides a good functional outcome in pediatric femoral shaft fractures. During the 1st month and 4th month follow-ups, two cases from stainless steel group had derotation screw tip breakage; this may be related to the less strength and rigid properties of stainless steel implants.[16] When shortening was evaluated at the 6th month follow-up, we found that patients who had varus collapse showed more shortening in both the groups which has been proved by a study conducted by Pauveldousa *et al.*[17] From the overall study findings, it was observed titanium and stainless steel nail shows no difference in relation to functional outcome, union, surgical site infection, and implant-related complications. However, there was the incidence of more implant-related complications in stainless steel nail group when compared to titanium nail group.[18]

LIMITATIONS AND RECOMMENDATIONS FOR THE FUTURE

Normally post implant removal all the nails should have been subjected in the metallurgical analysis to see any damage or loss of substance from the implant surface. By this method, we could have reached a conclusion regarding actual properties of both metal implants with respect to corrosion and biocompatibility, not done because we had no failures. Short duration and less number of subjects are also a limitation in our study.

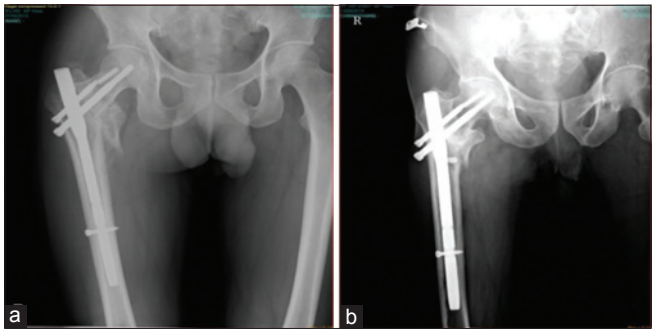


Figure 1: Derotation screw tip breakage in two patients stainless steel group

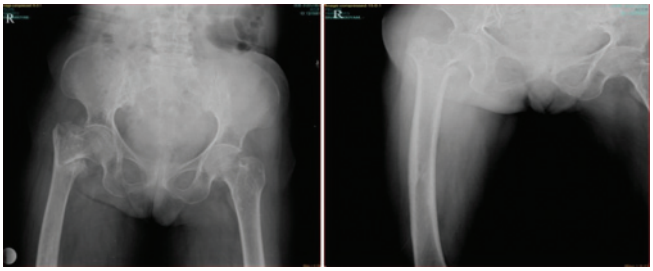
Figure 2: X-ray showing back out both screws in stainless steel group

CONCLUSION

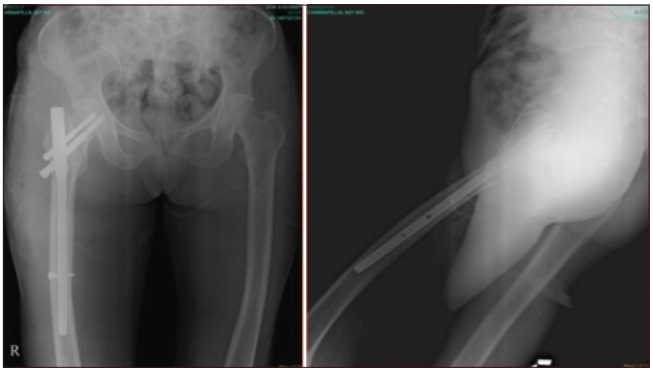
Functionally 76% of our patients had good and excellent Harris hip score. Both implants acted similarly with respect to union and achieved union in all the cases except one in titanium group. In our study, we did not encounter a single case of surgical site infection. Early full weight bearing mobilization with walker support helped in achieving a good outcome in both nail groups. In this study, the superiority of the properties of titanium nail does not make any significant difference with the stainless steel nail usage in relation to clinical and radiological outcome.

CASE ILLUSTRATIONS

Titanium nail (excellent outcome)



Pre-operative X-ray



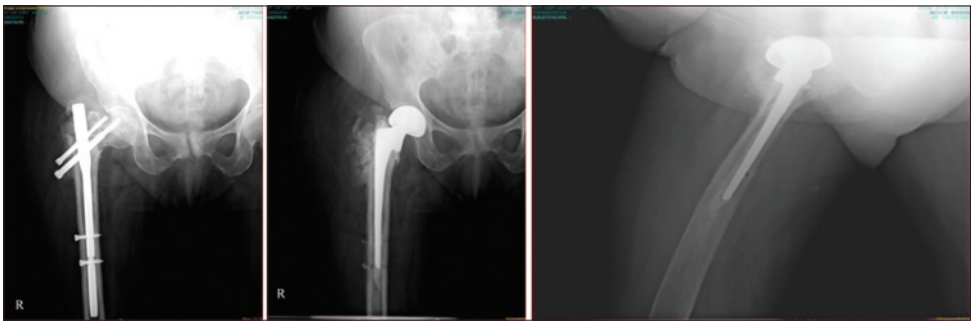


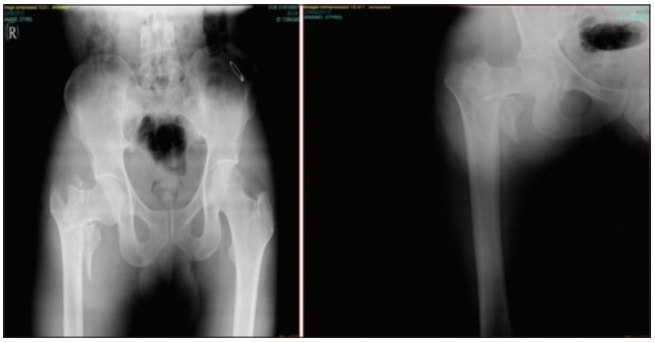
Figure 3: Titanium group complication showing varus collapse

6 months post-operative X-ray

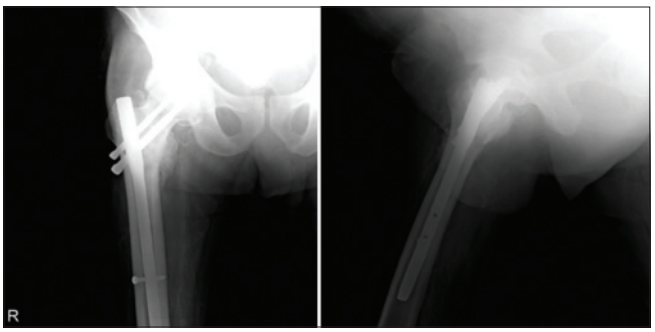
Titanium nail (excellent outcome)

Patient's clinical photographs

stainless steel (excellent outcome)



Pre-operative X-rays



6 months post-operative X-rays

Stainless steel nail (excellent outcome)

Bipolar hemiarthroplasty done after removal of proximal femoral nail and fracture mobility was checked under fluoroscopic which showed non-union

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Original Article

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Role of Adjuvant Lifestyle Modifications in Patients with Laryngopharyngeal Reflux Disease in Hilly Areas

Manpreet Singh Nanda

Associate Professor, Department of Otolaryngology Head & Neck Surgery Maharishi Markandeshwar Medical College & Hospital, Kumarhatti, Solan, Himachal Pradesh, India

Abstract

Introduction: Laryngopharyngeal reflux (LPR) is defined as a backflow of gastric contents into larynx and pharynx. This study aims to evaluate the effect of lifestyle modifications (LSM) as an adjuvant treatment along with proton pump inhibitors (PPIs) for the management of LPR disease.

Materials and Methods: A total of 200 patients with clinically and endoscopically diagnosed LPR disease were taken up in this study. 100 patients in the study group were asked to follow a list of LSM explained and given to them in their own language and were given oral rabeprazole tablet 20 mg twice daily 1 h before meals for 90 days. Remaining 100 patients in the control group were given 20 mg rabeprazole twice daily without LSM. The above treatment in both groups was given for 90 days. The patients in both groups were evaluated clinically and endoscopically after 45 days and 90 days of the treatment for improvement in clinical and endoscopic signs of LPR and patient satisfaction.

Results: The results showed that the major risk factors for LPR are spicy food and over intake of beverages along with habits like alcohol abuse and cigarette smoking. The results showed better and faster relief from reflux symptoms in the study group following LSM as compared to control group. There was a faster recovery of endoscopic signs in study group patients than the control group and greater patient satisfaction in the study group.

Conclusion: Hence, it can be concluded that life style modifications can be considered as an effective treatment if followed along with PPIs in patients with LPR disease.

Key words: Gastroesophageal reflux disease, Laryngitis, Laryngopharyngeal reflux, Lifestyle modifications, Proton pump inhibitors, Rabeprazole

INTRODUCTION

The prevalence of laryngopharyngeal reflux (LPR) among the population has increased dramatically at 4% a year.[1] It is a very common disease seen in ENT OPD and its treatment is a challenge for ENT surgeons as it affects half of patients with laryngeal and voice disorders.[2] LPR is defined as a reflux of stomach contents into larynx and pharynx[3] leading to tissue damage at upper airway level due to acidity of gastric juice.[4] There is an association between LPR and gastroesophageal reflux disease (GERD) with LPR being seen in 60% of patients with GERD.[3] The main manifestations of LPR are symptoms such as cough, sore throat, hoarseness, dysphonia, and globus, and laryngeal signs like erythema and edema seen at laryngoscopy.[5]

There is no standard treatment for LPR so far.[6] Since a long-time proton pump inhibitors (PPI) have been used as a potent suppressor of gastric secretions.[7] But its effect alone is doubtful. Many studies have failed to demonstrate any benefit of PPI alone.[8] A surgical treatment for LPR though tried but has also shown poor results in controlling the disease.[9]

Dietary and behavior modifications have been found to be a very effective in the management of LPR.[10] However,

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Corresponding Author: Dr. Manpreet Singh Nanda, H. No 554 Sector 36 B, Chandigarh, India. Phone: +91-8427187630/8894455504. E-mail: u_tell_me_80@yahoo.co.in

their effects have not been fully assessed. The results of various studies have remained controversial so far. Though recommended by many there is little evidence to prove their benefit. Even studies have shown that most general physicians do not believe in recommending and more than that insisting on lifestyle modifications as a part of treatment.[11] The main risk factors of LPR are dietary habits like alcohol, coffee, smoking, and psychological reasons.[12] Our institute being in hilly terrain here people are more habitual of beverages like tea, and there is a greater tendency to smoke and consume alcoholic drinks leading to greater incidence of LPR seen here. Hence, we have conducted this study to confirm whether lifestyle modifications (LSM) are effective in improving reflux symptoms and signs when given along with PPI in patients with LPR disease.

MATERIALS AND METHODS

This study was conducted in Department of ENT of our medical college and hospital which is located in hilly area from August 2013 to July 2014. 200 patients with diagnosed LPR were included in the study. The diagnosis of LPR was made by clinical history, endoscopic laryngeal findings and 24 h pH monitoring. The permission of local ethics committee was taken and written consent obtained from all the patients enrolled in the study. Only adult patients above the age of 18 years were included in the study. Exclusion criteria were patients known allergic to PPI, patients on any medications for chronic disorders like diabetes, hypertension, pregnant or nursing mothers, patients with diagnosed malignancies, achalasia and chronic peptic ulcers and patients unwilling to participate in the study.

All the 200 patients enrolled in this study underwent detailed history taking and diagnostic laryngoscopy examination at each visit. The patients were randomized alternatively into study and control group. 100 patients in the study group were advised to follow a set of LSM which were explained and given to them written in their own language (LSM details in the box below) along with tablet rabeprazole 20 mg twice daily 1 h before breakfast and evening meals. Remaining 100 patients in the control group were given tablet rabeprazole 20 mg twice daily 1 h before breakfast and evening meals without advising any LSM. The above treatment in both groups was given for 90 days.

The patients were assessed at the first visit, after 45 days and after 90 days of the treatment. The assessment points were as the following section.

1. The risk factors for LPR were investigated
2. The patients were assessed for clinical symptoms of LPR at each visit
3. The patients were assessed for endoscopic laryngeal signs at each visit
4. The patient satisfaction was assessed according to LIKERT SCALE at each follow-up visit.

10 point lifestyle modifications (LSM) for patients
To avoid hot, spicy and oily food
To avoid alcohol and cigarette smoking
To avoid beverages like coffee and tea
To avoid lying down for 1 h after meals
To avoid going to sleep for 2 h after dinner
Reduce to 3 meals a day with proper gap and a light dinner
Head end elevation while lying down
To drink small sips of water throughout the day
Voice rest
To avoid forceful throat clearing

RESULTS

About 200 patients who gave consent were enrolled in this study. All the patients underwent detailed clinical history taking and laryngoscopic examination at each visit. Data were collected on all patients. All the patients were above 18 years of age with the youngest patient of 20 years and eldest of 75 years of age. We found the majority of patients of lower middle age group (31-45 years 45%). There was a slight female predominance with male:female ratio of 1:1.3 (Table 1).

Regarding the risk factors of LPR, most of the patients had a habit to eat lots of spicy food (93%) and intake lots of tea during day time (96%). There was a tendency of cigarette or beedi smoking (42%) and alcohol intake abuse (38%) among the patients with LPR. (Figure 1) We found the habit of cigarette smoking and alcohol intake even among females in this area.

100 patients in the study group were advised to follow 10 point LSM as described earlier along with tablet rabeprazole 20 mg twice daily. Remaining 100 patients in the control group were given tablet rabeprazole 20 mg twice daily without advising any LSM. The above treatment in both groups was given for 90 days. The patients were assessed at the first visit, after 45 days and after 90 days of treatment.

Table 1: Age and sex distribution

Age group (years)	Male	Female	Total
<30	22	29	51
30-45	41	49	90
46-60	18	24	42
>60	7	10	17
Total	88	112	200

The major clinical symptom seen in our patients with LPR was foreign body sensation in throat or globus follow by change in voice or hoarseness. The other major symptoms were chronic non-productive cough, sore throat, heartburn, and post nasal discharge (Table 2). Regarding the endoscopic signs 59% patient in study group and 61% patients in control group had laryngeal congestion or edema at initial visit. The most common part of larynx was the posterior larynx involving arytenoids, interarytenoid area and posterior vocal cords. Around 25 % patients in both groups at initial visit had posterior pharyngeal wall congestion (Table 3).

Our results showed comparatively more number discontinued study in study group with LSM as compared to control group. This was due to difficulty in understanding and the following 10 points LSM by these patients in study group. On the contrary, much lower number of patients were lost to follow-up in study group at end of 90 days (14% in study group as compared to 24% in control group. This could be attributed to better cure rate in study group (Table 2).

Regarding the results 67% of patients had some improvement in their symptoms after 45 days in study group as compared to 50% in control group. This shows better and faster improvement in patients following 10 point LSM. There was greater patient satisfaction at the end of 90 days treatment in study group than control group (Table 4). There was much better faster improvement in clinical symptoms in study group as compared to control group (Table 2).

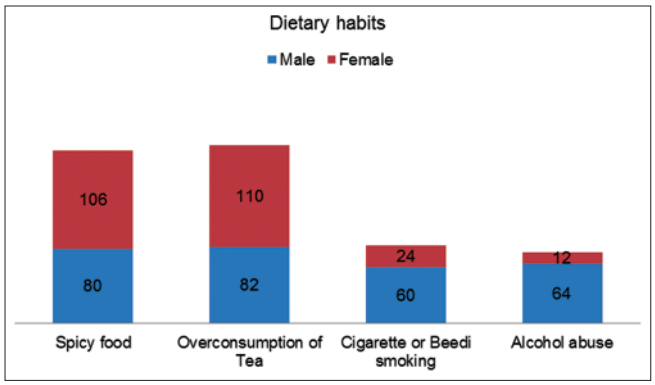

Figure 1: Risk factors of laryngopharyngeal reflux in the patients. The number denotes the number of patients

There was a better relief of laryngeal congestion and edema in study group than control group. This difference was a more remarkable after 45 days of treatment (Table 5). This shows faster relief of endoscopic signs of LPR when adjuvant lifestyle modifications were advised. Patients with posterior pharyngeal wall congestion were also much lower in study group.

We found in our results that most patients were able to follow this 10 point LSM as were they were explained and given to them in writing in their own language. Since the literacy rate of our region is high, and most of patients could read and understand in their native language we achieved a higher response rate of 74% patients in study groups following the treatment protocol and completing the study (Table 2).

DISCUSSION

The efficacy of LSM as adjuvant treatment along with PPI in patients with LPR was investigated in this study. The primary aim of this study was to evaluate the role of lifestyle modification in the treatment of signs and symptoms of LPR and the second aim was to evaluate the risk factors of the LPR.

We have devised a 10 point LSM in patient's own language so that the patient can understand and follow them in a better way and the response we got as explained earlier was very encouraging.

LPR is defined as backflow of stomach contents up the esophagus into larynx and pharynx leading to chronic laryngeal and pharyngeal disorders. There is growing prevalence of LPR in patients with GERD. The reflux

Table 2: Clinical symptoms in the patients at each visit

Symptom	First visit (%)		After 45 days (%)		After 90 days (%)	
	Study group	Control group	Study group	Control group	Study group	Control group
Foreign body sensation (Globus)	88 patients (88)	85 patients (85)	49 patients (60)	56 patients (70)	26 patients (35)	29 patients (42)
Change in voice (Hoarseness)	56 patients (56)	58 patients (58)	30 patients (37)	35 patients (44)	18 patients (24)	19 patients (28)
Chronic cough	30 patients (30)	31 patients (31)	16 patients (20)	20 patients (25)	10 patients (14)	11 patients (16)
Post nasal discharge	15 patients (15)	14 patients (14)	9 patients (11)	9 patients (11)	5 patients (7)	5 patients (7)
Sore throat	18 patients (18)	19 patients (19)	10 patients (12)	13 patients (17)	4 patients (6)	7 patients (10)
Difficulty in swallowing (Dysphagia)	3 patients (3)	3 patients (3)	2 patients (2)	2 patients (2)	2 patients (3)	2 patients (3)
Heart burn	18 patients (18)	20 patients (20)	8 patients (10)	12 patients (15)	4 patients (6)	7 patients (10)
Discontinued study	-	-	10 patients	5 patients	12 patients	7 patients
Lost to follow-up	-	-	8 patients	15 patients	14 patients	24 patients

of gastric contents contains harmful agents like acid and activated pepsin. Pepsin causes inflammation and mucosal damage of larynx leading to laryngitis. This disease according to studies is now prevalent in younger age group.[13] In our study, we found the most common age group affected to between 30 and 45 years of age (Table 1). According to Haruma *et al.* 58% of patients with reflux disease are females.[14] Similarly, in our study, we found female predominance among patients in our study and control group (Table 1). The major risk factors in our study were spicy food and overconsumption of tea along with alcohol and cigarette smoking (Figure 1) with similar findings in literature available.[12]

According to a study, the most common symptoms of LPR are a persistent cough (97%), globus (95%), and hoarseness of voice (95%).[15] In our study, we found globus to be the most common symptom followed by hoarseness, cough and sore throat (Table 2). Literature shows not all patients with reflux to have physical findings.[16] In our study, we found only 60% patients with reflux symptoms having laryngeal signs (Table 3). Lundy *et al.* found eythema of larynx to be the most common sign.[17] The literature shows that thickness, redness and edema of posterior larynx is most common in reflux laryngitis.[18] In our study, we found the most common region involved to be posterior larynx and most common sign seen was laryngeal congestion (Table 3).

The mainstay of treatment of LPR so far has been PPI. But its efficiency alone is doubtful.[8] Studies have shown that even after PPI treatment more than 30% patients fail to respond.[19] In our study, we found nearly half of the patients in control group with only rabeprazole given as treatment did not respond to the treatment with no improvement in their symptoms at end of 45 days treatment (Table 4). There is a lack of enough studies to prove the effect of LSM. Steward *et al.* found that lifestyle modifications for 2 months with PPI therapy improved chronic laryngitis symptoms.[20] Similar results regarding efficacy of LSM were obtained by Hamilton *et al.* in 1988.[21] According to studies for other diseases changes in lifestyle promotes a sense of well-being in the patient by shifting his focus from his disease.[22]

In our study, we found advising LSM (10 point LSM) along with PPI led to greater improvement in patients as compared to PPI alone after 90 days of treatment. We also obtained faster improvement in patients in study group as compared to control group after 45 days treatment (Table 4). This improvement was much better for clinical symptoms such as globus, hoarseness, chronic cough, heartburn, and sore throat at end of 90 days treatment in study group with 10 point LSM than control group and much faster relief after 45 days of treatment using LSM (Table 2). Laryngeal and posterior pharyngeal wall congestion was also much lesser in study group than control group after 45 and 90 days of treatment (Table 5).

Table 3: Diagnostic laryngoscopy findings at initial visit

Signs	Study group (%)	Control group (%)
Posterior larynx (arytenoids, interarytenoid area, posterior vocal cords) congestion or edema	41 patients (41)	42 patients (42)
Anterior larynx (anterior vocal cords, ventricles) congestion or edema	8 patients (8)	10 patients (10)
Diffuse laryngeal (both anterior and posterior) congestion or edema	10 patients (10)	9 patients (9)
Total patients with laryngeal signs	59 patients (59)	61 patients (61)
Posterior pharyngeal wall congestion	24 patients (24)	25 patients (25)

Table 4: Patient satisfaction in both groups

Satisfaction	After 45 days (%)		After 90 days (%)	
	Study group	Control group	Study group	Control group
Very comfortable (total relief)	20 patients (25)	14 patients (18)	26 patients (35)	22 patients (32)
Comfortable (improvement)	35 patients (42)	25 patients (32)	35 patients (47)	29 patients (42)
No change	25 patients (31)	39 patients (48)	11 patients (15)	16 patients (23)
Uncomfortable (worsened)	2 patients (2)	2 patients (2)	2 patients (3)	2 patients (3)

Table 5: Diagnostic laryngoscopy findings at follow-up visits

Signs	After 45 days (%)		After 90 days (%)	
	Study group	Control group	Study group	Control group
Laryngeal congestion or edema	33 patients (41)	40 patients (50)	19 patients (25)	23 patients (33)
Posterior pharyngeal wall congestion	14 patients (17)	16 patients (20)	8 patients (11)	10 patients (15)

CONCLUSION

Life style modifications when advised along with PPIs are effective in treating the signs and symptoms of LPR. When used as adjuvant treatment along with PPI they fasten the relief to the patients suffering from LPR. Patient satisfaction was much higher when 10 points LSM was followed by the patient along with rabeprazole. There is a need to properly explain the LSM in patient's own language to make him understand and gain his confidence.

The major risk factors of LPR are overconsumption of beverages like tea and too much spicy food. Habit like alcohol intake and cigarette smoking also contribute to LPR.

There is the scope of further studies along this line of management.

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Original Article

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Comparative Evaluation of Fracture Resistance of Tooth after Lateral and Vertical Obturation Filled with Gutta-Percha and Resilon Obturating Material: An *In Vitro* Study

Supratim Tripathi[1], Mubashir Baig Mirza[2], Mohammed Zaheer Kola[3]

[1]Assistant Professor, Department of Conservative Dentistry and Endodontics, Career Post Graduate Institute of Dental Sciences, Lucknow, Uttar Pradesh, India, [2]Faculty, Department of Conservative Dentistry and Endodontics, College of Dentistry, Prince Sattam Bin Abdul Aziz University, Alkharj Kingdom of Saudi Arabia, [3]Faculty, Department of Prosthodontics, College of Dentistry, Prince Sattam Bin Abdul Aziz University, Alkharj Kingdom of Saudi Arabia

Abstract

Introduction: Since long the obturating material and techniques have been discussed. The prime target of the material has always been to provide a three-dimensional obturation providing a monoblock concept thus strengthening the tooth.

Aim: The aim of the study was to evaluate the fracture toughness of the root canal treated teeth after being oturated with Gutta-Percha and Resilon by lateral and vertical compaction techniques.

Materials and Methods: A total of 75 human mandibular premolar teeth were taken and endodontically treated. All the teeth were divided into five groups with 15 samples in each. Access opening of all the teeth was done, and the cleaning and shaping were done up to 40 number file size. The samples were obturated with two materials which are Gutta-Percha and Resilon. All the teeth were subjected to compressive loading till the fracture occurred, and the readings were taken and compared. It was found that the teeth obturated with Resilon showed higher fracture resistance and that the obturating technique had no effect on fracture resistance.

Result: This study shows the relevant difference between the two groups and that the group with Resilon showed better fracture toughness when applied with universal testing machine.

Conclusion: This study concluded that Resilon is a better obturating material and that vertical condensation is better than lateral condensation.

Key words: Fracture resistance, Resilon, Vertical compaction and lateral compaction

INTRODUCTION

Endodontically treated teeth are widely considered to be a more susceptible to fracture than are vital teeth.[1,2] The reasons most often reported have been the water loss and loss of collagen cross-linking,[3,4] excessive pressure during obturation and the removal of tooth structure during endodontic treatment.[5,6] The strength of an endodontically treated tooth is related directly to the method of canal preparation and to the amount of remaining sound tooth structure.[7] It is commonly believed that the loss of dentin creates an increased susceptibility to fracture.[7] Resin-based dental materials have been proposed as a means to reinforce an endodontically treated tooth in the form of adhesive sealers in the root canal system. Dentin thicknesses, the radius of canal curvature and external root morphology have been proposed as factors potentially influencing fracture susceptibility.[8,9] This study deals with the fracture resistance of the tooth after being obturated with lateral and vertical obturating technique with Gutta-Percha and Resilon as two different

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Corresponding Author: Dr. Supratim Tripathi, Department of Conservative Dentistry and Endodontics, Career Post Graduate Institute of Dental Sciences, Lucknow, Uttar Pradesh, India. Phone: +91-7800302984. E-mail: t.supratim@yahoo.com

materials. The thinner the dentin, the more likely the tooth is to fracture.[10] However, bonding agents and resins studied to date as root filling materials had problems in working properties, radiopacity, and lack of re-treatability when used for endodontic purposes.[11] A low radius of canal curvature can act as a stress raiser area, which makes the root more susceptible to fracture.[11] In this study, the compressive load was subjected at a crosshead speed of 1 mm/min until the fracture of root occurred with a Universal testing Machine. The study was done in the Department of Conservative Dentistry and Endodontics, Career Post Graduate Institute of Dental Sciences, Lucknow, Uttar Pradesh, India, between December 2014 and March 2015.

MATERIALS AND METHODS

About 75 freshly extracted human mandibular premolars with fully formed apices, free of apical root resorption and caries were collected from the Department of Oral and Maxillofacial Surgery, Career Post Graduate Institute of Dental Sciences, Lucknow, Uttar Pradesh, India and were stored in 10% formalin.

List of materials used is as follows:

- Micro motor cord and straight piece
- Diamond disks
- Stainless steel files (10-40)
- Disposable syringe
- 5.25% sodium hypochlorite
- 17% EDTA
- Gates glidden drills
- Spreaders
- Plungers
- Lentulo Spiral
- Gutta-Percha
- AH 26 root canal sealer
- Resilon obturating materials (Pentron Clinical Technologies, Llc Wallingford, Ct).

The collected samples were cut at the cementoenamel junction (CEJ) with a diamond disk. The working length was established with 10 number file, 1 mm short to the apex. A crown down preparation technique was carried out in all the teeth. Preparations were irrigated between uses of each succeeding file with sodium hypochlorite (5.25%). After preparation the entire specimen were flushed with the EDTA, to remove smear layer and canal will be dried with paper points. Teeth were divided into 5 groups with 15 each. The canals were prepared up to 40 (k).

Group and its subgroups:

- A0: Control group. This group received no obturation; the canal opening was sealed with a temporary filling material (cavit).
- A1: Lateral condensation with Gutta-Percha. AH 26 sealer was used as a sealer. The cavity was sealed with cavit.
- A2: Vertical condensation with Gutta-Percha. Obtura II warm Gutta-Percha system was used with size 40 Gutta-Percha master cone point dipped in AH 26 sealer. The cavity was sealed with cavit.
- A3: Lateral condensation with Resilon. The primer was applied using paper point. Then, the sealer is mixed according to manufacturer's instructions. Resilon sealer was placed with a lentulo. After placing the master cone to the working length, accessory cones were placed dipped in Resilon sealer for the lateral condensation. The cavity was sealed with cavit.
- A4: Vertical condensation with Resilon. Vertical condensation was done using the heated pluggers and Obtura II warm Gutta-Percha system using a size 40 Resilon master cone dipped in resin sealer. The sealer was placed with a lentulo. After placing the master cone to the working length, we used heated pluggers to remove the Gutta-Percha point about 4 mm from the apex and for the vertical compression. After this procedure, the material was cured in the root canal for 30 s. The cavity was sealed with cavit.

The collected samples were cut at the CEJ with diamond disk. The working length was established with 10 no file, 1 mm short to the apex. Then, all the teeth were enlarged to the size 40 number. Preparations were irrigated between uses of each succeeding file with sodium hypochlorite (5.25%).

Preparation for Mechanical Testing

The root specimens were then prepared for mechanical testing. Apical root ends were embedded individually in phenolic rings with acrylic resin, living 9 mm of each root exposed, this was done so as to eradicate any chance of overfilling and to make sure that the obturating material did not come out of the apical foramen. Carbide bur was used to remove temporary material and to shape the root canal access to accept the loading fixture. Mounted cylinders were vertically aligned in the testing machine one at a time. Cylinders were mounted and aligned on the machine which has a fixed top standardizing the mounting. The compressive load was applied with a loading fixture with a spherical tip ($r = 2$ mm) at a crosshead speed of 1 mm/min until the fracture of root occurred. This load was applied at the canal opening. The amount of load obturated teeth can take was noted and it was evaluated which group of teeth can take maximum loads.

RESULTS

Fracture resistance of tooth in groups is measured, and the mean and standard deviation values of the applied force (mpa) according to groups are given in Tables 1-4 (Figure 1).

Table 1: Difference between the fracture resistance

Groups	Means	Standard deviation
A0	36.74	1.01
A1	31.82	0.61
A2	31.58	0.38
A3	32.19	0.63
A4	32.15	0.43
Total	32.90	2.05

Table 2: Comparison of five groups (A0, A1, A2, A3, and A4) with respect to applied force by one-way analysis of variance

SV	DF	SS	MSS	*F* value	*P* value	Significant
Between groups	4	242.90	60.7251	143.6443	0.0000	S
Within groups	60	25.36	0.4227			
Total	64	268.27				

Table 3: Pairwise comparison of five groups by Duncan's multiple comparison tests procedure

Groups	A0	A1	A2	A3	A4
Means	36.7380	31.8220	31.5850	32.1920	32.1540
A0	-				
A1	0.0001*	-			
A2	0.0000*	0.3567	-		
A3	0.0001*	0.1756	0.0315*	-	
A4	0.0001*	0.1976	0.0377*	0.8807	-

*Indicates significant at 5 level of significance (P<0.05)

Table 4: Pairwise comparison of five groups by student's unpaired *t*-test

Group	Mean	SD	*t* value	*P* value	Significant
A0	36.7385	1.0096	15.0430	0.0000	S
A1	31.8215	0.6080			
A0	36.7385	1.0096	17.2239	0.0000	S
A2	31.5846	0.3805			
A0	36.7385	1.0096	13.7715	0.0000	S
A3	32.1923	0.6304			
A0	36.7385	1.0096	15.0777	0.0000	S
A4	32.1538	0.4274			
A1	31.8215	0.6080	1.1911	0.2453	NS
A2	31.5846	0.3805			
A1	31.8215	0.6080	−1.5264	0.1400	NS
A3	32.1923	0.6304			
A1	31.8215	0.6080	−1.6122	0.1200	NS
A4	32.1538	0.4274			
A2	31.5846	0.3805	−2.9757	0.0066	S
A3	32.1923	0.6304			
A2	31.5846	0.3805	−3.5867	0.0015	S
A4	32.1538	0.4274			
A3	32.1923	0.6304	0.1821	0.8571	NS
A4	32.1538	0.4274			

SD: Standard deviation

Comparison between materials:

- As compared to A0, A1, A2, A3, A4 by the tests; there is a significant difference in fracture resistance of the root ($P < 0.05$).

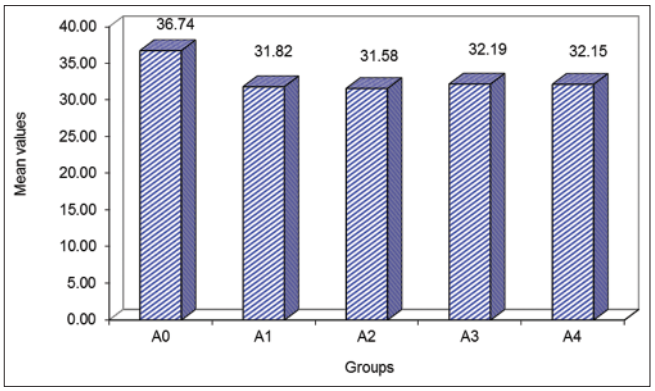

Figure 1: Comparison of five groups with respect to mean scores of applied force

- Overall result showed that Resilon increases the fracture resistance of the root compared to Gutta-Percha obturation.

DISCUSSION

In this study, the force was applied along the long axis of the root with a rounded punch, which produced root fracture when contact was made between the punch and walls of the canal opening and the force is applied. The roots used were narrower, and the standardization was done by doing the biomechanical shaping up to file size 40.[12,13] While going through results, we saw no differences between the lateral condensation and vertical condensation groups using the same material.[14,15] Many studies have suggested that as removal of tooth structure increases, fracture resistance of the tooth decreases. Root canal instrumentation is an unavoidable step in endodontic treatment.[16] However, it is understood that as dentin is removed during the instrumentation phase, a weakening effect on the root is inevitable. If we add the wedging forces of the spreader during lateral condensation or perform excessive dentin removal to facilitate pluggers for vertical condensation, the potential for root fracture is very real.[17] The concept of dentin bonding in restorative dentistry has been introduced in endodontic treatment, and promising results have been reported in methyl methacrylate tributylborane, or mma/tbb, - based resin sealer.[18] The resin composed of 4-methacryloxyethyl trimellitate anhydride, or 4-meta, and mma-tbb–which is known commercially as super bond c&b or c&b metabond has been reported to produce consistently high bond strengths and has been successfully used clinically for 15 years.[19] Some studies have suggested that the root canal sealer, especially glass ionomer cement, might strengthen root dentin.[2] Few studies have evaluated the potential of using dentin bonding agent and resins as obturation materials in nonsurgical root canal treatment.[20] Reasons for not using resins have centered on questionable results, difficult and

unpredictable methods of delivery into the root system and the inability to retreat the canal if necessary. However, these materials may have the potential to enhance the endodontic seal by reducing microleakage from both apical and coronal directions, thereby contributing to the success of orthograde endodontic treatment.[8-10] Trope and Roy, using maxillary and mandibular canine roots, showed that ketacendo strengthened roots weakened by canal instrumentation.[6] Lertchirakarn *et al.* suggested that ketac endo strengthened endodontically treated roots and may be used for weak roots, which are likely to be susceptible to vertical root fracture.[21]

CONCLUSION

This *in vitro* comparison study of fracture resistance of root filled with Resilon and Gutta-Percha with lateral and vertical obturation in the same diameter of the canal.

The vertical obturating technique is better than the lateral obturating technique. Resilon increases the fracture resistance as compared to the Gutta-Percha and AH 26. Under the conditions of this study, Resilon with vertical condensation technique performs better than Gutta-Percha and AH 26 sealer and to the lateral condensation technique.

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Original Article

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Outcome of Using Clinical Pathway in Laparoscopic Appendicectomy Patients – A Retrograde Analysis

Manuneethimaran Thiyagarajan[1], Saravanan Sanniyasi[2], Parimuthukumar Rajappa[1], Devamani Chalavadi[3]

[1]Assistant Professor, Department of General Surgery, Sri Ramachandra University, Chennai, Tamil Nadu, India, [2]Associate Professor, Department of General Surgery, Sri Ramachandra University, Chennai, Tamil Nadu, India, [3]Surgical Resident, Department of General Surgery, Sri Ramachandra University, Chennai, Tamil Nadu, India

Abstract

introduction: Appendicitis is a very common illness affecting all age groups of patients. It is the most common abdominal emergency. Open appendicectomy is a traditional method with its attendant complications. With the advent of laparoscopic surgeries, a laparoscopic appendicectomy has become one of the most common performed surgeries today. In many parts of the world, laparoscopic appendicectomy is a day care procedure.

Aim: To compare the efficacy of the pathway in appendicitis management in view of hospital stay, readmission rate, and complication rate.

Materials and Methods: A retrospective study was conducted in Sri Ramachandra University patients from 2008 to 2013. Comparison between the pathway group (2011-2013) and non-pathway (2008-2010) group was done. The duration of the hospital stay, complication rates, and readmission rate was compared between these two groups. In total of 893 patients, no clinical pathway was applied in 444 numbers of patients and pathway was applied 449 numbers of patients. Based on intraoperative findings both group patients are divided into appendicitis with peritonitis and appendicitis without peritonitis.

Results: The comparison between no pathway and pathway groups in the hours of hospital stay duration of appendicitis without peritonitis shows the statistical significance. The comparison between no pathway and pathway groups in the hours of hospital stay duration of with peritonitis shows no statistical significance. There was no difference in view of readmission rate and complication rate in both groups.

Conclusion: A standardized clinical pathway for simple appendicitis without peritonitis is very useful to reduce the duration of hospital stay without increase in readmission rate and complication rate. It gives favorable results on patient's outcome, hospital cost, and professional practice. Further modification of clinical pathway is essential to apply this in appendicitis with peritonitis patients to improve the outcome.

Key words: Appendicectomy, Clinical pathway, Laparoscopic appendicectomy

INTRODUCTION

Appendicitis is a very common illness affecting all age groups of patients. It is the most common abdominal emergency. The lifetime risk of developing appendicitis is approximately 7% with the highest frequency occurring at the ages from 10 to 30 years and usually requires surgical treatment.[1] The overall incidence of this condition is approximately 11 cases a 10,000 populations a year. The overall lifetime risk is 8.6% for males and 6.7% for females.[2] Open appendicectomy is a traditional method with its attendant complications. With the advent of laparoscopic surgeries, a laparoscopic appendicectomy has become one of the most common performed surgeries today. It has significant advantages in terms of less post-operative pain and early return to home. In many parts of the world, laparoscopic appendicectomy is a day care procedure. Hence, this has been selected for a clinical pathway to achieve our goal of making it a day care procedure. As a surgeon, it is very important to participate in the development of clinical pathways and

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Corresponding Author: Dr. Manuneethimaran Thiyagarajan, 107/F2, Anu Appartments, Vyasar Street, Kamatchi Nagar, Valasaravakam, Chennai - 60 0087, Tamil Nadu, India. Phone: +91-9952044955. E-mail: profmaran@gmail.com

clinical guidelines.[3] In 1998, the Southwestern Surgical Congress and the Southeastern Surgical Congress decided to publish the importance and efficacy of pathways in view of reducing length of stay and reducing the expenses for diagnosis. The practical guidelines, the motivation, the benefit and hazards of clinical pathways were analyzed by these surgical congresses.[4] In critical care patients, implementation of clinical pathways significantly improved the care processes with a good collaboration of healthcare professionals without any rise in the readmission rate.[5] There is significant improvement in length of stay, complication rate and financial outcomes in cancer patient by using evidence-based guidelines and clinical pathways.[6] The critical pathway for the management of acute heart failure provides computerized order sets that guide health care providers through accepted treatment regimens, providing documentation of treatment and assists with compliance data collection.[7] Pathway implementation in general surgery patients made a promising improvement in hospital care and patient satisfaction. Even though there are many clinical pathways used in clinical practice, pathway application for single surgical condition is rare. Since appendicitis is one of the commonest surgical emergencies in our practice, the pathway was applied for this condition in our hospital. Our aim is to compare the efficacy of the pathway in appendicitis management in view of hospital stay, readmission rate, and complication rate.

MATERIALS AND METHODS

This is a retrospective study conducted in Sri Ramachandra University patients from 2008 to 2013. All laparoscopic appendicectomy patients' details were collected from 2008 to 2010. There was no clinical pathway applied for laparoscopic appendicectomy patients in this period. From 2011 to 2013, all appendicectomy patients were treated with the clinical pathway. The exclusion criteria were open appendicectomy, laparoscopic appendicectomy converted to open, incidental appendicectomy, patients with symptoms that require intensive care unit (ICU) level of care, abscess appropriate for percutaneous drainage and initial non-operative treatment (intervention antibiotics, followed by interval appendectomy). After excluding these patients, only laparoscopically completed patients in this time period were selected for the study. Comparison between this pathway and non-pathway groups was done. The duration of the hospital stay, complication rates, and readmission rate was compared between these two groups.

Based on intraoperative findings, both group patients are divided into appendicitis with peritonitis and appendicitis without peritonitis.

In all patients, details like age, sex and diabetic status were collected. The duration of hospital stay was calculated in hours for every patient based on time of admission and time of discharge in the electronic record. The post-operative complications, such as wound infection, subacute intestinal obstruction, pelvic abscess, fecal fistula, and re-exploration rate, were collected from the case record. The readmission of patient within 1-month of post-operative period was collected from electronic records by using hospital admission number. The collected data were compared in both groups of patients.

Details of Clinical Pathway for Appendicectomy

Once patient was received in emergency department, emergency medical officer will assess the patient. If patient is provisionally diagnosed with appendicitis, pathway will be initiated. According to the pathway in Table 1, patient will be evaluated, and treatment will be started. Surgical consultant opinion should be obtained to all patients. Gynecologist opinion must be obtained for all female patients. The exclusion criteria for pathway are mentioned in Table 1. During the period of treatment if patient need higher level of care like ICU, prolonged nil per oral with parenteral therapy or if there is change in diagnosis intraoperatively, the patient will be excluded from the pathway. Patients undergo laparoscopic appendicectomy in the standard technique. Those who require conversion were excluded from the study. Pathway patients are divided into two groups based on intraoperative findings as, patients with peritonitis and patients without peritonitis. Antibiotics guideline was followed for both groups of patients. For patients without peritonitis, discharge planning will start on post-operative day (POD) 1 and most of them will be discharged on POD 2. If patient develops post-operative complications consultant can upgrade antibiotics if indicated and the reason for upgrading antibiotics must be documented in the case record. Patients with appendicitis with peritonitis are discharged on POD 4 and patients with abscess needing drain placement are discharged on POD 7.

Statistical Methods

The collected data were analyzed with SPSS for windows, version 16.0, Chicago Inc. To describe about the data descriptive statistics mean and standard deviation (SD) were used for continuous variables. To find the significant difference between the bivariate samples in Independent groups the unpaired sample *t*-test was used. In the above statistical tool, the $P < 0.05$ is considered as significant level.

RESULTS

A total of 893 patients were operated successfully with laparoscopic appendicectomy for the period of 6 years

Table 1: Appendicectomy pathaway used in Sri Ramachandra Medical University (from 2011 to 2013)

Patients to include on pathway: 1. Patients with a diagnosis of probable appendicitis
Patients to exclude from pathway: (1) Incidental appendectomy (2) Patients with symptoms that require ICU level of care. (3) Abscess appropriate for percutaneous drainage (4) Initial non-operative treatment (IV Antibiotics, followed by interval appendicectomy (5) Patient with complicating chronic conditions
Remove the patient from the pathway if the following occurs: (1) Significant post-operative complication such – Bowel obstruction Requiring a second operation or prolonged TPN (2) Transfer to a higher level of care (3) Change in diagnosis
Emergency department/OPD – Abdominal pain, Possibly appendicitis: Inpatient (A) – Acute appendicitis with generalized or localized peritonitis (B) – Acute appendicitis without peritonitis

Phase of care	Emergency room/admission/ preoperative	Day of surgery	1st POD	2nd POD (end of pathway for AC. appendicitis without peritonitis)	3rd POD	4th POD (end of pathway for appendicitis with peritonitis)	5th POD
Consults	(a) Surgical consult for abdominal pain (b) Gynecology opinion for a female patient						
Lab/tests	CBC, TC, DC urine analysis. If dehydrated, to do RFT, serum electrolytes. If diffusely tender abdomen, serum amylase. Urine pregnancy test			If still NPO, repeat RFT, serum electrolytes	CBC, TC, DC If febrile (38°C) or WBC or not tolerating diet		
Radiology	Acute abdominal series (X-ray, USG-abdomen) as requested by concerned surgeon						If febrile >38°C and WBC>14,000, CT of abdomen Any abscess is drained
Treatments	Insert IV	Wound care: infection: protection					
Medication	IV antibiotics cefazolin, metrogyl or clindamycin	To continue IV antibiotics as before			D/C IV antibiotics, if afebrile, tolerating diet WBC – (N) Start oral antibiotics	Oral anitibiotics	
Pain management	Comfort measures	Analgesics IV/IM			Paracetamol, codeine	Analgesics S.O.S	
Nutrition/hydration	NPO Start IV fluids DNS/NS/RL	(A) IV fluids (B) D/C IV after antibiotics Liquids advance diet	D/C IV When tolerating diet clear liquids Diet as tolerated	Liquid diet (N) Diet	Soft solid diet	(N) Diet	
Activity	Ad lib/As tolerated	(A) Up at bed side (B) Begin ambulation	Begin ambulation Ambulate	Ambulate Ambulate	Ambulate	Ambulate	
Assessment and monitoring	Physical vital signs Fluid monitoring Pain scoring	Physical vital signs Fluid monitoring Respiratory monitorin Pain scoring	Pain scoring Vital signs monitoring	Pain scoring Vital signs Monitoring	Pain scoring Vital signs Monitoring	Pain scoring Vital signs Monitoring	
Patient/family teaching	Explain diagnostic studies Provide patient/family with a copy of the Appendicitis/Appendectomy Teaching Handout Consent: Surgery consent for "Appendectomy" to be obtained after the surgeon/surgical resident has talked to the patient/family	Involve Pt/family in care	Discharge planning	Discharge planning Explain discharge criteria appointment for follow-up		Appointment for follow-up	

(*Contd*...)

Table 1: (*Continued*)

Phase of care	Emergency room/admission/ preoperative	Day of surgery	1st POD	2nd POD (end of pathway for AC. appendicitis without peritonitis)	3rd POD	4th POD (end of pathway for appendicitis with peritonitis)	5th POD
Other	If obstructed NG tube If dehydrated IV fluids and/or Foley catheter	Intraoperative protocol	Remove NG when BS+drainage less, Abd not bloated, Patient hungry. Remove Foley				
Expected outcome	No other X-rays or lab	No intraoperative complications compliance with Intraoperative protocol		(B) Discharge	(A) Afebrile (N) WBC	(A) Discharge	Discharge by day 7

TPN: Total parenteral nutrition, ICU: Intensive care unit, IV: Intravenous, POD: Post-operative day, CBC: Complete blood count, TC: Total count, DC: Differential count, RFT: Renal function test, WBC: White blood cell, USG: Ultrasonography, CT: Computed tomography, NS: Normal saline, DNS: Dextrose normal saline, RL: Ringer's lactate, IM: Intramuscular, NPO: Nil per oral

in Sri Ramachandra University (2008-2013). From 2008 to 2010, a number of patients operated with laparoscopic appendicectomy are 444 in which no clinical pathway was applied. However, pathway was applied from 2011 to 2013 for totally 449 numbers of patients. On comparing the age of the patients, the mean age in pathway and non-pathway groups are almost equal (30.36 ± 13.9 and 30.21 ± 12.6). The mean age of patients in appendicitis without peritonitis cases is significantly lesser (in pathway 29.22 ± 11.3 and no pathway 27.73 ± 12.3) than peritonitis cases (in pathway 34.48 ± 15.8 and in no pathway 38.32 ± 15.8). The male:female ratio of appendicitis patients is 1.2:1 (481 and 412, respectively). In total, 893 patients appendicitis with peritonitis is 201 (22.5%) and without peritonis are 692 (77.4%). In total, 201 peritonitis patients 111 (55.2%) patients are female patients and 90 (44.8%) patients are male patients. A number of patients with diabetic mellitus are 147 (16.5%). The diabetic status is significantly high in appendicitis with peritonitis patients (35.8% - 72/201) than appendicitis without peritonitis (10.8% - 75/692) (Table 2).

The comparison between no pathway and pathway groups in the hours of hospital stay duration shows a statistical significance ($P = 0.0005 < 0.01$) with the mean ± SD of the no pathway group (102.8 ± 35.0) and pathway group (90.6 ± 41.0) (Table 3 and Graph 1).

The comparison between no pathway and pathway groups in the hours of hospital stay duration of appendicitis without peritonitis shows a statistical significance ($P = 0.0005 < 0.01$) with the mean ± SD of the No pathway group (87.6 ± 23) and pathway group (72.8 ± 22.4). It was shown in Graph 2.

The comparison between no pathway and pathway groups in the hours of hospital stay duration of with peritonitis shows no statistical significance ($P = 0.462 > 0.05$) with

Table 2: Comparison of duration of hospital stay in total pathway and no pathway group

Groups	Mean	SD	*P* value
No pathway	102.8	35.9	0.0005**
Pathway	90.6	41.0	

**Highly significant at P<0.01 level. SD: Standard deviation

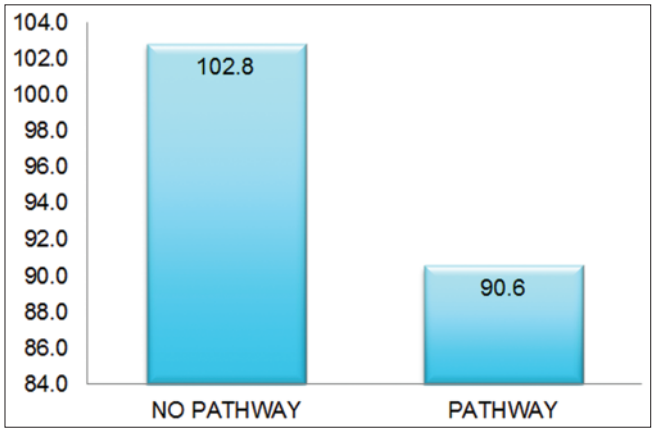
Table 3: Comparison of hospital stay in hours

Variables	Groups	Mean	SD	*P* value
Without peritonitis	No pathway	87.6	23.0	0.0005**
	Pathway	72.8	22.4	
With peritonitis	No pathway	152.6	23.2	0.462#
	Pathway	155.1	25.5	

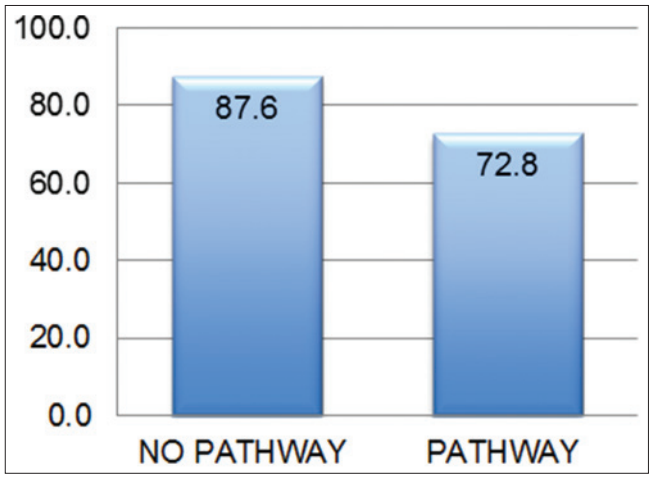
Pathway group without peritonitis versus No pathway group without peritonitis.
Pathway group with peritonitis versus No pathway group with peritonitis.
**Highly significant at *P*<0.01 level, #No significance. SD: Standard deviation

the mean ± SD of the No pathway group (151.6 ±23.2) and pathway group (155.1 ± 25.5) (Table 4).

Regarding post-operative complications, 22 patients (2.4%) had complications. The complication rate in pathway group is 2% (9 patients) and non-pathway group is 2.92% (13 patients). In appendicitis without peritonitis cases, only complication recorded is wound infection 0.1% (7 patients)



Graph 1: Comparison of duration of hospital stay in pathway and no pathway group



Graph 2: Duration of hospital stay in appendicitis without peritonitis

and there is no readmission and re-exploration found in this group. Wound infection rate in pathway group without peritonitis is 3 patients and in no pathway group without peritonitis is 4 patients. Hence, there is no difference in this group. But in appendicitis with peritonitis, the complication rate is 7.4% (15 patients). In pathway group, it is 6.2% and in non-pathway group it is 9.7%. It is again not statistically significant. The readmission rate in pathway group is 6.2% and in non-pathway group is 6.7%. The re-exploration rate in pathway and non-pathway group is 1% and 1.9%, respectively.

DISCUSSION

Acute appendicitis is one of the most common surgical emergencies in humans. Laparoscopic appendicectomy is the standard of care in these cases. However, there is a considerable variability in the diagnosis and management protocols across consultants. Clinical pathways have been able to bridge these gaps and provide significant improvement in clinical care in surgery.[8] Again pathways produce better teamwork and hence very useful in health organizations).[9] Clinical pathways in acute appendicitis are a common practice in many pediatric hospitals.[10-13] As part of quality improvement, pathway for acute appendicitis was introduced in our hospital in 2011. This 6-year retrospective analysis has given a lot of insight into the usefulness of a clinical pathway. One of the major advantages we were able to derive was the reduced hospital stay, which was on an average 12 h lesser after the introduction of the pathway, and this was statistically significant. Emil *et al.*,[10] Warner *et al.*[11] and Kenji Takegami *et al.*[14] have also brought out this significant advantage in their studies. The pathway could significantly reduce the hospital stay only in the group without peritonitis; there was no significant difference in the length of hospital stay in the group with peritonitis, similar to the study by Emil *et al.*[10] The complication, re-admission and re-exploration rates were similar in both the groups in our study. But the readmission rate was found to be significantly lesser in the pathway group by Emil. Drain

Table 4: Comparison of complication rate, re-admission rate and re-exploration rate

Post operative problems	Pathway (%)	No pathway (%)	Without peritonitis (%)		With peritonitis (%)	
			Pathway	No pathway	Pathway	No pathway
Complications						
Wound infection	7 (1.6)	8 (1.8)	3 (0.9)	4 (1.2)	4 (4.1)	4 (3.8)
Pelvic abscess	1 (0.2)	3 (0.7)	0	0	1 (1)	3 (2.9)
Subacute intestinal obstruction	0	1 (0.2)	0	0	0	1 (1)
Wound infection with pelvic abscess	1 (0.2)	0	0	0	1 (1)	0
Faecal fistula	0	1 (0.2)	0	0	0	1 (1)
Total	9 (2)	13 (2.9)	3 (0.9)	4 (1.2)	6 (6.2)	9 (9.7)
Readmission	6 (1.3)	7 (1.6)	0	0	6 (6.2)	7 (6.7)
Re-exploration	1 (0.2)	2 (0.5)	0	0	1 (1)	2 (1.9)

placement in patients with complicated appendicitis was significantly lesser in the pathway group in this study.[10] Other major advantages brought out by other studies are lesser antibiotic usage, decreased hospital charges, fewer unnecessary laboratory tests and decreased surgical site infections.[10-12,14,15] Clinical pathways are also a means of auditing surgical care and institute necessary modifications for the betterment of patient outcome.[15]

CONCLUSION

The results of the evaluation study show that a standardized clinical pathway for simple appendicitis without peritonitis is very useful to reduce the duration of hospital stay without increase in readmission rate and complication rate. It gives favorable results on patient's outcome, hospital cost, and professional practice. Further modification of clinical pathway is essential to apply this in appendicitis with peritonitis patients to improve the outcome.

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Original Article

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Clinico-microbiological Correlation of Genital Ulcer Diseases of Sexually Transmitted Diseases Origin

Raju G Chaudhary[1], Khushbu R Modi[2], Miral Bodar[2], Pratik Makwana[2]

[1]Associate Professor, Department of Dermatology, Smt. SCL Hospital, NHL Medical College, Ahmedabad, Gujarat, India, [2]Resident, Department of Dermatology, Smt. SCL Hospital, NHL Medical College, Ahmedabad, Gujarat, India

Abstract

Introduction: Genital ulceration disease is a vast and widely studied subject as genital ulcers and its varied clinical presentation as in many dermatological conditions in both sexually transmitted diseases (STDs) and non-STDs lead to lots of problem to a dermatologist while the most challenging aspect is proving an etiological diagnosis.

Aims: (1) To study clinico-microbiological correlation of genital ulcer disease (GUD) of STDs origin. (2) To study the pattern of STDs.

Materials and Methods: Present study was cross-sectional prospective and it included 150 cases of GUD of STD origin patients more than 19 years of age and ulcer on genital as a presenting feature. The presumptive clinical diagnosis was made on clinical examination of a characteristic of the genital ulcer as mentioned in the literature. Direct Gram-stain, direct Giemsa-stained smear, and Tzanck smear were prepared form genital ulcers. Venereal disease research laboratory and human immunodeficiency virus antibody test by enzyme-linked immunosorbent assay were done in each case of GUD of STDs origin. We compared clinical presumptive STD diagnosis with their microbiological findings of each patient.

Results: In the present study, we noticed higher number 75.33% of GUD of STDs origin in herpes progenitalis (HP) followed by 12.66% in chancroid cases. The present study showed and confirmed an increasing trend of STDs infections due to viral etiology. We found 42.66% (64 out of 150) clinico-microbiological correlation in the present study and 86 cases did not show any etiological agents. In our study, we found 57.89%, 75%, and 50% clinico-bacteriological correlation in chancroid, granuloma inguinale, and syphilitic ulceration of STD origin, respectively. GUD of HP and mixed infection showed 37.16% and 60% clinico-bacterial correlation.

Conclusions: The present study suggested that the need for combined clinical and microbiological and serological evaluation of genital ulcers of STD origin. For better understand of clinico-microbiological correlation of GUD of STDs origin, we have to improve diagnostic facilities and techniques with knowledge of changing pattern of STDs prevalence and varied clinical presentation.

Key words: Clinico-bacteriological correlation, Genital ulcer diseases, Sexually transmitted diseases

INTRODUCTION

Genital ulcer disease (GUD) can be defined as a genital lesion characterized by a defect in the epithelium of the skin or mucosa caused by a number of sexually transmitted infections (STIs)/sexually transmitted diseases (STDs) and non-STIs related dermatological conditions.[1] The major and consistent component of GUD is STDs. The importance of GUD must be stressed on as there is enormously growing evidence that GUD of STDs origin is a major risk factor for transmission of human immunodeficiency virus (HIV).[1,2]

GUD of STDs origin varies by population and by etiology and is more frequently noticed in developing countries than developed countries in the world. Developing countries like our nation India are likely to have constraints of manpower and resources and suffer from lack of proper diagnostic tests and incomplete reporting.

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Corresponding Author: Dr. Raju G Chaudhary, Department of Dermatology, Smt. SCL Hospital, Saraspur, Ahmedabad, Gujarat, India. Phone: +91-9727780221. E-mail: khushbumodi2610@gmail.com

To know the exact etiology of GUD of STDs origin is the common problem for both developed and developing countries.[3] Even better diagnostic facilities are available as in the developed countries; a specific microbiologic agent cannot be identified in 15-50% of STDs cases.[1]

GUD of STDs origin will remain a fascinating subject of varied etiology, and their clinical presentation for years to come, especially in the present era of acquired immune deficiency syndrome. Improving diagnostic facilities and techniques, awareness of changing pattern of STIs prevalence, and clinical presentation will determine the future course of GUD of STDs origin and its association with HIV infection.

The present study emphasized the correlation between the clinical presentations, microbiological, and serological findings of GUD of STDs origin.

MATERIALS AND METHODS

The present study was cross-sectional prospective and it included 150 cases of genital ulceration of STD origin presented in skin OPD at our tertiary care center from 1st April 2013 to 31st March 2015.

We enrolled patients more than 19 years of age and ulcer on genital as a presenting feature, and it was suspected clinically to be a venereal origin. In female genital ulcers on the mons pubis, labia majus and minus, introitus, posterior commissure, vagina, urethral meatus and vestibule, perianal and in male the glans, urethral meatus, corona, coronal sulcus, shaft, peno-scrotal junction, scrotum and perianal sites were involved in our study. Ulcerations on the perineum, groins, and buttocks were not included in our study. In the present and past history of oral and parenteral treatment, self-medication for last recent 2 weeks was excluded from our study. The patient with inquinal bubo or inquinal lymphadenopathy without ulcer as mentioned above sites was excluded from our study.

Demographic data of each individual was noted. Detailed sexual exposure history was taken of each individual including sexual partners, sexual behavior, and sexual practices.

Only strongly suspected cases of ulcers of STD origin were studied after thorough clinical examination. After clinical examination of ulcers (characteristics) of each individual patient, we put our presumptive clinical diagnosis. Each individual patient was also screened for the mucosal lesion, any skin lesion, and lymph nodes along with the systemic examination.

The smear was made with the help of sterile cotton-tipped swab from edge and floor of the ulcer after cleaning with normal saline. Then, Gram-stained for *Haemophilus ducreyi* (HD) and cocci and Giemsa-stained for Donovan body (DB) were prepared. Tzanck smear was made for all cases irrespective of their causes. We prepared a smear for DB and smear from urethral meatus in strongly suspected cases of granuloma inguinale (GI) and gonorrhea cases, respectively. *Treponema pallidum* hemagglutination (TPHA) test was done in all cases of syphilis and in mixed infection of chancroid with primary chancre.

Enzyme-linked immunosorbent assay (ELISA) for HIV and venereal disease research laboratory (VDRL)-SD for syphilis, serological tests were done in all 150 cases.

All patients were re-evaluated after 3 days as follows: Western blot assay for all ELISA HIV reactive patients. Each of individual was treated as per their causative etiology. Follow-up at 3 months: VDRL-SD for syphilis patient for falling titer and ELISA for HIV antibody test was repeated.

Finally, we collected data of all 150 cases and compared clinical presumptive STD diagnosis with their microbiological findings. Clinical and microbiological findings were correlated to each other.

RESULTS

In our study, we studied total 437 ulcers of STD origin. The majority of ulcers had been present from 1 to 30 days. The average duration was 20.5 days. The maximum number of ulcers, mainly of herpes progenitalis (HP) and chancroid were presented on prepuce. It showed that un-circumscribed male had a greater risk for acquiring STDs. Next common site was coronal sulcus. In female, we found maximum ulceration on labia majus and labia minus. Herpetic ulcers were found in the perianal region of all passive homosexual male and in four females having a history of peno-anus sex with their sexual partners. All cases of suspected HP and chancroid clinically had multiple ulcers (more than three). Single ulcer found in GI and syphilis. We noticed clinical examination findings of all ulceration except mixed infections of STDs conformed to the classic description as in literature.

DISCUSSION

GUD is a vast and widely studied subject as genital ulcers and its varied clinical presentation as in many dermatological conditions in both STDs and non-STDs lead to lots of problem to the dermatologist while the

most challenging aspect is proving an etiological diagnosis.[1] The main microbial causes of genital ulceration of STD origin are HD, *T. pallidum*, herpes simplex virus, *Chlamydia trachomatis* serovas L1, L2, and L3, i.e., the lymphogranuloma veneureum strains and calymmatobacterium granulomatis. Pyoderma, *Sarcotes scabiei*, *Pthirus pubis*, *Entamoeba histolytica*, *Trichomonas vaginalis,* and non-syphilis-spirochetes may occasionally cause GUD.[1,3] The role of *Neisseria gonorrhoeae* in genital ulcers is not clear though it is quite often isolated from GUD.[1] In this study, we studied clinico-microbiological correlation of genital ulceration of STDs origin only.

In our study, we enrolled total 150 cases of GUD of STDs origin. Among them, 40.7% were female and 59.3% were male (Table 1). Nayyar *et al.*,[4] Narayanan,[5] Sarkar *et al.*[6] reported the percentage of male predominance as our study. These figures conform to the predominance of males with genital ulceration seeking medical attention and attending general STD clinics. The low percentage of females is probably due to ignorance, social inhibitions, asymptomatic carriers, and importantly prostitutes who suffer from genital STDs and do not seek medical attention. The primary reason for this discrepancy may be that male as compare to female is believed to over report their sexual behavior.

The majority of males 25.33% and females 12.66% in present study belonged to the 19-30 years of age group (Table 1). In our study, the sexual behavior in STDs patients less than 30 years of age was significant over the sexual behavior in STDs patients more than 30 years of age ($P > 0.05$). Regardless of race or gender, data of Centers for Disease Control and Prevention show that sexually active adolescents and young adults are at increased risk for STDs when compared to older adults.[7] 21-40 years of sexually active age group was predominantly having STIs that reported by Vora *et al.*[8]

We found a high number of STDs in married male and female both (Table 2). In the present study, married women showed a high number of STDs than unmarried women because of the indirect risk of STDs. Many studies Narayanan[5] and Vora *et al.*,[8] reported a higher percentage of STIs in married patients. While other studies Nayyar *et al.*[4] and Bala *et al.*[9] reported more number of unmarried had STIs because of high-risk sexual practice.

We found 44.31% males and 35.48% female at direct risk for GUD of STD origin. We noticed GUD in 60.65%, 24.59%, and 9.81% in heterosexual, homosexual, and bisexual sexual behavior, respectively (Table 3). In present study, percentage of hetrosexual behavior (60.65%) was lower as compared to studies by Narayanan (95.9%),[5] and

Table 1: Age and sex distribution

Age group (in year)	Sex		Total (%)
	Male	Female	
19-30	38	19	57 (38)
31-40	31	20	51 (34)
41-50	8	17	25 (16.7)
51-60	6	4	10 (6.6)
61-70	5	1	6 (4)
>70	1	0	1 (0.7)
Total (%)	89 (59.3)	61 (40.7)	150 (100)

Table 2: Marital status

Sex	Single	Married	Total
Male	39	49	88
Female	28	34	62
Total	67	83	150

Vora *et al.* (97%),[8] and homosexual behavior (9.8%) was higher as compared to Vora *et al.* (0.5%).[8]

In our study, the patient with a past history of genital ulcer had a higher prevalence of STDs as compared to people without a past history. The same finding was reported by Rodrigues *et al.*[10]

We found 31.33% of STD in unprotected sexual exposure irrespective of the type of sexual practice. The correct and consistent use of latex condoms has been shown to be very effective in preventing transmission of STDs including HIV.[11]

In the present study, 8.6% of circumscribed male, all were Muslim having GUD of STDs origin. The role of circumcision in the prevention of HIV/STIs is still controversial. Some studies Nayyar *et al.*[4] and Rodrigues *et al.*[10] showed a low prevalence of HIV/STIs in circumscribed male while Chao *et al.*[12] showed that lack of circumcision is not associated with risk of HIV and STI.

Overall in the present study, the most common sexual pattern seen was that of young, sexually active heterosexual male having unprotected peno-vaginal intercourse.

In the present study, we noticed higher number 75.33% of GUD of STDs origin in HP (Figure 1a) followed by 12.66% in chancroid (Figure 1b) cases. 2.66% of GUD of STDs origin was found in both syphilis (Figure 1c) and GI (Figure 1d). 6.66% GUD of STDs origin was found in mixed infection (Figure 2a and b, Table 4).

The present study showed an increasing trend of STDs infections due to viral etiology as compared with bacterial. The present study confirmed a similar pattern and showed

an increasing trend of HP. Many Indian studies Vora *et al.*,[8] Jain *et al.*,[13] Chandragupta *et al.*,[14] and Choudhry *et al.*[15] reported marked declines in bacterial STIs were resulting in an apparent increase of the viral STIs. In our country, there was an increasing trend of viral STIs with a reduction in those of bacterial origin because of higher and better antibiotics used empirically by general practitioners.

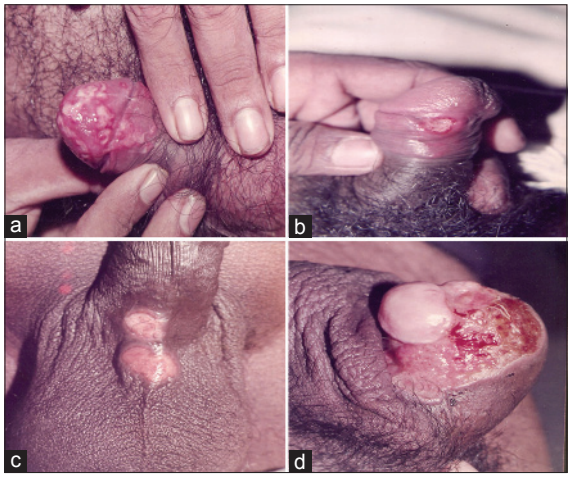

Figure 1: (a) Multiple ulcers of herpes progenitalis (b) Chancroid (c) Kissing ulcers of primary syphilis (d) Granuloma inguinale

Figure 2: (a) Mixed infection chancroid + herpes progenitalis (b) Mixed infection chancroid + herpes progenitalis

The presence of Gram-negative cocco-bacillary forms in pair of short chains in Gram-stained smear (Figure 3a and b) was considered highly suggestive of HD in this study.[16]

In the present study, 11 out of 16 cases of clinically diagnosed chancroid proved HD on direct Gram-stain smear (Table 5). In the present study, HD was isolated in 12 cases by selective media and 5 cases by Mueller-Hinton agar. Selective media was found to be far superior to culture results on Mueller-Hinton agar. We did not use selective media for all patients due to our certain limitation. Many studies have stated that the direct Gram-stained smear

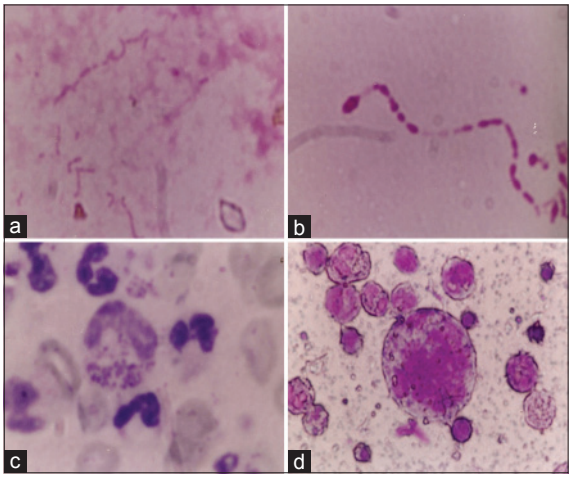

Figure 3: (a) Direct Gram-stain *Haemophilus ducreyi* (HD) (b) Gram-stain HD from culture colony (c) Donovan Bodies Giemsa-stained smear (d) Multinucleated giant cells seen in herpes progenitalis

Table 3: History of sexual exposure and sexual behavior

Sex	Sexual exposure			Sexual behavior		
	Single	Multiple	Denying sexual exposure	Hetrosexual	Homosexual	Bisexual
Male (88)	15	24	49	18	15	6
Female (62)	14	8	40	19	0	0
Total (150)	29	32	89	37	15	6

Table 4: Presumptive STDs in our study

STDs	Chancroid	Mixed infection	Granuloma inguinale	Syphilis	Herpes progenitalis	Total
Male	11	7	3	3	64	88
Female	8	3	1	1	49	62
Total (%)	19 (12.66)	10 (6.66)	4 (2.66)	4 (2.66)	113 (75.33)	150 (100)

STDs: Sexually transmitted diseases

Table 5: Smear, serology test, and STDs

STDs	Chancroid	Mixed infection	Granuloma inguinale	Syphilis	Herpes progenitalis
Gram-stain					
H. ducreyi	11	5	-	-	-
Diplococci	-	2	-	-	-
Staphylococci	9	7	3	2	15
Streptococci	2	2	2	1	2
Diphtheroids	1	2	2	1	2
Anaerobes	-	-	-	-	-
Giemsa-stain					
Treponems	-	1	-	2	-
Donovan bodies	-	2	3	-	-
MNGC	-	4	-	-	31
Chlamydia	-	3	-	-	-
CMV	-	1	-	-	-
Wright stain					
Donovan bodies	-	-	2	-	-
Tzanck smear MNGC	-	-	-	-	42
TPHA	-	1	-	2	-
S VDRL	-	1	-	2	-
HIV ELISA	-	2	-	-	-

STDs: Sexually transmitted diseases, TPHA: *Treponema pallidum hemagglutination*, VDRL: Venereal disease research laboratory, HIV: Human immunodeficiency virus, ELISA: Enzyme-linked immunosorbent assay, CMV: Cytomegalovirus, MNGC: Multinucleated giant cells, *H. ducreyi: Haemophilus ducreyi*

is not sensitive or specific for the detection of HD.[17,18] Therefore, the isolation of HD is necessary in all cases. In the present study, we used both Mueller-Hinton agar and selective media by Borchardt Hoke method as a culture technique for isolation of the HD.

Staphylococci coagulase negative which is present in normal cutaneous flora was the most common organism co-existing with HD followed by alpha hemolytic streptococci and diphtheroids. Pathogenic strains of staphylococci and streptococci appear to play a role in ulcers clinically resembling chancroid.[19] The isolation of staphylococci coagulase positive and beta-hemolytic streptococci along or in combination in the absence of HD tempts one to suspect them as primary pathogens in the ulcers.[19] Anaerobic bacteria were not detected in any of the ulcers in this study. One case in the present study showed growth of staphylococci coagulase positive and beta-hemolytic streptococci along with HD. Two cases showed growth of only staphylococci coagulase positive and two cases showed growth of beta-hemolytic streptococci. None of the microbiological investigations raised suspicious of Ducreyi Like Bacillilus[18] in cases that did not grow HD and were clinically chancroid.

Diplococci were seen on Gram-stain smear in 2 cases of chancroid, both extra and intra cellular. Cultured techniques detected HD and *N. gonorrhoeae* both from the same ulcer.

Direct smears attained with Giemsa-stain were prepared in all 150 cases in our study (Table 5). Dunlop discussed the direct detection of treponemal forms by microscopic examination and suggested the disadvantages of examination of fixed specimens.[20] In our study, Giemsa smear showed trponenms in three patients. One out of three patients was of chancroid with weekly positive VDRL test. Two out of three had primary syphilis, showed 1:16 VDRL titer and positive TPHA in all three cases. Multinucleated Giant cells were not detected in any cases of chancroid by direct Giemsa-stain smear, but it was found in 4 cases of mixed infection and 21 cases of HP. Geimsa-stained smear alone detected treponems in one case, chlamydial inclusions in three cases, and cytomegalovirus (CMV) in 1 case. DB detected in 2 cases of microbiologically proved chancroid. Thus, ulcers of chancroid have a polymicrobial flora.[17,21]

Therefore, whenever possible, in cases of chancroid with a high index of suspicion based on clinical criteria even if smear and culture on other hand do not detect HD on selective media should be employed as an HD is known to be a fastidious organism. Chapel *et al*.[21] showed that the difficulty in obtaining a microbiological confirmation from clinically typical ulcers of chancroid often results in a diagnosis of chancroid based on clinical appearance and exclusion of other STDs.

Giemsa-stained direct smear detected DB in ulcers (Figure 3c). 2/4 was positive for DB by crushed tissue smear and direct smear. ¼ cases, crushed tissue smear was negative, but direct smear was positive. Neither smear was positive in 1 case of GI. Ideally, both smears should be prepared for every genital ulcer clinically looks like GI. That the ulcers of GI were mono microbial as compared to chancroid, multiple organisms being detected in many cases of the latter. Ulcero-granulomatous of GI lesions has higher yields of DB on smear than hypertrophic and

exuberant variety. Cases of typical ulcers which are too early or too chronic, necrotic or sclerotic, and resembling malignancy may also be negative for DB on smear.

Multinucleated giant cells were detected in 4 cases of mixed infections and 21 cases of HP by direct Giemsa-stain smear (Figure 3d). Multinucleated giant cells were detected in 42 cases of HP by Tzanck smear stained with Wrights' stain (Table 5). Solomon *et al.*[22] have assessed the accuracy of Tzanck smear in cutaneous herpes simplex; they found the lowest possibility from crusted-ulcer lesions (16%). In the present study, 18 direct Gram-stain smear of herpetic ulcers showed staphylococci and streptococci. HD was isolated from 4 cases of clinically diagnosed HP in our study. The coexistence of herpes simplex virus (HSV) and HD has been reported by Chapel *et al.*[21]

In our study, we found 57.89% clinico-bacteriological correlation in chancroid ulceration of STD origin (Table 6). This could be interpreted as HD is a fastidious organism. Culture techniques employed in this study were not sensitive enough, and chancroid ulcers were more common then realized.

4 cases were clinically diagnosed as GI and 3 showed DB. We found 75% clinico-bacteriological correlation in GI ulceration of STD origin (Table 6).

4 cases were clinically diagnosed as syphilitic chancre; one case showed cutaneous manifestations of secondary syphilis with primary chancre. We found 50% clinico-bacteriological correlation in syphilitic ulceration of STD origin (Table 6).

Only 42 cases out of 113 diagnosed HP showed multinucleated giant cells on Tzanck smear. This indicates that superior diagnostic techniques such as culture and serology are required, and Tzanck smear alone is not enough (Table 6).

6 cases out of 10 clinically diagnosed as mixed infection were correlated microbiologically (Table 6). This indicates that cases of mixed infections and coexisting STDs are on the rise with often more than one pathogen being isolated.[23] The most common mixed infection seen was chancroid + HP. Others were chancroid + primary chancre, chancroid + GI. Polymicrobial flora were seen most commonly with proved cases of chancroid, the organisms being *T. pallidum*, gonococci, HSV, DB, chlamydiae, staphylococci, streptococci and one case of CMV. The importance is that antimicrobial therapy for the STDs should be such that it can combat more than one type of STD organism. Polymicrobial flora was highest in ulcers of chancroidin this study. ELISA test for HIV infection was positive in 2 cases of mixed infection which was confirmed by western blot. Multiple episodes of GUD can result in sero-conversion of an HIV-infected individual,[2] hence the correct and consistent use of latex condoms is necessary to prevent transmission of STDs, including HIV.

Overall we found 42.66% (64 out of 150) clinico-microbiological correlation in our study and 86 cases did not show any etiological agents.[24,25] It required better diagnostic techniques (Table 6).

Nowadays, the field of microbiology could be applied to the GUD of STDs with amazing results. This was soon followed by immunology and serology and since then the whole new world has opened up giving us a better insight into the etiology of genital ulcerations, better rates of detection of the microbial organisms involved and hence more complete diagnosis, at the same time revealing some unusual clinico-bacteriological findings.

The present study had limitations that we did not enroll the patients of genital discharge without genital ulceration and lake of better diagnostic techniques at our center.

The present study fulfilled its aims and highlighted the need for combined clinical and microbiological and serological evaluation of genital ulcers of STD origin. Clinical features had been proved inadequate and as a dermatologist, we cannot reliable on it as the sole diagnostic criteria of GUD of STD origin.

CONCLUSION

Improving diagnostic facilities and techniques, awareness of changing pattern of STIs prevalence and its clinical presentation are the main factors to better understand of clinico-microbiological correlation of GUD of STDs origin. In future, more and more studies are required to determine the future course of GUD of STDs origin.

Table 6: Clinical and microbiological correlation

STDs	Chancroid	Mixed infection	Granuloma inguinale	Syphilis	Herpes progenitalis	Total
Presumptive clinical diagnosis	19	10	4	4	113	150
Microbiological diagnosis	11	6	3	2	42	64
No microbiological diagnosis	8	4	1	2	71	86
% of co-relation	57.89	60	75	50	37.16	42.66

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Original Article

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Morphological and Histological Features of Human Fetal Thyroid Gland

A Anupriya[1], R Kalpana[2]

[1]Assistant Professor, Department of Anatomy, Sri Muthukumaran Medical College Hospital & Research Institute, Chennai, Tamil Nadu, India, [2]Professor, Department of Anatomy, Sri Muthukumaran Medical College Hospital & Research Institute, Chennai, Tamil Nadu, India

Abstract

Introduction: The thyroid gland regulates the basal metabolic rate, somatic growth, and psychic growth. Hence, the thyroid gland plays a major role for the normal growth of a fetus during the prenatal period. It is the first endocrine gland which starts to develop by 24 days after fertilization. The aim of our study is to study the morphological and histological features of the thyroid gland in various age group fetuses.

Materials and Methods: 40 intact fetuses of different gestational ages ranging from 11 to 36 weeks were studied in the Department of Anatomy, Sri Muthukumaran Medical College & Research Institute, Chennai. The fetuses were preserved in 10% formalin solution. Midline dissection of the neck was done to expose the thyroid gland. The situation, shape, and measurements of the gland were noted. Then, sections of the gland were taken for histological study. These sections which were preserved in 10% formalin was processed and stained with hematoxylin and eosin.

Results: It was observed that the thyroid gland was situated in its definitive location anterior to 1st-6th tracheal ring in all fetuses. The gland was horse-shoe shaped in all fetuses, except in one fetus (22 weeks), where isthmus was absent. The isthmus was related to 1-4th tracheal rings. The fetuses were categorized into three gestational age groups as: Group I: 10-17 weeks, Group II: 18-22 weeks, and Group III: 23-36 weeks. The mean and ranges of the length, breadth, and thickness of the right and left lateral lobes were measured in each group. The observation of the histological features revealed that development of thyroid gland has three stages as: Colloid formation stage, folliculogenesis stage, and mature follicular growth stage. These stages were correlated with gestational age.

Conclusion: The present study helps us to understand and correlate the morphological and histological changes during the development of thyroid gland. Such knowledge helps the clinicians to understand the anatomical and histo-pathological changes in certain thyroid gland disorders.

Key words: Fetal thyroid, Histogenesis of thyroid gland, Histological differentiation, Histology of thyroid, Thyroid gland

INTRODUCTION

The thyroid gland is the first endocrine glandular structure to be differentiated. It begins to form about 24 days after fertilization and by 7 weeks, thyroid gland assumes its definite shape and reaches its final site in the neck. By the 11th week, it starts its function of synthesis of thyroid hormones.[1,2] The thyroid gland is an unpaired derivative of the primitive pharyngeal floor, and most human embryologists are of the opinion that in man it follows the typical vertebrate pattern.[3] The morphology and histological structure of the thyroid gland were examined in fetuses to assess the peculiarities of thyroid differentiation before birth. The study of histological differentiation helps us to understand the morphological changes during the development of human thyroid. The thyroid gland regulates the basal metabolic rate, somatic growth, psychic growth, calcium metabolism, and circadian rhythm. Hence, thyroid gland plays a major role for the normal growth of the fetus during the prenatal period. Thyroid gland abnormalities both anatomical and functional are seen in approximately one in 2000-4000 new infants.[4] The main objective of our study is to study the morphological and histological features of the thyroid gland in various age group fetuses.

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Corresponding Author: Dr. A Anupriya, Flat No 3, "Aashish Apartments," AL 33 (Old No AL 121), IIIrd Street, Anna Nagar, Chennai - 600 040, Tamil Nadu, India. Phone: +91-94442-12457. E-mail: dr_anu_priya@yahoo.co.in

MATERIALS AND METHODS

40 intact fetuses of varying gestational ages ranging from 11 to 36 weeks were studied in the Department of Anatomy, Sri Muthukumaran Medical College Hospital & Research Institute. The fetuses were preserved in 10% formalin solution. Following is the procedure followed for the exposure of the thyroid gland. Midline dissection of the neck was done. The situation and shape of the gland was noted. Measurements of the length, breadth, and thickness of the right and left lateral lobes and isthmus of the gland were noted for each fetus.

Processing was done for the histological study of sections taken from the thyroid gland of fetuses. These sections were preserved in 10% formalin. They were subjected to routine processing by dehydration in graded alcohols, clearing in xylol and were embedded in paraffin sections. Sections of 5 μm thickness were cut and stained with hematoxylin and eosin and mounted in Canada balsam. The histological features were observed using a light microscope and correlated with the gestational age.

Based on the histological differentiation and organization, the fetuses were grouped into three gestational age groups as: Group I: 10-17 weeks, Group II: 18-22 weeks, and Group III: 23-36 weeks. The histological features were same for all fetuses belonging to a particular group.

The mean and ranges of the length, breadth, and thickness of right and left lateral lobes and isthmus were calculated for the fetuses in each group.

RESULTS

In the present study, 40 intact fetuses of different gestational age and of both sexes were studied for morphological and histological features.

Morphological Features

Shape

The thyroid gland was "horse-shoe shaped" in all fetuses, except in one fetus where it was "irregular in shape" because isthmus was absent (2.5%).

Extent

The lateral lobes extended from middle or lower border of the thyroid cartilage to 3rd or 4th tracheal ring in all fetuses. The isthmus was related to 1st-4th tracheal rings. 2.5% (1 out of 40) specimens showed the absence of isthmus (Figure 1). Pyramidal lobe (PL) was seen in 30% (12 out of 40) specimens (Figure 2). Levator glandulae thyroidea was present in 15% (6 out of 40) specimens (Figure 3).

Figure 1: Absence of isthmus (shown by arrow) seen in a fetus

Figure 2: Pyramidal lobe (shown by arrow) seen in a fetus

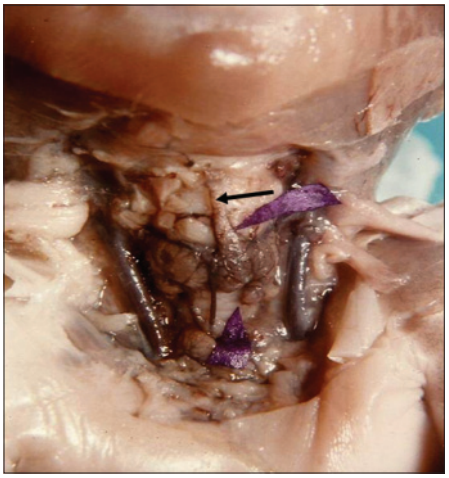

Figure 3: Levator glandulae thyroidea (shown by arrow) seen in a fetus

Dimensions

The mean and ranges of the length, breadth, and thickness of lateral lobes were measured and tabulated for each group as given in Table 1.

From the Table 1, it is observed that during the fetal life the mean of length, breadth, and thickness of lateral lobes for gestational ages 10-36 weeks ranged from 5.6 to 12.1 mm, 2.8 to 4.5 mm, and 1.8 to 2.9 mm, respectively.

The mean and ranges of the length and breadth of isthmus were measured and tabulated for each group as given in Table 2, after excluding one specimen in Group II as the isthmus was absent.

Hence, as noted from the Table 2, the mean of length and breadth of isthmus for gestational ages 10-36 weeks ranged from 4.07 to 10.6 mm and 2.2 to 5.6 mm, respectively, during the fetal life.

Histological Features

Group I (10-17 weeks): Colloid formation stage

In this stage, it was observed that the capsule was seen with septa dividing the gland into incomplete lobules. Cluster and cords of epithelial cells with very few follicles were seen in the central core of the glands. Follicles which were seen in the periphery were of small size and were irregular in shape. Follicular cells were simple cuboidal cells with darkly stained nuclei. Thin rim of colloid were present in few developing follicles. Colloid was absent in most of the follicles. Sinusoids were present between the follicles. Vascularity increased as gestational age increased. Hence, this stage is considered as "colloid formation stage" (Figure 4).

Table 1: The mean and ranges of the length, breadth, and thickness of lateral lobes

Groups (*n*=40)	Lateral lobes Mean and range (mm)					
	Length		Breadth		Thickness	
	Mean	Range	Mean	Range	Mean	Range
Group I (10-17 weeks) *n*=13	5.6	3-9	2.8	2-4	1.8	1-4
Group II (18-22 weeks) *n*=12	9.5	7-12	4.2	3-6	2.75	2-4
Group III (23-36 weeks) *n*=15	12.1	7-18	4.5	2-6	2.9	2-5

Table 2: The mean and ranges of length and breadth of isthmus

Groups (*n*=39)	Isthmus Mean and range (mm)			
	Length		Breadth	
	Mean	Range	Mean	Range
Group I (10-17 weeks) *n*=13	4.07	1-6	2.2	0.5-4
Group II (18-22 weeks) *n*=11	8.9	3-13	4.9	4-5
Group III (23-36 weeks) *n*=15	10.6	8-13	5.6	3-9

Group II (18-22 weeks): Folliculogenesis stage

In this stage, capsule and septae were present but were incomplete. The periphery and central core of the gland showed increase number of follicles. In the periphery of the gland, follicles were round to oval shape with lumen showing thin rim of colloid. In the central core of the gland, developing follicles were seen which were small in size with or without a lumen. Sinusoids were abundantly present. Hence, this stage is considered as "folliculogenesis stage" (Figure 5).

Group III (23-36 weeks): Mature follicular stage

It was observed in this stage that the capsule and septae were well-defined. Connective tissues between follicles

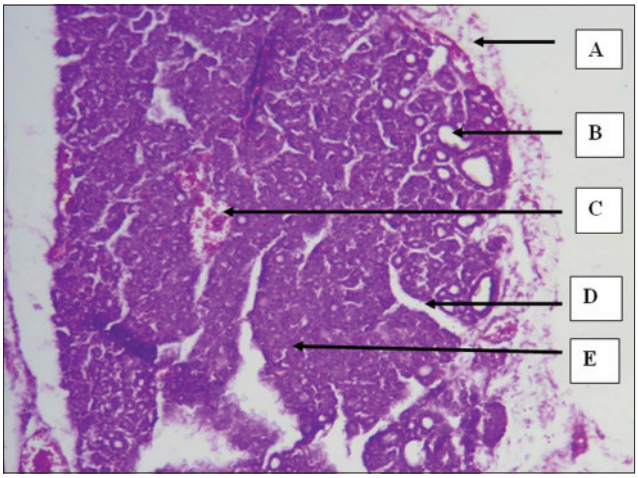

Figure 4: Colloid formation stage: (a) Capsule, (b) peripheral follicle, (c) sinusoids, (d) septa, (e) developing follicles as cluster of cells

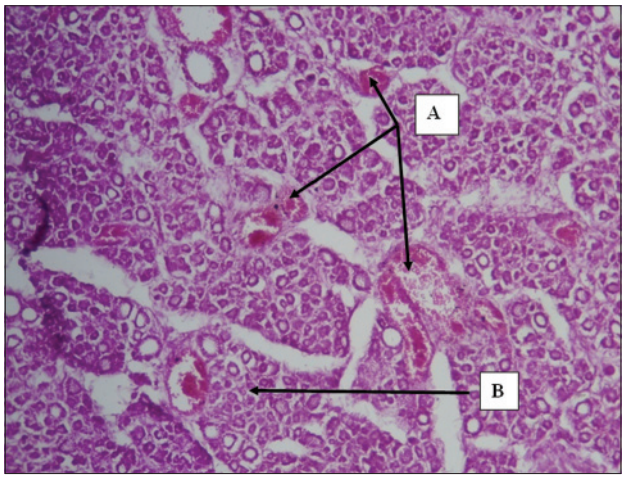

Figure 5: Folliculogenesis stage: (a) Abundant sinusoids, (b) developing follicles in central part of gland

showed abundant vessels. There was an increase in the number of follicles and follicles of varying sizes were also seen. More number of mature thyroid follicles was present in this group which showed simple cuboidal epithelium with centrally placed nucleus. Some follicles showed irregular eroded colloid with vacuoles in it. Hence, this stage is considered as "Mature follicular stage" (Figure 6).

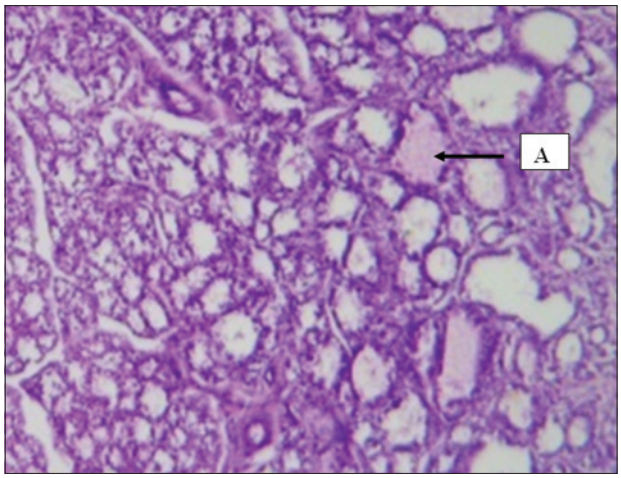

Figure 6: Mature follicular stage: (a) Follicle showing irregular eroded colloid with vacuoles in it

DISCUSSION

In the present study, it was observed that the thyroid gland was "horse-shoe shaped" in all fetuses, except in one fetus where it was "irregular shape" because isthmus was absent (2.5%). Harjeet *et al.*[5] observed different shapes of isthmus such as horse-shoe shaped (36.8%), irregular shape (5.1%), and glands with separate lobes (7.9%). The absence of isthmus was also observed by Lokanadham and Devi[6] in 6.6% specimens and Marshall *et al.*[7] in 10%. This agenesis can be due to an anomaly of embryological development, where there is a high division of thyroglossal duct leading to dysorganogenesis like the absence of isthmus or any one lobe.[8,9] The knowledge of the absence of isthmus is significant for surgeons when performing thyroidectomy as it causes difficulty in identifying vessels and hence leading to major complications.

The knowledge of the presence of PL is important because it causes hindrance during surgery. It also misleads diagnosis of scintigraphical images.[10] The incidence of PL in other studies conducted in different populations is shown in Table 3. In our study, PL was present in 12 out of 40 fetuses (30%).

Table 3: Incidence of pyramidal lobe in different populations

Authors	Presence of pyramidal lobe (%)	Populations
Braun *et al.*[10]	55	Austria
Gangbo *et al.*[11]	76.8	Korea
Lokanadham and Devi[6]	7	South India
Sadat[12]	41.6	Bangladesh
Present study	30	South India

In the present study, the dimensions of thyroid gland increased proportionately with the gestational age, as there is an increase in colloid formation and increase in number and size of the follicles in the gland.

According to the present study, based on the histological differentiation and organization, the fetuses were grouped into three gestational age groups:

1. Colloid formation stage: 10-17 weeks
2. Folliculogenesis stage: 18-22 weeks
3. Mature follicular stage: Above 22 weeks.

This staging differed from staging done by Jyothi *et al.*[13] where four stages were done as follows: Precolloid (upto 12 weeks), colloid formation (13 to maximum 20 weeks), folliculogenesis (14-20 weeks), and secretory stage (20-24 weeks).

In the present study, the capsule was observed from 11 weeks, and it became thick and vascularity increased as age advances. This was also observed by Arthur[14] and Jyothi *et al.*[13] reported that the capsule started to appear as a thin layer by 12 weeks and became thick as age advanced.

In the present study, thyroid follicles started to develop from the periphery of the gland as observed in Group I. According to Jyothi *et al.*,[13] differentiation of follicles started from the periphery as vascularity was more in the periphery than the central part of gland throughout the gestational age of the fetus. Potter[15] observed that epithelial cords are arranged to form small follicles which are solid at first then becomes hollow and filled with colloid. In our study, the epithelial cords formed small solid follicles then it matured to become colloid-filled follicles as age advanced. Hence, Group III fetuses showed few solid follicles in the center and many colloid-filled follicles in the periphery.

As was observed in our study, the number and size of follicles increased as gestational age increased. Follicles were lined by low cuboidal epithelium and appeared empty in sections. According to Shepard *et al.*,[16] connective tissues between follicles decreased as the vasculature increased, and there was a progressive increase in diameter of follicles as gestational age increased. Folliculogenesis is more prominent by 14-20 weeks[13] and 10-18 weeks,[17] and in our study, it was very well-established between 11 and 22 weeks.

Shepard *et al.*[16] observed that human thyroid follicles do not develop synchronously throughout, instead different stages of maturity was seen in fetuses belonging to same age group. Even in large fetuses, there were some areas in which follicles had not developed. Such immature follicles were also seen in Group III fetuses of our study.

In the present study, colloid appeared as a thin rim in the developing follicles of Group I fetuses and increased as gestational age advanced. Colloid in follicle is indicated by its affinity for acidic dyes. Clear vacuoles in colloid and apical position of epithelial cells indicate secretory activity of follicular cells.[18] In our study, it was seen in specimens belonging to Group III.

Junqueira *et al.*[19] observed an irregular outline of colloid in active follicles of fixed and stained histological preparation. Arthur[14] reported that colloid seems to have shrunken away from follicular epithelium in such a way as to present a serrated outline when the gland is active. In the present study, a colloid in the follicles appeared irregular and eroded at the periphery in Group III fetuses indicating secretory activity (Figure 6). According to Shepard *et al.*,[16] the scallop like vacuolization of the outer part of the colloid cavity is indicative of utilization of thyroid hormones. This stage corresponds with the time at which radioiodine has been found to accumulate as observed by authors such as Chapman *et al.*[20] and Hodges *et al.*[21]

This study helps us to correlate the morphological changes with histological changes during the development of fetal thyroid gland. Any delay between the stages of histological differentiation leads to hyperplasia of the gland as mentioned by Lokanadham and Devi.[6] The staging of histological differentiation helps us to understand the morphological and functional disorders of the thyroid glands which were also stated by Lokanadham and Devi.[6]

CONCLUSION

The present study helps us to understand and correlate the morphological and histological changes during the development of thyroid gland. Such knowledge helps the clinicians to understand the anatomical and histopathological changes in certain thyroid gland disorders.

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Original Article

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Comparison of Effect of Adding Intrathecal Magnesium Sulfate to Bupivacaine Alone and Bupivacaine-Fentanyl Combination during Lower Limb Orthopedic Surgery

Rajesh Vasure[1], Inder Dev Ashahiya[2], Rekha Mahendra[3], Neeraj Narang[2], Raj Kumari Bansal[4]

[1]Senior Resident, Department of Anesthesiology, Netaji Subash Chandra Bose Medical College, Jabalpur, Madhya Pradesh, India,
[2]Assistant Professor, Department of Anesthesiology, Netaji Subash Chandra Bose Medical College, Jabalpur, Madhya Pradesh, India,
[3]Professor and Ex. HOD, Department of Anaesthesiology, Netaji Subhash Chandra Bose Medical College, Jabalpur (Madhya Pradesh)
[4]Post-graduate Student, Department of Pharmacology, Netaji Subash Chandra Bose Medical College, Jabalpur, Madhya Pradesh, India

Abstract

Background: Spinal anesthesia is a simple technique that provides a fast surgical block. It has certain limitations such as limited duration of the blockade and post-operative analgesia.

Materials and Methods: This randomized study was conducted in 60 patients of the American Society of Anesthesiologists Classes I and II aged between 20 and 50 years scheduled for elective lower limb orthopedic surgery. Patients were randomly divided into three groups of 20 each. Group I patients received bupivacaine (0.5%) 2.5 ml with $MgSO_4$ (50%) 0.1 ml, Group II patients received bupivacaine (0.5%) 2.5 ml with fentanyl (50 mg/ml) 0.5 ml, whereas Group III patients received bupivacaine (0.5%) 2.5 ml with $MgSO_4$ (50%) 0.1 ml and fentanyl (50 mg/ml) 0.5 ml, to a total volume of 3.1 ml in each group. The parameters assessed were onset and duration of sensory block, time to reach the maximum height of the sensory block, duration of analgesia, and incidence of side effects.

Results: It was found that in Group I, there was a significant delay in the onset of sensory block and time to reach maximum sensory block level when compared with Groups II and III. While the duration of sensory and motor block was significantly higher in Group III than Groups I and II. The moreover, duration of analgesia was prolonged when compared with Group II. In addition of magnesium sulfate provide, a more stable hemodynamic profile and causes less side effects.

Conclusion: The addition of 50 mg magnesium sulfate as adjuvant to intrathecal bupivacaine significantly prolongs duration of analgesia with a lesser side effect. It is suggested that magnesium may be a useful adjuvant to opioids for spinal anesthesia.

Key words: Anesthesia, Bupivacaine, Fentanyl, Magnesium sulfate, Post-operative analgesia

INTRODUCTION

Post-operative pain relief has two practical aims. The first one is the provision of subjective comfort which is desirable for humanitarian reasons. The second is inhibition of trauma induced nociceptive impulses to blunt autonomic and somatic reflex responses to pain and to enhance subsequent restoration of function by allowing the patient to breath, cough, and move more easily[1]. Spinal anesthesia is a simple technique that provides a deep and fast surgical block through the injection of small doses of local anesthesia solution in subarachnoid space. It provides excellent operating conditions for surgery below the umbilicus[2]. Spinal anesthesia using bupivacaine heavy is one of the most frequently used techniques for lower limb and lower abdominal surgeries. In last few decades, many agents have been used along with bupivacaine intrathecally to prolong the intra- and post-operative analgesia, the opioid being the most common. Fentanyl is a synthetic primary mu opioid receptor agonist. It is a lipophilic

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Corresponding Author: Dr. Inder Dev Ashahiya, D-503 Acropolis, Near Gulati Petrol Pump, Madan Mahal, Jabalpur - 482 002, Madhya Pradesh, India. Phone: +91-9691205305. E-mail: drinderdevgwl@gmail.com

opioid with rapid onset of action following intrathecal administration which provide better intraoperative analgesia for the management of early post-operative pain and do not cause delayed respiratory depression. The multimodal approach to the management of perioperative pain has become routine both to improve efficacy and to minimize the side effects of opioids. Magnesium (Mg) has been one of the agents investigated for this purpose as it is known to inhibit calcium entry into cells and to exhibit non-competitive blockade of the N-methyl-D-aspartate (NMDA) receptor. It does not appear that magnesium has any primary analgesic effect in its own right, but it does offer secondary analgesic effects that may enhance the action of other analgesic agents. The purpose of this study is to investigate and compare the effect of magnesium sulfate in spinal anesthesia and post-operative pain relief with bupivacaine alone and with the bupivacaine-fentanyl combination in lower limb orthopedic surgeries[3-6].

MATERIALS AND METHODS

A total of 60 patients were enrolled for the study after the approval from Institutional Ethics Committee. The design of the study was randomized, double-blinded in patients who have undergone lower limb orthopedic procedures and fulfilling the criteria for regional anesthesia. A detailed history, thorough physical examination, routine investigation like complete blood count, blood sugar, renal profile, serum electrolytes, and any special investigation if required was done for the study. An informed written consent was taken from all the patients. Obviously, the patients who had coagulopathy, sepsis at the site of intrathecal injection, major organ pathology like heart disorder, hepatic, and renal disorder were excluded from the study. The patients were randomly divided into three groups of 20 each. The three groups were named as Groups I, II, and III. Group I patients received injection bupivacaine (0.5%) 2.5 ml with injection $MgSO_4$ (50%) 0.1 ml, Group II patients received injection bupivacaine (0.5%) 2.5 ml with injection fentanyl (50 mg/ml) 0.5 ml, whereas Group III patients received injection bupivacaine (0.5%) 2.5 ml with injection $MgSO_4$ (50%) 0.1 ml and injection fentanyl (50 mg/ml) 0.5 ml. The appropriate volume of normal saline was added to each study solution so as to make the injectate volume comparable. Material required for this is spinal trolley with 25 G spinal needle, 5 ml disposable syringe, injection bupivacaine (0.5%), injection magnesium sulfate (50%), injection fentanyl (50 mcg/ml), tuberculin syringe, normal saline, emergency drugs/intubation kit and resuscitation kit. After we received the patients in the operation room, a careful pre-operative examination was done and monitors were attached including non-invasive blood pressure, pulse oximetry and electrocardiogram. An intravenous line was secured using an 18 G cannula on the right forearm vein. The patients were preloaded with ringer lactate solution 15 ml/kg over 20 min. The patient received a spinal injection in sitting position using the study solution. Intraoperative episodes of hypotension (define as ≥30% fall in mean blood pressure [MBP]) were treated with intravenous 6 mg ephedrine injection. Intraoperative episodes of bradycardia (defined as pulse rate <60 bpm) were treated with intravenous injection of 0.3 mg atropine. Various parameters were then assessed and recorded on a prescribed proforma like onset of sensory block (time elapsed from the end of study solution to absence of pinprick sensation at T10 dermatome), maximum height achieved of sensory block, time to reach the maximum height of sensory block (time elapsed from the end of injection to attain maximum height [level] of sensory block), duration of sensory block (time elapsed from the end of injection to regression of sensory block by two dermatomes), and duration of analgesia. Onset, height and duration of sensory block were assessed by pinprick method. The duration of analgesia was recorded as the time from intrathecal injection until the patients request for additional analgesia in post-operative period which was assessed by a visual analogue score of ≥4. The intensity of post-operative pain was evaluated using a visual analogue scale, one end ("0" point of VAS) of which shows no pain and other end ("10" point of VAS) shows worst possible pain. Demographic parameters, such as age and sex, were also recorded on a prescribed proforma. Intraoperative hemodynamic variables like pulse rate per min, systolic blood pressure, diastolic blood pressure, MBP were recorded preoperatively and at 10^{th} min, 30^{th} min, and 150^{th} min. Though the mean surgery was around 115 min, which means that 150^{th} min recording of hemodynamic variable was recorded in the post anesthesia recovery unit. Our study also entailed recording of various side effects like the incidence of nausea-vomiting, pruritis and shivering. Randomization of the subjects was done using standard random number table. The study was double-blinded in which both the patients and assessor of parameters were blinded for the type of injection used in the spinal anesthesia. All case report forms were checked for completeness and inappropriate or illogical responses. All the data pertaining to the demographic characteristic, sensory block, hemodynamic analysis. The forms were filled using Microsoft 2007 Excel worksheet. The databases were validated, and all inconsistencies and differences were resolved. Statistical analyses were performed using STATA 12 for Windows (StataCorp LP, Texas, USA). Categorical data are presented as frequency counts (percentage) and compared using the Chi-square or Fisher's exact statistic as appropriate. Odds ratio and 95% confidence intervals were also presented for 2 × 2 contingency tables. Continuous data are presented as means (±standard deviation) and

compared using the *t*-test or analysis of variance as appropriate.

RESULTS

Table 1 shows age and sex distribution of the three groups. Among the three groups, the most patients were of male gender. However, there was no statistically difference the demographic parameters of age and sex.

Table 2 depicts the maximum level of sensory block achieve among the three groups. Maximum patient of Group II had the maximum sensory level block until T_4 dermatome. There was statistically difference observed among the groups especially between Groups I and II for the maximum level of sensory block observed at T_4 dermatomes.

Table 3 demonstrate the onset of sensory block in the study population. The mean onset time for the sensory block was observed to be 4.45, 1.62 and 3.30 min for Groups I, II and III, respectively, ($F = 70.60$; $P < 0.0001$).

Mean time to reach maximum sensory block level was 10.40, 5.65, and 9.55 min, respectively, for Groups I, II, and III. It was found that the mean difference between Groups I and II and Groups II and III were statistically highly significant ($P < 0.0001$), whereas the result was statistically significant ($P < 0.05$) between Groups I and III.

The duration of sensory block was 136, 180 and 232 min in Groups I, II and III, respectively. Which was statistically significant ($F = 160.53$; $P < 0.0001$).

The duration of analgesia was significantly higher in Group III. It was 164, 238 and 368 min in Groups I, II and III ($F = 786.0$; $P < 0.0001$).

The mean surgical time duration was 111.5, 113.1 and 117.9 min in the three groups, respectively. The data were comparable.

Table 4 shows the incidence of side effects among all the groups.

Table 1: Demographic data

Age category (in year)	Group I (%)		Group II (%)		Group III (%)	
	Male	Female	Male	Female	Male	Female
21-30	3 (15)	0	3 (15)	0	3 (15)	2 (10)
31-40	5 (25)	3 (15)	6 (30)	2 (10)	5 (25)	2 (10)
41-50	6 (30)	3 (15)	4 (20)	5 (25)	7 (35)	1 (5)
Total	14	6	13	7	15	5

P>0.05 in significant

Table 2: Level of sensory block

Level	Group I (%)	Group II (%)	Group III (%)
T4	1 (5)	17 (85)	10 (50)
T5	8 (40)	3 (15)	5 (25)
T6	10 (50)	0 (0)	5 (25)
T7	1 (5)	0 (0)	0 (0)

Table 3: Sensory block parameters

Parameters	Group I	Group II	Group III	Significance (mean difference)
Onset of sensory block (min)	4.45±0.74	1.62±0.62	3.30±0.88	1/2=2.88 1/3=1.15 2/3=1.67 *P*<0.0001 *F*=70.60
Time to reach maximum sensory level (min)	10.40±0.94	5.65±1.04	9.55±1.09	1/2=4.75; *P*<0.0001 1/3=0.85; *P*<0.05 2/3=3.90; *P*<0.0001
Duration of sensory block (min)	136±8.21	180±12.56	232±25.26	1/2=44 1/3=96 2/3=52 *P*<0.0001
Duration of analgesia (min)	164±10.46	238±14.96	368±21.91	1/2=74.5 1/3=204 2/3=129 *P*<0.0001 *F*=786.0
Duration of surgery (min)	111.5±15.62	113.1±8.59	117.9±9.36	*P*>0.05

Table 4: Incidence of side effect

Side Effects	Group I (%)	Group II (%)	Group III (%)
Nausea vomiting	1 (5)	3 (15)	2 (10)
Pruritis	0	2 (10)	0
Shivering	0	3 (15)	0

DISCUSSION

The intrathecal route is attractive, as it obviates the problems of systemic administration and it solves the problem of transport of the agent across the blood brain barrier. Various intrathecal adjuvants such as NMDA antagonists, clonidine, and neostigmine have been assessed as possibilities for improved pain relief without side effects.[7-9] Magnesium exerts its analgesic action as a non-competitive NMDA receptor antagonist, blocking ion channels in a voltage-dependent manner.[5] In the dose range necessary for the effective enhancement of opiate-based analgesia, there is no evidence that magnesium is harmful to neuronal tissue.[10] Indeed, it may offer some degree of protection against hypoxia and ischemia through

a combination of spinal cord vasodilatation, calcium antagonism and blockade of the NMDA channel.[11] However, magnesium is ineffective as a primary analgesic and must be used in conjunction with opiates to provide a useful analgesic extension. The combination of magnesium and opiates appears to offer enhanced opioid analgesia, a reduction in the risk of secondary hyperalgesia and possibly a reduction in the risk of the development of post-operative chronic pain syndromes.[12,13]

Previous studies have used the dose of 50 mg neuraxial magnesium sulfate either as intrathecal or epidural dose and reported an increase in duration of analgesia and found to be safe and effective.[14-16] In contrast, very high doses of magnesium sulfate produce a transient toxic effect. Khalili *et al*.,[17] also demonstrated that the application of a larger dose (100 mg) could not produce any further desirable effects compared to 50 mg magnesium sulfate except prolonging the duration of sensory block with no effect on duration of spinal analgesia.

Since all the groups were demographically similar ($P > 0.05$ in all the comparisons), it can be presumed that the groups are comparable for the purpose of the study. No premedication was used in the study population, it can, therefore, be presumed that recording of parameters pertaining to sensory analgesia was consistently accurate. All the patients were preloaded to offset the effect of relative hypovolemia or hypotension.

In this study, we showed that magnesium 50 mg when added to bupivacaine-fentanyl combination for spinal anesthesia could provide prolonged post-operative analgesia without additional side effects in patients undergoing lower limb orthopedic surgery. Furthermore, it significantly delays the onset of the sensory block as well as time to reach maximum sensory block and also prolongs the duration of sensory blockade. Magnesium 50 mg alone when added to bupivacaine too leads to delay in onset of sensory block and prolongation of time to reach maximum sensory block but without prolongation of sensory block duration and duration of post-operative analgesia.

Onset of sensory block in the present study was defined as time taken for loss of pinprick sensation at T10. Mean time for onset of sensory block and time to reach maximum sensory level was significantly higher in Group I as compare to Groups II and III.

These results are consistent with studies of Ozalevli *et al*.,[14] who too observed a similar delay in onset of spinal anesthesia when magnesium is added to fentanyl and isobaric bupivacaine. Malleeswaran *et al*.,[18] also observe similar results in their study when they used a mixture of bupivacaine-fentanyl and magnesium intrathecally in patients with mild preeclampsia undergoing caesarean section. Arcioni *et al*.,[19] also observed that intrathecal and epidural magnesium sulfate potentiated and prolonged motor block. These findings are in agreement with various studies.[17,20-22] The authors suggested that the difference in pH and baricity of the solution by addition of magnesium contributed to the delayed onset, which may also be the case in our study.

The mean duration of sensory was significantly higher in Group III than Groups I and II. These results are in corroboration with Malleeswaran *et al*.,[18] Unlugenc *et al*.,[20] who showed prolongation of the duration of sensory block in magnesium group.

Jabalameli and Pakzadmoghadam[22] used different doses of magnesium, i.e., 50, 75 and 100 mg with 0.5% bupivacaine in caesarean section and observed maximum duration of sensory block with 100 mg group, Khalili *et al*.,[17] observed prolongation of the duration of the sensory block with 100 mg intrathecal magnesium. Sayed and Fathy,[23] showed the prolongation of onset as well as time to regression of sensory block was more with 100 mg of magnesium as compared to 50 mg.

The combination of fentanyl and magnesium sulfate is hyperbaric as compared with CSF and would limit cephaled spread. This explained the delay by the difference in pH and baricity of the solution containing magnesium.[14,18,24]

The mean duration of analgesia was significantly higher in III than Groups I and II ($P < 0.0001$). In our study, duration of analgesia was taken as the period from spinal injection to the time of administration of first rescue analgesia for pain postoperatively when requested by the patient. Malleeswaran *et al*.,[18] found that the addition of intrathecal magnesium increased the duration of spinal anesthesia by 42 min. Dayioglu *et al*.,[25] also conclude that addition of magnesium sulfate to spinal anesthesia prolonged the time to first analgesic requirement. Khezri *et al*.,[21] demonstrated that the addition of $MgSO_4$ (50 mg) to 15 mg of spinal bupivacaine (0.5%) failed to prolong the time to first analgesic requirement, as seen with fentanyl and bupivacaine combination.

In Group I, where only magnesium is added to bupivacaine show minimum duration of analgesia in comparison to other two groups. There are a few possible reasons why magnesium failed to prolong the time to the first analgesic requirement. First of all, it has been claimed that the effects of magnesium sulfate on the NMDA receptor complex are weaker than those of some other NMDA receptor antagonists. The second possible cause is that

magnesium sulfate which most likely vasodilator around the injection site will eventually accelerate the systemic uptake of local anesthetic, thereby prolonging the onset time of block. Third, magnesium sulfate might activate bupivacaine hydroxylation by the cytochrome P450. Therefore, the addition of intrathecal magnesium sulfate to spinal bupivacaine may alter bupivacaine pharmacokinetics and cause a more rapid elimination of bupivacaine.[26] Furthermore, magnesium sulfate is reported to have been successfully used to attenuate the bupivacaine-induced toxicity in the central nervous system and heart.[21]

In the present study, there were no clinically significant changes in vital parameters. There was initial fall in MBP and heart rate from pre-operative value in patients of all three groups which was statistically but not clinically significant and easily corrected with administration of mephentermine, additional fluids or atropine for hypotension and bradycardia. This may be attributed to the absence of systemic vasodilator effects of spinal magnesium. Higher dose of magnesium (100 mg) might result in increasing some of the side effects (hypotension, nausea and vomiting).[22]

In our study, the incidence of nausea and vomiting showed no significant difference among groups and this may be related to similar hemodynamic and absence of significant hypotension among groups.

Pruritus and shivering were observed only in patients of Group II. The incidence of post-anesthetic shivering in Group II was 15% as against none in rest of the two groups. Magnesium causes peripheral vasodilatation which probably improves the cutaneous circulation, thus decreasing the incidence of shivering.[23,27]

CONCLUSION

To summarize, our results shows that addition of 50 mg magnesium sulfate in patients undergoing lower limb orthopedic surgery lead to prolonged duration of analgesia significantly without increasing the incidence of side effects. Furthermore, there was a significant delay in the onset of sensory block and prolongation of sensory block duration.

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Original Article

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Effect of Dexamethasone as an Adjuvant to Local Anesthetic in Supraclavicular Brachial Plexus Block

B T Arish[1], D Dinesh Babu[2], Suneeth P Lazarus[3], D Dilip Chandar[2], S Balasubramanian[4], K Suresh Kumar[4]

[1]Post-graduate Resident, Department of Anaesthesiology, Sri Manakula Vinayagar Medical College and Hospital, Puducherry, India, [2]Assistant Professor, Department of Anaesthesiology, Sri Manakula Vinayagar Medical College and Hospital, Puducherry, India, [3]Professor, Department of Anaesthesiology, Sri Manakula Vinayagar Medical College and Hospital, Puducherry, India, [4]Associate Professor, Department of Anaesthesiology, Sri Manakula Vinayagar Medical College and Hospital, Puducherry, India

Abstract

Introduction: Brachial plexus block is the most preferred anesthetic technique for upper limb surgeries. This study was done to study the adjuvant effect of dexamethasone when added with local anesthetics in supraclavicular brachial plexus block.

Objective: The objective of the study was to evaluate dexamethasone as an adjuvant to bupivacaine in patients undergoing upper limb surgeries by supraclavicular brachial plexus block.

Materials and Methods: After Ethics Committee Approval this randomized, double-blinded, control study was conducted in the Department of Anaesthesiology, Sri Manakula Vinayagar Medical College and Hospital, Puducherry. A total of 50 patients who met the inclusion criteria were enrolled into the study and were randomized to receive plain bupivacaine and bupivacaine with dexamethasone in supraclavicular brachial plexus block. The onset of analgesia, the onset of motor blockade and hemodynamic parameters oxygen saturation, heart rate, systolic and diastolic blood pressures were recorded during and 1 h after the procedure. The duration of analgesia and motor blockade were also noted in the post-operative period.

Results: There was no statistically significant difference in the onset of sensory and motor blockade between both the groups. The mean duration of sensory blockade in study group was 1075.20 ± 144.831 min and in control group was found to be 288.00 ± 103.923 min and the mean duration of motor blockade in study group was 475.20 ± 114.787 min and in control group was found to be 218.40 ± 64.52 min and was statistically significant ($P \leq 0.001$).

Conclusion: We conclude that when dexamethasone used as an adjuvant along with local anesthetic in brachial plexus block, it effectively prolongs the duration of both sensory and motor blockade with no side effects.

Key words: Adjuvant, Brachial plexus, Dexamethasone, Supraclavicular

INTRODUCTION

Brachial plexus block is the most preferred anesthetic technique for upper limb surgeries. It has its own advantages by avoiding untoward effects of general anesthetic drugs and upper airway instrumentation. Various approaches of brachial plexus blocks have been described, but the supraclavicular approach is the easiest and most consistent method for anesthesia and perioperative pain management in surgery below the shoulder joint.[1] In a supraclavicular approach, the brachial plexus is blocked where it is most compactly arranged at the level of nerve trunks and rapid onset can be achieved, with a high success rate for elbow, forearm, and hand surgery because all the branches of the brachial plexus can be reliably blocked.[2]

Investigators have tried mixing local anesthetic with adjuvant drugs in an attempt to prolong analgesia from nerve blocks. Drugs like morphine, pethidine, clonidine, dexmedetomidine, butorphanol, buprenorphine are commonly used as adjuvant along with local anesthetic. Adjuvants including epinephrine, clonidine,[3,4] opioids,[5,6] ketamine,[7,8] and midazolam[9] have met with limited success.

Recent pre-clinical and clinical studies show that the glucocorticoid dexamethasone appears to be effective as

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Corresponding Author: Dr Dilip Chandar, Assistant Professor, Department of Anaesthesiology, Sri Manakula Vinayagar Medical College and Hospital, Puducherry, India. Email id: dilipchandar2000@gmail.com

an adjuvant to local anesthetics.[10-13] This study was done to study the adjuvant effect of dexamethasone when added with local anesthetics in Supraclavicular brachial plexus block.

MATERIALS AND METHODS

After obtaining approval from the Institutional Ethics Committee approval, this study was conducted in Department of Anesthesiology at Sri Manakula Vinayagar Medical College and Hospital, Pondicherry between November 2013 and May 2015. The study was designed to be of double blinded randomized control study following good clinical practice guidelines of the WHO. After taking thorough history and pre-operative assessment, 50 patients who were satisfying the inclusion criteria were enrolled into the study. The inclusion criteria were defined as patients aged between 18 and 60 years of American Society of Anesthesiologists I to II physical status, who were planned to undergo below shoulder upper limb surgeries (both elective and emergency) under brachial plexus block. Patients who refused to give consent, pregnant women, history of local anesthetics allergy, peptic ulcer disease, diabetes mellitus, peripheral neuropathy and patients with contraindications for brachial plexus block like bleeding disorder, patients on anticoagulants, severe respiratory disease, neurological deficit involving brachial plexus local infection at the injection site were excluded from the study.

After explaining the procedure properly in their native language, a written informed consent was taken from all the participants of the study. The study subjects were randomized by using block randomization using sealed concealed envelopes into two groups namely Group D and Group S each consisting of 25 patients. In the pre-operative room, intravenous access was secured with 18-G cannula on the contralateral hand and baseline parameters such as heart rate, mean arterial pressure, oxygen saturation was observed and recorded.

The brachial plexus block was carried out after thorough explanation of the procedure and emphasizing the need for patient cooperation. In the operation theater, monitors were connected (pulse oximetry, electrocardiography and noninvasive arterial blood pressure monitoring). Oxygen was administered via a Hudson mask at a rate of 5 L/min. Supraclavicular brachial plexus block was performed under aseptic precautions with the patient in supine position, and head turned slightly to the opposite side. A small pillow was placed in between the shoulders. The arm to be anaesthetized is adducted and the hand extended along the side towards the ipsilateral knee as far as possible. We used a nerve stimulator with a 22-G, 5 cm insulated needle for precise localization of the brachial plexus. A skin wheal with local anesthetic was raised in the 1.5-2 cm posterior to the midpoint of the clavicle. The subclavian artery is usually palpable at this site. The nerve stimulator frequency was set at 1 Hz, and the intensity of the stimulating current was initially set to deliver 2 mA. The insulated needle was inserted through the skin wheal in a posterior, caudal and medial direction until a distal motor response is elicited. The position of the needle was considered acceptable when an output current ≤0.4 mA still elicited a distal motor response. At this point, the local anesthetic mixture was injected in increments after negative aspiration for blood and air. The local anesthetic mixture for patients belonging to respective groups as follows.

Group D (study group): Patients in this group received 0.25% bupivacaine (38 ml) plus dexamethasone 8 mg (2 ml) making a total volume of 40 ml (care was taken not to exceed the maximum drug dosage).

Group S (control group): Patients in this group received 0.25% bupivacaine (38 ml) plus 0.9% normal saline (2 ml) making a total volume of 40 ml.

The site of injection was sealed with a tincture benzoin. During the conduct of block and thereafter, the patient was observed vigilantly for any complications and toxicity of the drugs injected. After injection of the local anesthetic, the following parameters were studied:

1. The onset of sensory block, i.e., the time from injection to onset of analgesia in each of the major peripheral nerve distribution (ulnar, radial, medial and musculocutaneous) was assessed by pinprick using the blunt end of a 27-G needle at 0, 2, 5, 10, 15, 20 and 30 min. Sensory block was graded according to the following scale: 0 = no block (normal sensation), 1 = partial block (decreased sensation), and 2 = complete block (no sensation)
2. Onset of motor block, i.e. the time from injection to the inability of the patient to move his/her fingers or raise hand. Motor block was measured at 0, 10, 20, 30 and 40 min by assessing the following motor functions: Flexion at the elbow (musculocutaneous nerve), extension of the elbow and the wrist (radial nerve), opposition of the thumb and index finger (median nerve), and opposition of the thumb and small finger (ulnar nerve). Motor block was graded according to the following scale: 0 = no block (full muscle activity), 1 = partial block (decreased muscle activity), and 2 = complete block (no muscle activity)
3. A duration of analgesia was assessed during the procedure. Anesthesia was considered satisfactory if the patient did not complain of any pain or discomfort and if no sedation was necessary. Post-operative

follow-up was carried out in the recovery and post-operative ward. The duration of analgesia was noted according to 0-10 visual analogue score (VAS) for pain at every 1 h until first 10 h and thereafter 2nd hourly until 24 h. When the patients began to experience pain (VAS = 4), it was considered that analgesic action of the drugs was terminated, and rescue analgesic (injection diclofenac 1-1.5 mg/kg IM) was given

4. Duration of motor block, postoperatively was assessed every hourly by asking the patients to move their fingers and to see whether the elbow flexion could be done against gravity or not. This time was recorded and taken as cessation of motor block effect
5. Possible complications of brachial plexus block such as pneumothorax, hematoma, signs and symptoms for local anesthetic toxicity was looked for and noted, if any.

The above assessments were carried out by the principal investigator who was blinded to the drugs administered in the plexus block. In the circumstance of inadequate or patchy action of the block, the block was supplemented with general anesthesia. If in case surgery is unduly prolonged and the effect of the block wore off, general anesthesia was given.

RESULTS AND OBSERVATIONS

Sample Size Determination

The sample size was determined considering mean difference of 1.75 min as proposed in the previous study done by Talukdar *et al.*,[14] with a confidence interval of 95% and 80% power of the study, the sample size of 23 in each group was considered adequate. Considering non-response, we concluded to a sample size of 25 in each group (total $n = 50$).

The data were analyzed using statistical software using Epi info 3.5.3 and SPSS version 20. Results are represented as mean ± standard deviation. Student's unpaired "*t*" test was used to compare the age, weight, baseline parameters, perioperative parameters and for onset and duration of sensory and motor blockade. Fisher's exact test was used for sex distribution. Chi-square test was used for site of surgery. Mann–Whitney *U*-test was used for assessing VAS score parameters. A $P = 0.05$ or less was considered for statistical significance. The results and observations are summarized as Tables 1-6 and Figures 1-12. Side effects like pneumothorax, hematoma, signs and symptoms for local anesthetic toxicity, nausea, bradycardia, and hypotension were not significant in between the study groups.

The Figure 5 shows the perioperative heart rate changes in both the groups. The Figure 6 the perioperative systolic blood pressure changes in both the groups. The Figure 7 the perioperative diastolic blood pressure changes in both

Table 1: Demographic and clinical characteristics of study participants

Patient characteristics	Group D	Group S	*P* value
Age	36.88±11.501	37.32±11.814	0.894 (NS) - Student's unpaired *t*-test
Sex			
Male	22	19	0.463 (NS) - Fisher's exact test
Female	3	6	
Weight	59.60±4.472	60.04±4.208	0.722 (NS) - Student's unpaired *t*-test
ASA status			
I	19	19	1.000 (NS) - Chi-square test
II	6	6	

NS: Not significant, ASA: American Society of Anesthesiologists

Table 2: Site of surgery distribution

Site of surgery	Study groups		Total
	Group D	Group S	
Arm	4	2	6
Elbow	5	6	11
Forearm	11	12	23
Hand	2	0	2
Wrist	3	5	8
Total	25	25	50

Chi-square test, Degree of freedom=3, P=0.849 (not significant)

Table 3: Onset of sensory block

Parameters	Groups	*N*	Mean	SD	*P* value
Onset of sensory (min)	Group D	25	28.00	4.082	0.451 (NS)
	Group S	25	28.80	3.317	

Student's unpaired *t*-test; NS: Not significant, SD: Standard deviation

Table 4: Onset of motor block

Parameters	Groups	*N*	Mean	SD	*P* value
Onset of motor (mins)	Group D	25	38.80	3.317	1.000 (NS)
	Group S	25	38.69	3.317	

Student's unpaired *t*-test; NS: Not significant, SD: Standard deviation

Table 5: Duration of sensory block

Parameters	Groups	*N*	Mean	SD	*P* value
Duration of sensory (min)	Group D	25	1075.20	144.831	<0.001*
	Group S	25	288.00	103.923	

Student's unpaired *t*-test; *Significant

Table 6: Duration of motor block

Parameters	Groups	*N*	Mean	SD	*P* value
Duration of motor (mins)	Group D	25	475.20	114.787	<0.001*
	Group S	25	218.40	64.529	

Student's unpaired *t*-test; *Significant

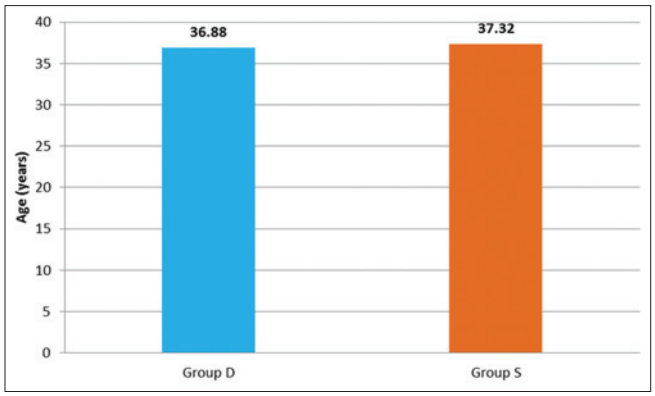

Figure 1: Age-wise distribution of study participants

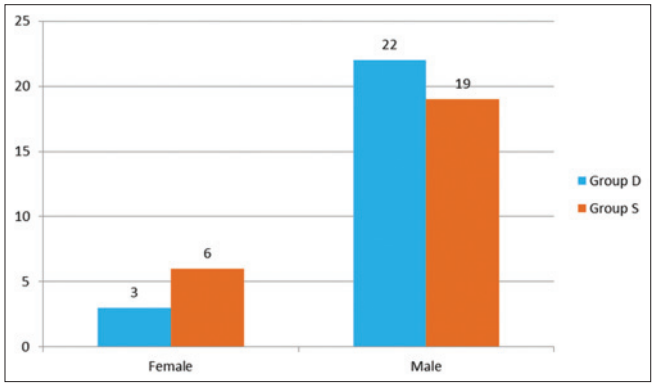

Figure 2: Sex-wise distribution of study participants

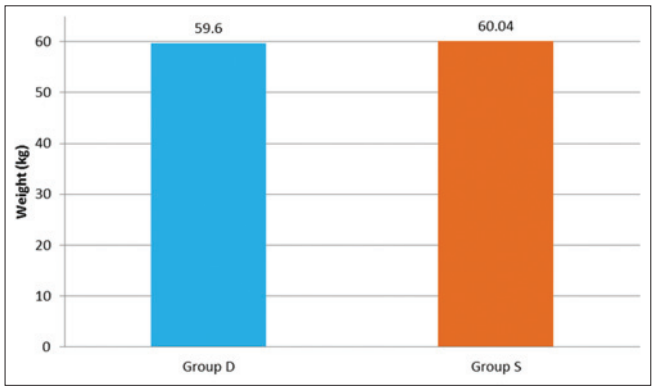

Figure 3: Mean weight of the study participants in both groups

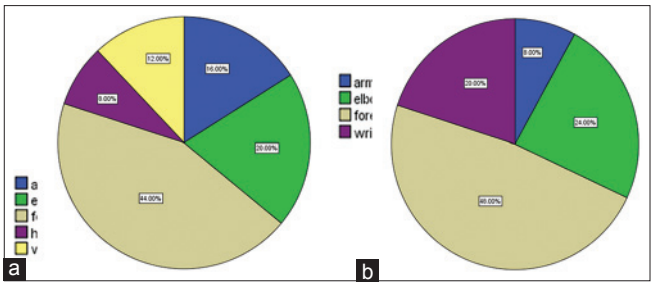

Figure 4: (a) Site of surgery in Group D, (b) site of surgery in Group S

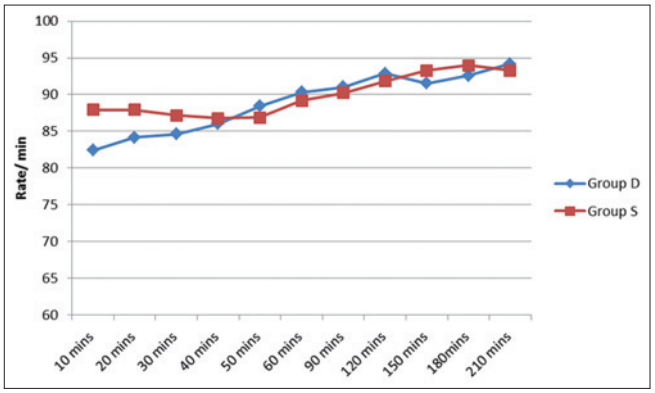

Figure 5: Perioperative heart rate

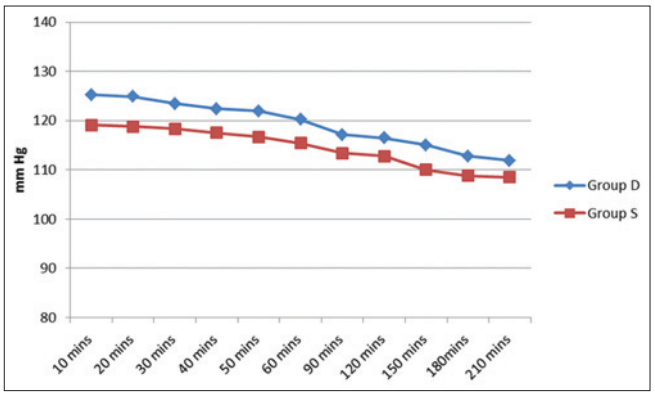

Figure 6: Perioperative systolic blood pressure

the groups. The Figure 8 shows the perioperative SpO_2 changes in both the groups. The mean duration of sensory blockade in group D was 1075.20 ± 144.831 mins and in group S was found to be 288.00 ± 103.923 mins and was statistically significant (*P* value = <0.001) (Figure 11).

DISCUSSION

The word "pain" derived from the Latin word "*Poena*" which means penalty or punishment. International society for the study of pain defines pain as an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage. Inadequate pain relief in the perioperative period increases the patient morbidity and often associated with poor surgical outcomes.

Regional anesthesia is a boon in the present era of patient care because of its simplicity of the technique, preservation of consciousness, avoidance of airway instrumentation and rapid recovery with adequate post-operative analgesia (Miller's, 1994). The techniques of peripheral neural blockade were developed early in the history of anesthesia. The American surgeons Halsted and Hall[15] described the injection of cocaine into peripheral sites, including the ulnar, musculocutaneous, supratrochlear, and infraorbital nerves, for minor surgical procedures in the 1880s. Regional

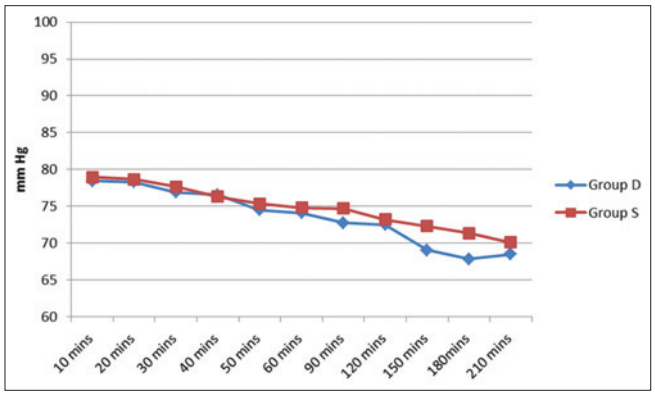

Figure 7: Perioperative diastolic blood pressure

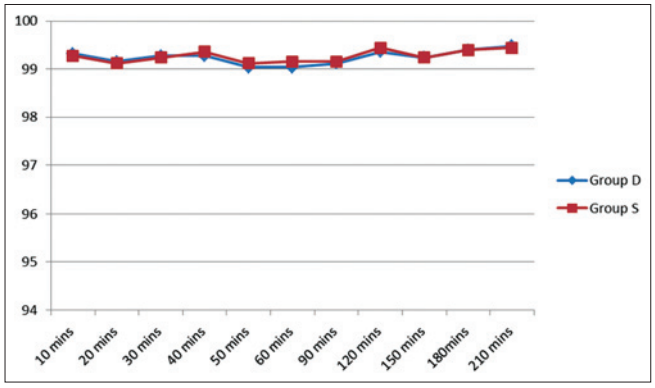

Figure 8: Perioperative SpO_2

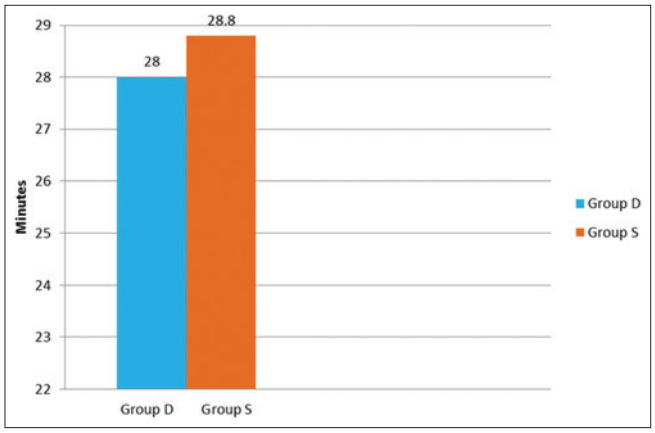

Figure 9: Mean onset of sensory block in both groups

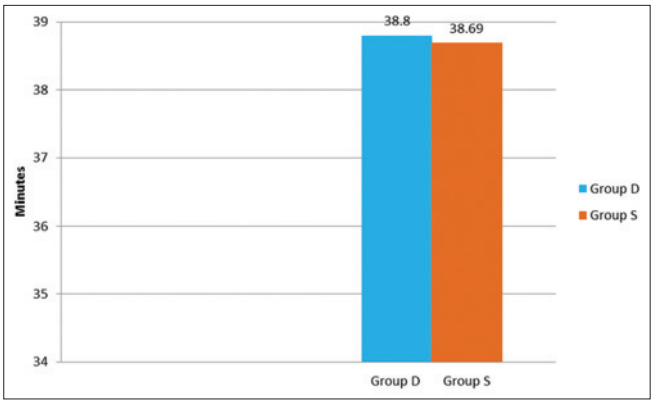

Figure 10: Mean onset of motor block in both groups

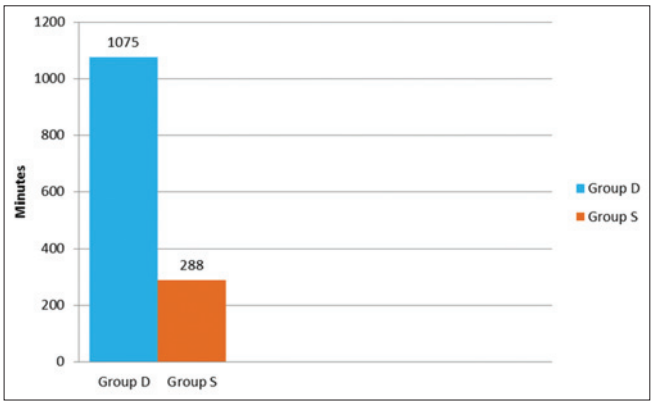

Figure 11: Comparison of mean duration of sensory block

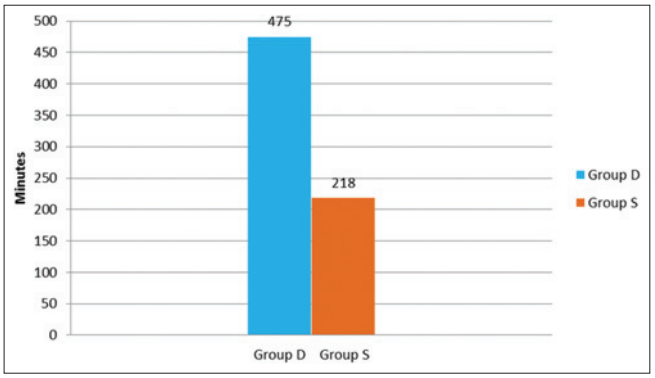

Figure 12: Comparison of mean motor block

anesthesia of the upper extremity requires knowledge of brachial plexus anatomy from its origin, where the nerves emerge from the intervertebral foramina to its termination in the peripheral nerves. Kulenkampff introduced the supraclavicular brachial plexus block[16] a few months after Hirschel described the axillary approach. Kulenkampff injected his own plexus with 10 mL of procaine at complete anesthesia of the arm.

The supraclavicular brachial plexus block provides a satisfactory anesthesia and analgesia for the upper extremity surgery and also provides anesthesia of the entire upper extremity in the most consistent manner of any brachial plexus techniques. Currently, local anesthetics can provide analgesia for limited period of time when used as a single injection. When plain Bupivacaine used as a sole anesthetic in brachial plexus block, it produces a block with the relative duration of action with bupivacaine is 2-4 h[17] and also it has its own unfavorable properties like cardiac toxicity and slower onset of action.

Different drugs have been used as adjuvant to achieve quick, dense and prolong block.[18] Adjuvant improves analgesia,

reduces systemic side effects and reduce total dose of local anesthetic required. Drugs like morphine, pethidine, clonidine, butorphanol, midazolam are commonly used along with local anesthetics for this purpose. Clonidine has been used as an adjuvant to local anesthetics since the 1980s in various regional techniques to extend the duration of block because of the side effects like heavy sedation, respiratory depression and psychomimetic effects seen with morphine, pethidine, butorphenol.

There has always been a search for adjuvants to the regional nerve block with drugs that prolong the duration of analgesia but with lesser adverse effects. The search for the ideal additive led us to try the novel glucocorticoids-dexamethasone as an adjuvant to local anesthetics in brachial plexus block in this study because respiratory depression is not a major problem with its use. Steroids have nerve block prolonging effects. They block the nociceptive impulse transmission along the myelinated C fibres.[19,20] Steroids are very potent anti-inflammatory and immunosuppressive agents. Perineural injection of steroids is reported to influence post-operative analgesia.

We assessed sensory blockade using pin prick method using the blunt end of a 27-G needle at 0, 2, 5, 10, 15, 20 and 30 min. In our study, the mean time taken for onset of sensory blockade in dexamethasone group was 28.00 ± 4.082 min and in the saline group was 28.80 ± 3.317 min; we did not find any statistically significant difference between both the groups in terms of time taken for onset of sensory blockade ($P = 0.451$).

We assessed the motor blockade at 0, 10, 20, 30 and 40 min by assessing the motor functions of each nerve individually. The mean time taken for onset of the motor blockade in dexamethasone group was 38.80 ± 3.317 min and in the saline group was 38.80 ± 3.317 min; we did not find any statistically significant difference between both the groups in terms of time taken for onset of motor blockade ($P = 1.000$).

With our observations, we found out that addition of dexamethasone did not have any impact on the time taken for onset of sensory and motor blockade.

Our observations in terms of time taken for onset of the sensory blockade and motor blockade concur with the studies done by Parringtonet,[21] Movafegh *et al.*,[12] and Shaikh *et al.*[22]

We assessed the duration of analgesia among study subjects by using VAS score every hourly in the first 12 h and every 2nd hourly in the next 12 h. The mean duration of analgesia in the study subjects belonging to the dexamethasone group was 1075.20 ± 144.831 min and the normal saline control group was 288.00 ± 103.923 min. The mean duration of analgesia in dexamethasone group was statistically significant ($P \leq 0.001$). The mean duration of analgesia was 3 times more prolonged in the dexamethasone group compared to the control groups.

In our study, the patients belonging to dexamethasone group had no pain from 1st-10th h, The VAS score remained within a range of 4-6 until 14 h of post-operative period. The VAS score in both the groups were similar in the first 3 h after initiation of block; later the VAS score in the control group started to rise progressively and by the 6th h majority of the patients had inadequate pain relief necessitating rescue analgesia. Our observations show that comparatively dexamethasone group had 3 folds prolonged post-operative analgesia with respect to the control group.

Our findings in terms of duration of analgesia concur with the studies done by Shrestha *et al.*,[23] Cummings *et al.*,[24] Pathak *et al.*,[25] and Choi *et al.*[26]

Dexamethasone used as an adjuvant in brachial plexus blocks clearly prolongs the duration of sensory and motor blockade.

Limitations of our study are we did not use ultrasound-guided block because of unavailability in our institution during the study period. We did not study the impact of dexamethasone on glucose homeostasis on wound healing and we did not follow-up the patients for long periods, i.e., >3 months for chronic neurological effects of dexamethasone.

Recent studies point out that caution must be used while using dexamethasone as an adjuvant in patients with diabetic neuropathy, because of their property to exacerbate neuropathy.[27,28] The outcomes associated with perineural dexamethasone is still unexplored, Christopher *et al.*,[15] from his meta-analysis on multiple studies which used dexamethasone as an adjuvant, did not find any favorable evidence pointing out to dexamethasone-induced neuropathy or neurotoxicity.

From the available data, we can cautiously conclude that perineural adjuvant dexamethasone is not overtly neurotoxic at 8 mg and has the potential for safe use as an adjuvant in regional anesthesia.

Furthermore, more randomized controlled trials would require prohibitively large sample sizes. The dose what we used in our study is a safe dose, which was proved in several clinical trials and no significant side-effects were noted in the study group in our study.

CONCLUSION

We conclude that when dexamethasone used as an adjuvant along with local anesthetic in brachial plexus block, it effectively prolonged the duration of both sensory and motor blockade with no side effects.

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Original Article

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Effect of 3% Hypertonic Saline and Mannitol on Brain Relaxation during Supratentorial Brain Tumor Surgery

C S Mishra[1], B Godwin Rajan[2], A Sethi[3], N Narang[2]

[1]Senior Resident, Department of Anesthesiology, Gandhi Medical College, Bhopal, Madhya Pradesh, India, [2]Assistant Professor, Department of Anesthesiology, Netaji Subhash Chandra Bose Medical College, Jabalpur, Madhya Pradesh, India, [3]Associate Professor, Department of Anesthesiology, Netaji Subhash Chandra Bose Medical College, Jabalpur, Madhya Pradesh, India

Abstract

Introduction: Patients with brain tumor usually have increased intracranial pressure due to swelling of the brain tissue. To ease surgical tumor removal, measures are taken to reduce brain swelling, often referred to as brain relaxation. Administration of osmotherapy is one of the interventions used to produce cerebral relaxation in elective neurosurgeries. The objective of the present study is to compare brain relaxation after the administration of hypertonic saline (3%) and mannitol (20%) in patients undergoing supratentorial brain tumor surgery.

Materials and Methods: A prospective, case-control study included total 60 patients of ASA I and II between age 18 and 70 years were scheduled for supratentorial brain tumor surgery. Two groups were formed; Group HS received 3% hypertonic saline (3 ml/kg), and Group M received 20% mannitol (0.75 g/kg) via peripheral intravenous line over 30 min before dural opening. Outcome measurements were brain relaxation, fluid input, urine output, and blood loss.

Result: Brain relaxation in Group HS was better than those in Group M ($P < 0.0017$). The mean intraoperative urine output in Group HS was lower 881.0 ± 112.1 ml as compared to the Group M 1155.0 ± 145.2 ml ($P < 0.05$). There were no significant differences in fluid input and blood loss in between the two groups.

Conclusion: We conclude that the use of 3% hypertonic saline provides better brain relaxation as compared to 20% mannitol.

Key words: Brain relaxation, Brain tumor, Hypertonic saline, Mannitol

INTRODUCTION

Patients with brain tumor usually have increased intracranial pressure due to swelling of the brain tissue. To ease surgical tumor removal, measures are taken to reduce brain swelling, often referred to as brain relaxation. Brain relaxation is essential in anesthesia for intracranial surgery; it has been considered a neuroprotective measure as it can reduce surgical compression, local hypoperfusion, cerebral ischemia, and blood loss.[1]

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Administration of osmotherapy at the onset of craniotomy before opening the dura mater is one of the interventions used to produce cerebral relaxation in elective neurosurgeries.[2] It has been the cornerstone of the medical management of cerebral edema, irrespective of its etiology, for decades; the mannitol is the most widely used agent.[3]

Mannitol is a six carbon sugar compound. It exerts its intracranial pressure lowering effects via two mechanisms - an immediate effect because of plasma expansion and a slightly delayed effect related to its osmotic action. The early plasma expansion reduces blood viscosity and this, in turn, improves regional cerebral microvascular flow and oxygenation.[4]

The effects of hypertonic saline were first described by Weed and Mckibban in 1919. In addition to an osmotic action, hypertonic saline has hemodynamic, vasoregulatory, immunological, and neurochemical effects, relaxes arteriolar

Corresponding Author: Dr. Rajan B. Godwin, Vandana Vila, CMS Church compound, Nehru ward Ghamapur Jabalpur, Madya Pradesh, India. E-mail: drrjngodwin@gmail.com

vascular smooth muscle and in association with a reduction in cerebral endothelial cell edema, improves cerebral microcirculatory flow.[5] It also expands intravascular volume, thereby potentially augmenting cerebral perfusion pressure.[6,7]

The modern day concept of cerebral edema is based on the theory of Klatzo[8] who proposed two different types of edema, cytotoxic, and vasogenic. Edema associated with the brain tumors is considered to be vasogenic. In vasogenic edema, vascular permeability is increased, under normal conditions a sink effect is provided by the ventricles and subarachnoid cerebrospinal fluid to allow steady circulation and replenishment of the extracellular space, this sink effect is overwhelmed in vasogenic edema resulting in extracellular fluid accumulation. Aquaporin 4 (AQP4) is a water channel protein strongly expressed in the brain parenchyma and major fluid compartment, including cerebrospinal fluid and blood AQP4 deletion, aggravates vasogenic brain edema produced by tumor.[9]

On a molecular level morphologically disrupted tight junctions in newly formed brain tumors capillaries are associated with a paucity or lack of proteins such as occludins, claudins, or the junctional adhesion molecules.[10-12] The transmembrane proteins, such as Zo-1, Zo-2, and Zo-3, are in the coupling of tight junctions to the actin cytoskeleton of endothelial cells.[13] Decrease in expression or function of these tight junction proteins leads to opening of the junction and to the formation of edema.[12,13]

The objective of the present study is to compare cerebral relaxation after the administration of hypertonic saline (3%) and mannitol (20%) in patients undergoing supratentorial brain tumor surgery. Blood loss was also evaluated during surgery.

MATERIALS AND METHODS

After obtaining approval of the Ethics Committee, the study was carried out in the Neurosurgery Operation Theatre, Department of Anesthesiology, Netaji Subhash Chandra Bose Medical College and Hospital, Jabalpur, Madhya Pradesh, India. 60 adults of ASA physical status I and II between ages 18 and 70 years undergoing supratentorial brain tumor surgery were included in this study. A detailed history was taken. Thorough physical examination, routine investigations, and any special investigations if required were done.

It was a prospective case-control study in which two groups were formed, in Group A received 3% hypertonic saline (3 ml/kg) via peripheral intravenous (IV) line over 30 min and those in Group B received 20% mannitol (0.75 g/kg) via peripheral IV line over 30 min before dural opening.

Sample size was derived using a right size sample size calculator. Total 30 cases in each group were selected assuming that the minimum requirement of the cases in each group considered the 95% confidence interval with 5% precision of error.

In the operating room after standard preparation and setting up of monitors and preoxygenation with 100% oxygen for 3 min, anesthetic induction was done using propofol 2 mg/kg. Just before induction IV glycopyrrolate 0.01 mg/kg and fentanyl 2 μg/kg were given. Tracheal intubation was performed 3 min after administration of 0.1 mg/kg vecuronium. Anesthetic maintenance was done with isoflurane at (1.2 minimum alveolar concentration) with oxygen at the rate of 5 L/min and vecuronium was given when required and was repeated according to need. Every patient received 4 mg dexamethasone IV before skin incision. Foley's catheterization was done for all patients to monitor urine output. The impression of neurosurgeon about brain relaxation was assessed on a scale ranging from 1 to 4 where:

1. Perfectly relaxed
2. Satisfactory relaxed
3. Firm brain
4. Bulging brain.

Patients without satisfactory brain relaxation after surgical appraisal received another bolus of the same osmotic agent.

Assessment of blood loss:
Blood loss = Estimated blood volume × ln (hematocrit 1/hematocrit 2).[14]

Where hematocrit 1 is the pre-operative hematocrit and hematocrit 2 is the post-operative hematocrit. Those who required intraoperative blood transfusion were excluded from the study.

Statistical Analysis

Data are presented as the mean ± standard deviation or as the median with ranges. Differences between the HTS and M groups were analyzed using a χ^2 test (demographic variables), a Mann–Whitney *U*-test (brain relaxation scores), and an unpaired Student *t*-test for multiple measurements (fluid input, urine output, blood loss). $P < 0.05$ was considered significant.

OBSERVATIONS AND RESULTS

This prospective case-control study was carried out in the Department of Anesthesiology, NSCB Medical

College. 60 selected cases were included under the study to compare the cerebral relaxation after the administration of hypertonic saline (3%) and mannitol (20%) in patients undergoing supratentorial brain tumor surgery.

Analysis of the demographic characteristics of the studied patients has shown that all groups were matched as regarding age, gender, and weight and it was insignificantly different among the groups (Table 1).

The median of brain relaxation in Group A was 1 and in Group B was 3 by applying Mann-Whitney *U*-test. We found a $P = 0.0017$ which implies a statistically significant difference between the two groups ($P < 0.01$) (Table 2) (Graph 1).

The mean intraoperative fluid input in Group A was 1911.7 ± 131.1 and in Group B was 1891.7 ± 168.2 ml. We did not found any significant different in both studied groups ($P > 0.05$).

The mean intraoperative urine output in Group A was 881.0 ± 112.1 ml and in Group B was 1155.0 ± 145.2 ml, and there was statistically significant different in both groups ($P < 0.05$)

The mean intraoperative blood loss in Group A was 257.1 ± 47.1 ml and in Group B was 266.0 ± 48.2 ml, and there was no statistically significant difference between the two groups ($P > 0.05$) (Table 3).

Table 1: Demographic data

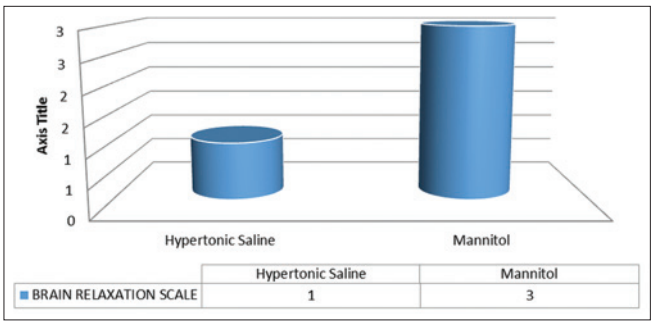
Parameters	Group A (3% HS)	Group B (20% M)	*P* value
Age (years)	38.47±12.9	38.03±14.17	0.89
Sex ratio (male:female)	12:18	18:12	0.19
Weight (kg)	56.5±3.8	55.8±7	0.114
ASA grading (1:2)	7:23	22:8	0.78

Table 2: Brain relaxation scale

Group	Brain relaxation scale
Hypertonic saline	
Median	1
Range	1-4
Mannitol	
Median	3
Range	1-4
P value	0.0017

Table 3: Intraoperative parameters

Parameters	Group A (3% HS)	Group B (20% M)	*P* value
Fluid input (ml)	1911.7±131.1	1891.7±168.2	0.607
Urine output (ml)	881.0±112.1	1155.0±145.	0.045
Blood loss (ml)	257.1±47.1	266.0±48.2	0.460



Graph 1: Brain relaxation scale

DISCUSSION

Administration of hypertonic saline or mannitol increases serum osmolarity and decreases intracranial pressure and brain water content in not injured brain areas. The principal mechanism underlying these effects is the induction of water shift from brain tissue to the intravascular space by the hyperosmolarity of hypertonic saline and mannitol because the blood brain barrier is impermeable to sodium and mannitol.

We performed the study as a prospective case control. The demographic data of our study showed that all patients were 18-70 years of age. The mean age of patients in Group A was 38.47 ± 12.9 years and in Group B was 38.03 ± 14.17 years. There was no statistically significant difference in both groups ($P > 0.05$).

We found that 3% hypertonic saline provided better brain relaxation than mannitol. Our study was in agreement with the study of Wu *et al.*[15] in showing the superiority of hypertonic saline over mannitol for providing satisfactory brain relaxation. Rozet *et al.*[16] and Li *et al.*[17] found a significant decrease in dural tension score in patients receiving hypertonic saline as compared to mannitol ($P < 0.05$). Our findings concurred with the findings of Li *et al.* in showing the superiority of hypertonic saline over mannitol. However, our study was more significant with respect to the sample size taken. The effectiveness of the hyperosmolar solute depends on the reflection coefficient which determines the relative impermeability of an intact blood-brain barrier to the solute. RC of 1 means an absolutely impermeable solute and RC of 0 means ideally permeable solute. Hypertonic saline may present a theoretical advantage over mannitol because sodium has a higher osmotic RC than does mannitol (1 vs. 0.9), a lower solute leakage may evoke a greater increase in serum osmolarity and a higher transendothelial osmotic gradient

in the vascular compartment may lead to increased brain water extraction into the intravascular space.[15,16]

All the patients in both the groups remained hemodynamically stable, with no significant changes in Heart rate, systolic, diastolic, and mean blood pressure.

The mean intraoperative fluid input in Group A was 1911.7 ± 131.1 ml and in Group B was 1891.7 ± 168.2 ml. We did not found any significant difference between both groups ($P > 0.05$).

Being an osmotic diuretic, infusion of mannitol leads to significant diuresis. We found that the mean intraoperative urine output was more in the mannitol group as compared with HS ($P < 0.05$). These findings are in concordance with earlier studies.[15-18]

Accurate assessment of blood loss is a problem in neurosurgery, estimation of actual blood loss during neurosurgery with traditional methods, such as measuring the loss of blood in suction bottles, drapes, and swab are difficult. Estimated blood loss is not a good predictor of calculated blood loss. Laboratory investigations are better than significant difference with the routine method of visual estimation. Accurate assessment of blood loss is of critical importance in these patients to maintain oxygen delivery to the brain. So, keeping this view in mind in the present study, we did an assessment of blood loss based on laboratory calculations with pre and post-operative hematocrit values. There was no statistically significant difference between both groups ($P > 0.05$). However, blood loss was slightly less in 3% hypertonic saline group as compared to 20% mannitol group. It was compatible with the study did by Romani *et al.*[19] In which median intraoperative blood loss was 200 ml.

CONCLUSION

Administration of the mannitol and HS provided acceptable brain relaxation. HS resulted in a significant increase in osmolarity compared with mannitol, without diuretic effect. Thus, we conclude that HS can be routinely used in place of mannitol to achieve perfectly relaxed brain relaxation, superior neurosurgical access, and better hemodynamic stability in elective supratentorial craniotomies.

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Original Article

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A Clinical Study of Sigmoid Volvulus

Bantu Rajsiddharth[1], Sridhar Reddy Patlolla[2], Bachannagari Srinivas Reddy[3], Sreedhar Sriramoju[4], Bharath Kumar Palley[4], Karthik Maripeddi[4]

[1]Associate Professor, Department of General Surgery, Kakatiya Medical College/Mahatma Gandhi Memorial Hospital, Warangal, Telangana, India, [2]Senior Resident, Department of General Surgery, Kakatiya Medical College/Mahatma Gandhi Memorial Hospital, Warangal, Telangana, India, [3]Consultant Surgeon, Department of General Surgery, Area Hospital, Mahboobnagar, Telangana, India, [4]Post-graduate Student, Department of General Surgery, Kakatiya Medical College/Mahatma Gandhi Memorial Hospital, Warangal, Telangana, India

Abstract

Introduction: Volvulus of the sigmoid colon is a common cause of intestinal obstruction. Typically, an elderly patient presents with constipation, abdominal pain, and distension of sudden onset. Delay in the diagnosis and treatment can lead to serious complications such as like bowel gangrene, perforation, peritonitis' and sepsis.

Materials and Methods: This study is a prospective study of 32 cases of sigmoid volvulus, carried out as regards to the etiological factors which predispose to the sigmoid volvulus, the clinical features, modes of treatment and the outcomes, at Mahatma Gandhi Memorial Hospital, Warangal, for a period of 2-year.

Results: Patients were younger relatively healthy, physically active prior to the onset of the volvulus. An absence of associated diseases was a notable feature. Almost all patients were consuming high residual vegetable and cereal diet. Most of them belonged to poor socio-economic group. The overall mortality was 18.75% in this series. Those who survived the episode were able to return to their earlier vocation.

Conclusion: Sigmoid volvulus is a common disorder in this region accounting for 40% of large bowel obstruction cases. Almost all our patients were consuming high residual vegetable and cereal diet. Most of them belonged to poor socio-economic group. The role of strong anterior abdominal wall is not allowing distension of the colon (which is so common in high cereal and vegetable diet), forcing the colon to shift sideways, is the causative factor for volvulus to occur is to be considered.

Key words: Complications, Intestinal obstruction, Mortality, Sigmoid volvulus, Surgery

INTRODUCTION

Sigmoid colon volvulus, defined as an abnormal twisting of the sigmoid colon around its mesentery, is an infrequent cause of colonic obstruction.[1] Sigmoid volvulus accounts for 2-3% of all intestinal obstructions. Yet it is the most common strangulating obstruction of the colon, being second, only to carcinoma as a cause of colonic obstruction.[2]

The mean age of sigmoid volvulus patients is 49 years (range 19-75).[3] Typically, an elderly patient presents with constipation, abdominal pain, and distension of sudden onset. This classical clinical picture together with plain radiographs is usually sufficient to diagnose the condition. Diagnostic difficulties, however, are not uncommon A recent report from Finland, where the disease is endemic, confirms the problem of poor diagnostic accuracy.[4]

Sigmoid volvulus affects both sexes, with males being affected more. It is believed that wider pelvis which provides space of spontaneous untwisting, and a lax abdomen are said to be the reasons for lesser rate in females.[5]

The etiology of sigmoid volvulus is:

A. Congenital: Idiopathic, narrow attachment of the sigmoid mesentery, long mobile loop of the sigmoid colon, Hirschprung disease, pseudo megacolon and congenital bands.
B. Acquired and predisposing factors: Post-operative adhesions, loaded colon resulting from chronic constipation, dietary-large, heavy course diet, old age

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Corresponding Author: Dr. Sridhar Reddy Patlolla, C/o Dr. B. Rajsiddharth, 1-9-1015, Basith Nagar, Postal Colony, Subedari, Hanamkonda, Warangal - 506 010, Telangana, India. Phone: +91-9676143980/9866666650. E-mail: sridhar258@gmail.com

and drugs like anti-cholinergics, ganglion blockers anti-parkinsonian drugs-and tranquilizers also have been said to produce megacolon or megacolon syndrome.[6]

In many instances, the etiology and level of obstruction can be identified radiologically. When a dilated loop of bowel is seen, clinicians have to identify the level of obstruction, the loop of dilated bowel proximal to it, as well as the undilated bowel distal to it. An abdominal radiograph is usually sufficient for diagnosing the level of bowel obstruction.

Although surgical exploration itself is an accepted mode for diagnosing acute abdomen, accurate pre-operative diagnosis will reduce the morbidity and mortality. Delay in diagnosis and treatment may lead to sigmoid ischemia, infarction, peritonitis, and septicemia, resulting in mortality of up to 60%.[7] In most instances, decompression can be done non-operatively with insertion of a rectal tube, or performing flexible sigmoidoscopy.[8] However, sigmoidoscopy should not be performed in patients who have developed clinical evidence of bowel gangrene (such as those with sepsis, fever, or peritonitis).[9]

Emergency laparotomy and resection with or without primary anastomosis is indicated when non-operative methods fail, or when there is evidence of strangulation, infarction, or perforation.[10] Post-operative mortality ranges from 6% to 60%. Factors associated with poor prognosis include advanced age, delay in diagnosis, presence of intestinal infarction, peritonitis, and shock at presentation.

MATERIALS AND METHODS

Source of Data

For this study, the patients admitted in all surgical units of Mahatma Gandhi Memorial Hospital, Warangal, due to sigmoid volvulus were selected.

This study is a detailed study of 32 cases of sigmoid volvulus, carried out as regards to the etiological factors which predispose to the sigmoid volvulus, the clinical features, modes of treatment and the outcomes. The duration of study was 2 years and was conducted from November 2012 to October 2014.

Inclusion Criteria

All the patients who presented to surgical Outpatient Department at Mahatma Gandhi Memorial Hospital, Warangal, with large bowel obstruction due to sigmoid volvulus.

Exclusion Criteria

All cases of large bowel obstruction other than due to sigmoid volvulus were excluded.

RESULTS

Incidence

Males and females were affected in 25 and 07 cases, respectively (Figure 1).

It would appear that sigmoid volvulus occurs almost with equal frequency between the age groups 21-30 years, 31-40 years, and 41-50 years and these groups accounted for 52.5% of patients. The maximum number, i.e. 25% were belong to 51-60 age group. This disease is very uncommon below the age of 20 years and above the 70 years (Table 1).

All our patients were active and physically fit prior to the onset of the sigmoid volvulus. Majority of these patients (72.5%) were involved in strenuous work for their lively hood.

All our patients belonged to poor socio-economic status and mainly consumed diet rich in roughage and bulky in quantity.

The dietetic habits are also on the general predictable lines. 90% of our patients consumed mainly vegetarian diet and the remaining consumed mixed diet (Table 2).

In the present study distention of the abdomen (100%) was the most common symptom followed by constipation (93.75%) and pain abdomen (75%) (Table 3).

When the bowel was viable, 93.75% of the patients survived irrespective of the surgical procedure carried out. One patient (6.25%) died in the hospital (Table 4).

Table 1: Age distribution of cases

Age in years	Total no	Percentage
11-20	3	7.5
21-30	4	12.5
31-40	6	20.0
41-50	6	20.0
51-60	8	25.0
61-70	4	12.5
71-80	1	2.5

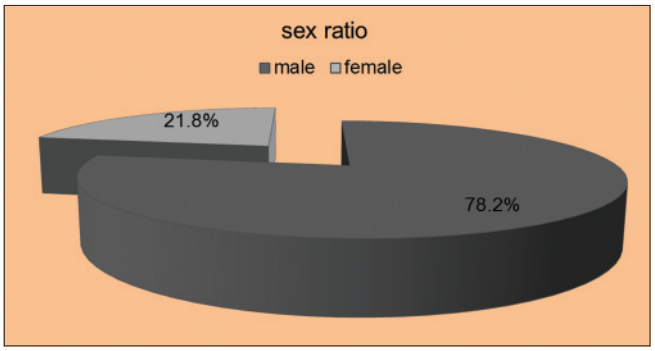

Figure 1: The ratio of male and female is 3.5:1 in this study

Amongst the patients with gangrenous bowel (16), 56.25% (9) patients survived. 5 patients (31.25%) expired and 2 patients (12.5%) left against medical advice. It would be more appropriate to group these patients as probably died (Figure 2).

DISCUSSION

Clinical Features

In the present study of sigmoid volvulus, 80 cases of large bowel obstruction were studied, among which 32 cases were due to sigmoid volvulus (Table 5).

In the present study, the most common age group was 51-60 years (25%) and mean age being 55.5 years (Table 6).

The male to female ratio in patients with sigmoid volvulus is variable. However, the review of the literature indicates that there is a general male preponderance (Table 7).

Treatment

The treatment of sigmoid volvulus has been varied. These variations depended on many factors such as general health of the patient prior to the onset of the disease, condition at the time of operation, availability of ancillary help such blood, investigations facility, and individual preference of the surgeon. The fact that many operative procedures have been described in the treatment of sigmoid volvulus and would probably mean that no single operation is suitable in all patients, or there is the difference in the outlook of a pattern of the disease.

The basic problem in management of the patients is a high incidence of recurrence of sigmoid volvulus after the commonly performed procedures such as rectal tube deflation, laparotomy and simple derotation, and operative derotation and fixation of the "omega loop" to the lateral or anterior abdominal wall. High incidence of post-operative recurrence has been noted by Shepherd,[18] Anderson and Lee.[8]

Resection of the sigmoid colon almost prevents recurrence noted by Hines *et al.*,[19] Chakrabarty *et al.*,[20] Anderson and Lee,[8] Khanna *et al.*[17] Resection and end to end anastomosis as an emergency procedure, in an un prepared bowel, in conditions like that make the situation far from ideal and in our under nourished patients has its own price in the increased morbidity and mortality.

Díaz-Plasencia *et al.* subjected 15.4% of patient for this treatment and found 100% cure rate. In our present study, 31.2% patients underwent derotation and fixation to abdominal wall procedure with 100% cure rate (Table 8).

Díaz-Plasencia *et al.*[21] subjected 56.9% of patients for this treatment and found 87% cure rate and 13% mortality. Peoples *et al.*[10] study 47.6% of patients were subjected to primary resection and end to end anastomosis, however, 73.7% of patients were cured and 26.3% mortality. In our present study, 31.2% of patients underwent primary resection and end to end anastomosis with cure rate 60% and mortality 30%. One patient left against medical advice (Table 9).

Table 2: Occupation of the patients

Occupation	Number of patients	Percent
Cooli	19	60
House wife	9	27.5
Agriculture	4	12.5

Table 3: Modes of presentation

Symptoms	Number of patients	Percent
Pain in abdomen	24	75
Distension of abdomen	32	100
Constipation	30	93.75
Vomiting	15	47.5
Retention of urine	02	6.25
Fever	01	3.12

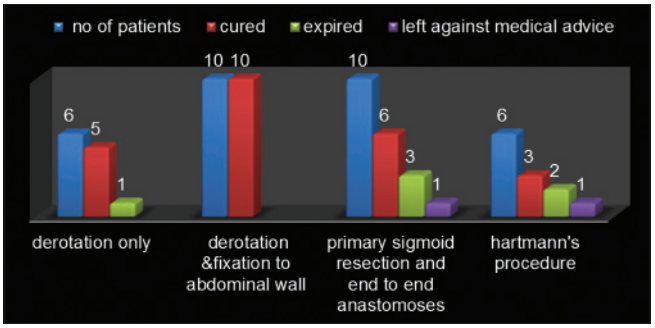

Figure 2: Various types of surgeries and its outcome

Table 4: Various types of surgery performed and outcome of the procedure

Procedure	Number of patients	%	Cured (%)	Expired (%)	Left against medical advice (%)
Derotation only	6	18.75	5 (83.3)	1 (16.7)	-
Derotation and fixation to abdominal wall	10	31.25	10 (100)	-	-
Primary sigmoid resection and end to end anastomosis	10	31.25	6 (60)	3 (30)	1 (10)
Hartmann's procedures	6	18.75	3 (50)	2 (33.3)	1 (16.7)

Table 5: Incidence of sigmoid volvulus in large bowel obstruction

Study group	Sigmoid volvulus as a percentage of large bowel obstruction
Ballantyne *et al.*[11]	43
Echenique Elizondo and Amondaraín Arratíbel[12]	52
Present study	40

Table 6: Age incidence by various authors

Study group	Mean age (years)
De *et al.*[13]	45.06
Ballantyne *et al.*[11]	68.5
Connolley *et al.*[14]	78
Atamanalp[15]	58.6
Present study	55.5

Table 7: Sex incidence by various authors

Study group	M:F ratio
Atamanalp[15]	4.7:1
Sankaran[16]	5:1
De *et al.*[13]	2.07:1
Ballantyne *et al.*[11]	1.4:1
Connolley *et al.*[14]	5:3
Khanna *et al.*[17]	2.5:1
Present study	3.5:1

Table 8: Derotation and fixation to abdominal wall

Study group	Number of patients	%	Cured (%)	Expired (%)
Díaz-Plasencia *et al.*[21]	19	15.4	19 (100)	0
Present study	10	31.2	10 (100)	0

Díaz-Plasencia *et al.*[21] subjected 28.7% of patients for this treatment and found 68.6% cure rate and 37.4% mortality. In Peoples *et al.* study 26.6% of patients were subjected to Hartmann's procedure with 87% cure rate and 13% mortality. In present study, 18.75% of patients were subjected to Hartmann's procedure with cure rate of 50% and mortality 33.3%. One patient left against medical advice (Table 10).

De *et al.*[13] conducted surgery on 196 cases of sigmoid volvulus. Derotation and fixation to abdominal for 1 case, primary sigmoid resection and end to end anastomosis in gangrenous bowel of 195 cases, and mortality was 1.01%.

In the present study, 32 cases of sigmoid volvulus various types of surgeries conducted, in cases of derotation and fixation to the abdominal wall, there is no mortality. However, in case of Hartmann's procedure the mortality rate is high i.e., 33.3%. So the overall mortality is less in viable bowel compared to the gangrenous bowel.

Table 9: Primary sigmoid resection and end to end anastomosis

Study group	Number of patients	%	Cured (%)	Expired (%)
Díaz-Plasencia *et al.*[21]	69	56.9	60 (87)	9 (13)
Peoples *et al.*[10]	19	47.5	14 (73.7)	5 (26.3)
Present study	10	31.2	6 (60)	3 (30)

Table 10: Hartmann's procedures

Study group	Number of patients	%	Cured (%)	Expired (%)
Díaz-Plasencia *et al.*[21]	35	28.7	24 (68.6)	11 (37.4)
Peoples *et al.*[10]	15	26.6	13 (87)	2 (13)
Present study	6	18.75	3 (50)	2 (33.3)

CONCLUSION

A study of 32 cases who presented with sigmoid volvulus was conducted at Mahatma Gandhi Memorial Hospital, Warangal, during the period November 2012 to October 2014.

Emergency laparotomy was conducted in all the cases. Sigmoid volvulus is more common in males than females, and highest incidence is seen in 5th and 6th decade of life. Sigmoid volvulus constituted 40% of the total large bowel obstructions.

The outcome of the surgical procedures, such as derotation and fixation to abdominal wall were good. These procedures were carried out in viable bowel.

Mortality was observed to be higher in procedures like resection and anastomosis and Hartmann's procedures which were carried out in gangrenous bowel.

- Sigmoid volvulus is a common disorder in this region accounting for 40% of large bowel obstruction cases
- The male:female ratio is 3.5:1
- Our patients were younger relatively healthy, physically active prior to the onset of the volvulus. An absence of associated diseases was a notable feature
- Almost all our patients were consuming high residual vegetable and cereal diet. Most of them belonged to poor socio-economic group
- The role of strong anterior abdominal wall is not allowing distension of the colon (which is so common in high cereal and vegetable diet), forcing the colon to shift sideways, is the causative factor for volvulus to occur is to be considered. This at best is speculative
- In most of our patients, the diseases progressed gallopingly
- Delay in seeking medical aid resulted in gangrene.

Understandably, the mortality was more in patients with gangrene than without gangrene

- When the sigmoid colon was gangrenous, resection and end to end anastomosis was carried out. This had a high mortality
- In old debilitated patients, with associated gangrenous bowel Hartmann's procedure were conducted. This has got high mortality
- There is no single universal etiological factor, progress of the diseases is varied, the physical and mental status of patients is different in different areas, and finally, there is no single operative procedure useful in all patients
- The overall mortality was 18.75% in this series. Those who survived the episode were able to return to their earlier vocation.

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Review Article

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Patient Safety Practices in Dentistry: A Review

Abhishek Jadhav[1], Sourab Kumar[1], Siddharth Acharya[2], Payoshnee Bhalinge[3], Shravani Ganta[4]

[1]Senior Lecturer, Department of Oral Pathology, Dr. D. Y. Patil School of Dentistry, Navi Mumbai, Maharashtra, India, [2]Senior Lecturer, Department of Public Health Dentistry, Dr. D. Y. Patil School of Dentistry, Navi Mumbai, Maharashtra, India, [3]Senior Lecturer, Department Oral Pathology, M.A. Rangoonwala College of Dental Science, Pune, Maharashtra India, [4]Senior Lecturer, Department of Public Health Dentistry, Jaipur Dental College, Jaipur, Rajasthan, India

Abstract

Dental literature reports have indicated the maximum number of deaths occurring due to negligence in clinical practice. Patient safety in today's practice is one of the most important roles for dentists. There must be the development of multi-professional curriculum guide for patient safety monitoring. For patient safety, adequate communication must be among treating dentists, clinical staff, patients, and their families. Everyone plays an important role in creating a patient safety culture in a clinical environment. Safety culture can be developed by implementing qualities of leadership, commitment, routine audits and risk assessment of hazards, safe practices, continuing educational activities for staff and patients, proper accounting.

Key words: Curriculum, Death, Dentists, Implementing, Risk

INTRODUCTION

Dentists handle dangerous drugs and use advanced technical appliances (e.g. lasers, electrocautery, ionizing radiation) cause serious harm. Dentists and dental assistants come into contact with blood and body fluids that can transmit infectious diseases. Promotion of patient safety is an ethical obligation in any health care profession. Hippocratic principle promotes the principle "Primum Non Nocere" (first, do no harm). Minimize danger inherent in treatment and avoid the occurrence of any possible complications. Any dental care in which all possible risk factors can be controlled represents highest-quality dental care, and there is a clear relationship between the quality of treatment and the success of outcomes.[1] Quality assurance/improvement provide better legal security for dental practitioners.

Safety of patient and henceforth practitioner are correlated. Continuous investigations are prevailing regarding particular knowledge pertaining to accidents and complications which are associated with the use of materials, general procedures and clinical facilities.[2] It is multifactorial and very complex. The focus must be on the latent risks, way in which clinical information is transmitted between professionals, requirements that staff work excessively long hours and installation of floor warning sensors that becomes slippery when it is wet.[3] It is a part of the non-punitive character that patient safety doesn't seek to punish the guilty.

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Methodological Peculiarities

It is of prime importance regarding classification and analysis of adverse events and taking proposed corrective measures.[4] Prospective analysis would be identify the potential risks associated with treatment, work organization, appliances or new materials failure mode and effects analysis. Retrospective analysis would be regarding events important with frequency, characteristics, severity (sentinel events), health care error, an accident in office, poorly treated clinical complications.[5-10]

Root cause analysis considering the organization of labor; the materials and appliances available; patient characteristics; the continuing education of professionals; the transmission and storage of information.[11] Preparing a risk map with procedures that practitioners wish to start applying and allows for the implementation of measures to reduce the likelihood of these risks materializing, or, at least, limit their consequences if they do emerge. Analysis of problems acquired during daily practice, acquired habits, time pressure, haste, inertia, and fatigue.

Corresponding Author: Dr. Sourab Kumar, Department of Public Health Dentistry, Dr. D. Y. Patil School of Dentistry, Nerul, Navi Mumbai - 400 706, Maharashtra, India. Phone: +91-7715085880. E-mail: sourab.birla@gmail.com

Safety Culture

It is the product of individual and group values, attitudes, perceptions, competencies and patterns of behavior that determine the commitment to, and the style and proficiency of an organization's health and safety management.[12-15] It compels us to share our experiences and data, both good and bad, with our colleagues so that everyone can learn from them. Providing a firm organization goal, mission and culture along with cores of leadership, teamwork, provision of evidence-based care, communication, learning, patient-centered. Making an institutional culture of patient safety through strategic planning, learning from errors, commitment to leadership, documenting and improving patient safety, encouraging and practicing teamwork, spotting potential hazards and using systems for reporting and analyzing adverse events and measuring improvement.[16,17]

What Needs to be Done

The policy-makers must ensure measures to improve the culture of safety. Academicians must incorporate principles into educational curricula and organizations must promote patient safety. There must be a multidisciplinary team training of dentists, continuous quality improvement tools, innovative human resources, practices, and policies.[18]

Measurement of Patient-safety Climate

Methods of analysis according to purpose to which they will be put. The need to tailor different or even unique strategies that accommodate particular circumstances of each organization.[19]

Patient Safety in Dentistry

Applying safety measures like:

1. Educating staff regarding patient safety culture
2. Understanding our current situation
    a. Recall and analyze adverse events encountered
    b. Check correctness of 20 medical records chosen at random
    c. Review our protocols for cleaning and sterilizing non-disposable instruments
    d. Review our protocols for action in a life-threatening emergency.
3. Devising protocols to make maneuvers and activities in potentially less dangerous criterias
4. Establishing "Safety Instructions" (red lines)
    a. Do not perform Root Canal Treatment (RCT) without rubber dam
    b. Never re-use containers designed for single-use only
    c. Never prescribe any drug without consulting patient clinical record and without directly asking the patient about allergies or other health problems
    d. Never take X-ray in a woman of child-bearing age without protection and without asking possible pregnancy
    e. Sharing experiences in patient safety with our colleagues.[21,22]

Errors in Clinical Documents, Information, and Referral of Patients

1. Histories which lack essential data (clinical and allergic background and updated information about medication)
2. Use of abbreviations (or bad handwriting) that lead to confusion on the part of other professionals at the same center using the same history
3. Failure to provide adequate information to the patient about the procedure, its potential risks or recommendations that must be followed to avoid complications
4. Inaccuracies in patient referrals to other professionals that may lead them to make mistakes.

Prescribing Errors

1. Errors in the indication for the drug (in relation to the type of drug, dose or duration of treatment)
2. Allergic reactions that occur because of a lack of adequate medical records
3. Drug interactions that occurs because the prescribing practitioner lacks the relevant pharmacological knowledge or fails to update the list of drugs taken by the patient
4. Wrong dose of the drug (especially common in children and in patients with alterations in the metabolism or elimination of drugs)
5. Duplication of drugs (especially common with anti-inflammatories) because of a lack of coordination among the various professional prescribing for the same patient.[23]

Surgical Events

1. Errors in treatment planning (sometimes associated with lack of adequate clinical records previous to treatment)
2. Errors in the type of procedure performed (motivated by incorrect patient identification or inadequate clinical history)
3. Errors in the area of intervention (Wrong-site surgery) that occur as a result of forgetfulness or the inappropriate interpretation of records by the professional
4. Errors in pre-operative prophylaxis in medically compromised patients
5. Errors in the monitoring and control of operated patients (no post-operative instruction sheet or lack of post-surgical control)

6. Post-surgical infections (detected late or inadequately treated).[16]

Accidents

1. The patient falls (due to poorly organized furniture, architectural barriers, slippery floors, etc.)
2. Heavy or sharp instruments or apparatus fall on the patient
3. The patient suffers accidental cuts and burns
4. The patient ingests/inhales small dental material
5. The patient suffers eye damage.[23]

Goals of Patient Safety

1. Correctly identify the patients
2. Effective communication
3. Safety alert for High-alert medicines
4. Eliminate errors like wrong-side, wrong-patient, wrong procedure surgeries
5. Reduce the health-care acquired diseases
6. Reduce risk of patient hurt against equipment, falls.[20]

CONCLUSION

Patient safety can be improved using proper protocols, education, communication, learning initiatives from hazards that had taken place earlier, rectification, six-sigma monitoring, and safety standards. Every clinician must make it mandatory to follow the patient safety standards. The strict body must be maintained who monitors and regulates these principles being followed in hospitals and clinics.

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Review Article

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Maxillary Impacted Canine: Diagnosis and Contemporary Ortho Surgical Management Guidelines

Nitubroto Biswas[1], Soma Halder Biswas[2], Ajoy Kr Shahi[3]

[1]Professor, Department of Periodontia and Implantology, Buddha Institute of Dental Sciences and Hospital, Patna, Bihar, India, [2]Clinical Tutor, Department of Orthodontics, Dr. R. Ahmed Dental College and Hospital, Kolkata, West Bengal, India, [3]Professor, Department of Oral and Maxillofacial Surgery, Buddha Institute of Dental Sciences and Hospital, Patna, Bihar, India

Abstract

Canines contribute significantly in functional occlusion and form the foundation of an esthetic smile. So, any factor that interferes with the normal development and eruption of canine has serious consequences. Surgical exposure and orthodontic traction of impacted canine demand patient cooperation, long treatment duration, high cost, and chances of damage to the tooth and adjacent structure. Early diagnosis of canine impaction is essential for proper deimpaction of canine. Determination of the prognosis of the impacted canine is essential before orthosurgical approach for management of this specific malocclusion. Proper knowledge of the position of canine in relation to the other anatomical structure is very important in surgical exposure and orthodontic management of impacted maxillary canine. In the present article, with an overview of incidence and etiology, we have mostly concentrated on diagnosis, prognosis, and orthosurgical management of impacted canine.

Key words: Diagnosis, Impacted canine, Management, Prognosis

INTRODUCTION

Impacted tooth is one that fails to erupt and will not attain its anatomical position beyond the chronological eruption date even after its root completion. The impacted maxillary canine is a frequently encountered clinical problem.

Maxillary canine is the most commonly impacted teeth, second only to third molars.[1] The permanent maxillary canine is frequently misplaced teeth in relation to other teeth in the maxilla. The prevalence of non-eruption and ectopic eruption of this tooth has been reported to be 0.9-2.0% in samples not previously selected for orthodontic treatment. The canine is the most frequently found palatal to the lateral incisor. Impactions are twice as common in females. 8% have bilateral impactions.[2] Approximately, one-third of impacted maxillary canine is located labially, and two-thirds are located palatally.[3]

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ETIOLOGY

Several etiologic factors are responsible for impaction of maxillary canine broadly termed under localized, systemic, and genetic.

Buccally impacted canine is mostly due to tooth size-arch length deficiency. Study shows only 17% of labial impacted canine shows insufficient space, whereas palatally impacted canine has sufficient space in 85% cases for eruption.[4]

Etiology of palatally impacted canine is related to two major theories - guidance theory and genetic theory.

The guidance theory proposes that canine erupts through a long, tortuous path. Lateral incisors serve as a guide to canine during the course of the eruption. If the root of lateral incisor is missing or malformed, the canine will not erupt. The presence of the lateral incisor root with the right length, formed at the right time, is an important

Corresponding Author: Dr. Soma Halder, Department of Orthodontics, Dr. R. Ahmed Dental College and Hospital, 114, A. J. C. Bose Road, Kolkata -14, West Bengal, India. Phone: +91-09475679714. E-mail: stdc32@gmail.com

variable needed to guide the mesially erupting canine in a more favorable distal and incisal direction.[5]

The genetic theory points genetic factor as primary etiology of palatally impacted canine and may be associated with missing or small lateral incisor.[6] It has been suggested that transcription factors such as MSX1 and PAX9 might be involved in the genetic control of palatally displaced canines. Some studies reported that palatally impacted canines in association with enamel hypoplasia, small lateral incisor, aplasia of the second premolar, and infra occlusion of primary molars signifies genetic involvement.[7]

ROOT RESORPTION OF MAXILLARY LATERAL INCISORS

Ericsson and Kurol[8] found that resorption of maxillary lateral incisors in relation to impacted canine was found to be more common in girls than in boys. The sex ratio was 3:1. The position of the cusp of the maxillary canine was positioned more mesially in the resorption group.

DIAGNOSIS

The diagnosis of canine impaction is based on both clinical and radiographic examinations.

Clinical Evaluation

It has been suggested that the following clinical signs must be correlated with chronological and dental age of the patient for proper diagnosis of maxillary canine impaction.[9]

- Delayed eruption of the permanent canine or prolonged retention of the deciduous canine beyond 14-15 years of age
- Absence of a normal labial canine bulge
- Presence of a palatal bulge (Figure 1)
- Delayed eruption, distal tipping, or migration of the lateral incisor.

Radiographic Evaluation

Extraoral radiographs such as cephalogram determine the relationship of the impacted teeth to the other facial structure and orthopantomograph (OPG) used to localize impacted teeth in all three planes. Intraoral radiographs such as occlusal radiograph (OR) determine the position of the impacted teeth relative to the midline. Intra-oral periapical radiograph determines the integrity of lamina dura.

Most widely recommended technique of localization of impacted canine is the parallax method. In radiologic terms, parallax (image/tube shift) is the apparent displacement of an image, relative to the image of a reference object, caused by an actual change in the angulation of the X-ray beam. The reference object is normally the root of an adjacent tooth. The image of the tooth that is farther away from the X-ray tube moves in the same direction as the tube, and the image of the tooth closer to the X-ray tube moves in the opposite direction to the tube. A tube shift may be carried out in either the horizontal or the vertical plane.

Clark used two periapical radiographs in different horizontal angulation for a horizontal tube shift technique.

Keur used the combination of panoramic (PR) and ORs for a vertical tube shift (VTS).[10] A PR is often taken as an initial radiograph, this combination of radiographs only requires one additional exposure, the OR. The PR tube is actually positioned behind the head at an angle of −7° to the occlusal plane. The OR is taken at an angle of +60-65° to the occlusal plane, i.e. there is an effective difference of 53-58° between the taking of the two films. The image of the canine that is farther away from the X-ray tube moves in the same direction as the tube. If impacted teeth move more downward in OR than in OPG it is buccal in location if it moves upward, it is palatal in location. If the position is same in both radiographs, the tooth may be in mid alveolus (Figures 2 and 3).

VTS technique is preferred because OPG, which provides information about all the teeth, jaws, and the surrounding structures, is often taken as an initial radiograph and this combination only requires one additional exposure the OR. 50° of differences between the two radiographs makes it less technique sensitive procedure.[11]

Complex and severe cases may demand a cone beam computed tomography (CBCT) for better visualization and precise surgical planning. Extent of damage of the adjacent tooth root, amount of bone surround each tooth, size of the follicle and precise buccolingual location can be determined from CBCT images. A comparison of two-dimensional image with CBCT shows a 21% disagreement in mesiodistal location and 16% disagreement in buccopalatal location.[12]

Determination of Prognosis

Prognosis of deimpaction of canine depends on the age of the patient, availability of space in the arch, favorable position of the impacted canine in the maxilla.

To determine the favorable position of the impacted canine one highly relevant classification is sector classification.[13] It predicts the chance of future canine impaction as well as chances of correction by early intervention. Ericson and Kurol found that tip of impacted canine located more close to dental midline are

more prone to impaction.[14] On the basis of this sector, classification was created. One line each was drawn a tangent to the mesial and distal height of contour of lateral incisor. The long axis of lateral incisor was drawn.

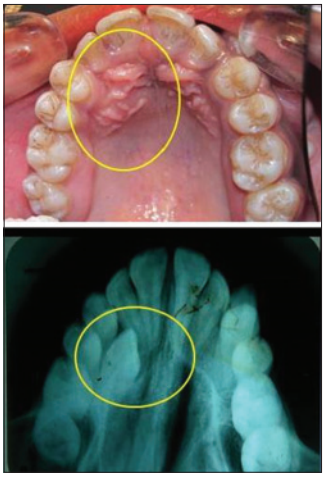

Figure 1: Palatal bulge in impacted palatal canine

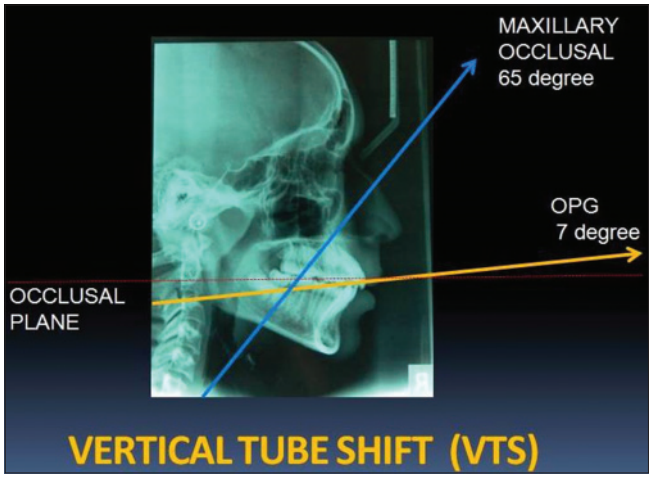

Figure 2: Diagrammatic representation of vertical tube shift technique

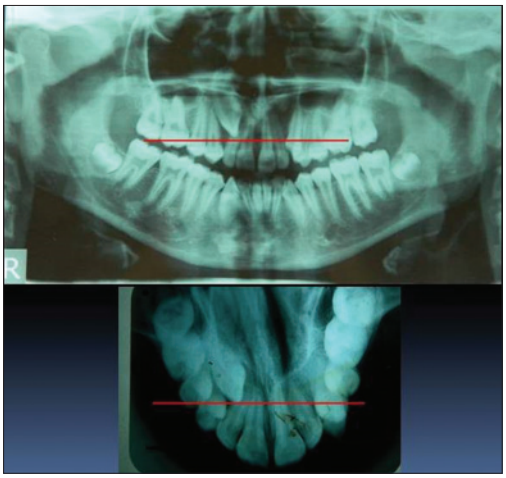

Figure 3: Vertical tube shift showing palatal impaction of canine

So, the area were divided into four sectors I, II, III, and IV from distal to mesial (Figure 4). 78% of the canines are destined to be impacted if their cusp tips are located in the sectors I, II, and III.

Another method of prediction of chances of canine impaction is the calculation of angulation of long axis of canine to the midline in OPG.[15] If the angulation is more than 31 degree, the chance of spontaneous eruption after preventive treatment is less (Figure 5).

Management of Impacted Canines

Ideal approach for the management of impacted canine is interdisciplinary management comprises of a team of an orthodontist, oral surgeon, and periodontist. Intervention at an early age (10-13 years) with extraction of deciduous canine spontaneous eruption of permanent canine increases by 75% cases and severity of impaction decreases by 94% cases.[16] Removal of physical barrier like a supernumerary tooth, odontome, fibrous bands, and tooth sac are helpful in tooth eruption. Creation of sufficient space by maxillary

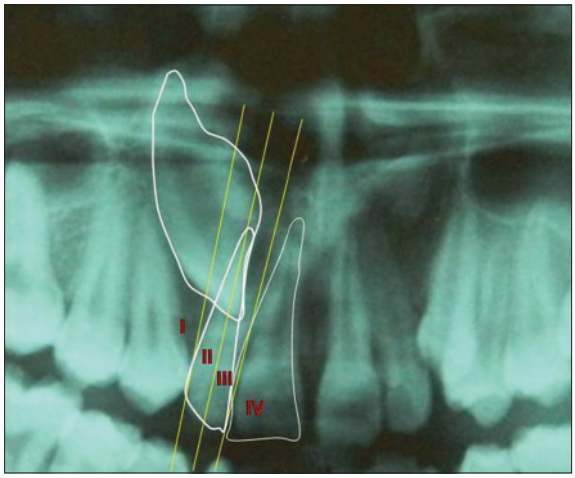

Figure 4: Sector classification

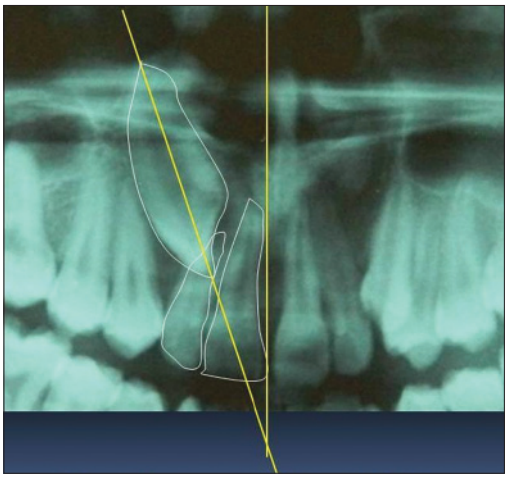

Figure 5: Angulation of canine to the midline

expansion and molar distalization improves the prognosis of canine impaction.

Surgically assisted orthodontic guidance is required when a definitive diagnosis of impaction is established, and possibilities of spontaneous eruption are exhausted. It is considered after complete root apex formation.[17]

Two different methods of surgical exposure of impacted canine have evolved, one method is commonly known as the open eruption technique, and the other method is called the closed eruption technique.

Open eruption involves the surgical excision of a wedge-shaped section of the overlying palatal mucosa after removal of the bone covering the ectopic canine. A surgical or periodontal pack is then placed over the exposed tooth for 7-10 days. After pack removal, the ectopic canine is often left to erupt naturally for a period of 4-6 day before a bonded attachment is placed, and orthodontic traction is commenced. This technique is mostly used for palatally impacted canines (Figure 6).

An alternative closed eruption method of surgical exposure is preferred by many oral surgeons and orthodontists. This technique usually involves raising a large full thickness flap with a minimum degree of bone removal to uncover the ectopic canine. Efforts are made not to uncover the cementoenamel junction or not to disturb the periodontal ligament. Instead, an attachment or bracket with a braided wire ligature or gold chain connected to it is bonded to the crown of the exposed canine during surgery. The mucosa is then sutured back into place with the end of the wire ligature extending into the mouth either through the wound margin or through an incision placed in the flap. Orthodontic traction is usually commenced soon after the surgical exposure. This technique is mostly used for labially impacted canines (Figure 7).

When considering the periodontal implications of surgical exposure, an apically repositioned flap or closed eruption through keratinized gingival tissue is recommended for a labially ectopic canine. The soft tissues on the buccal aspect of the maxilla comprise keratinized attached gingiva at the alveolar margin and mobile non-keratinized tissue in the sulcus. There is conclusive evidence that an open eruption approach through non-keratinized gingiva should be avoided. Long-term periodontal health is better when the more resilient keratinized gingival tissue is maintained on the labial aspect of the canine.[18]

For palatally impacted canine significantly deeper mean pocket depths found palatal to the previously ectopic canine for those patients treated by the closed eruption technique than those patients treated by the open eruption. The removal of palatal mucosa during the open eruption technique had the same effect as a gingivectomy in reducing pocket depth. The mean attachment loss on the palatal aspect was significantly greater for the patients treated by open eruption than the patients treated by the closed eruption, but it has limited esthetic value. The interdental bone levels did not differ significantly.[19]

Figure 6: Open eruption technique

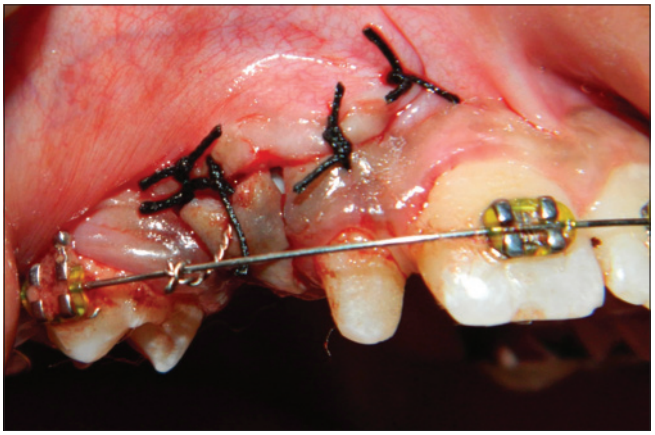

Figure 7: Closed eruption technique

Orthodontic Management

For applying orthodontic traction following considerations are recommended:

- Creation and maintenance of sufficient space before surgical exposure
- Attachments should preferably low labiolingual profile, preventing flap tearing and buttonholing
- Orthodontic traction application is recommended soon after surgical exposure; the canine is pulled directly to its correct position and prevented from adopting a more anterior or palatal position and takes less treatment time[20]
- Light force ranging around 60 g for orthodontic traction is used. The direction of orthodontic traction

is intended for vertical eruption away from the roots of the incisors
- Provision of arch wire of sufficient stiffness
- Torquing auxiliaries are used only in finishing stages. Ectopic canines requiring torquing root movements had 4% less bony support than those aligned by tipping or extrusive movements.[21]

Contemporary orthodontic devices are "Ballista spring"[22] attached on the buccal surface of the posterior teeth, with a transpalatal arch as anchorage, provide a comfortable and controlled movement of the uncovered palatally impacted canine. For labially impacted canine stainless steel archwire auxiliary, cantilever spring, and titanium molybdenum alloy box loop, Australian helical archwire are used.[23,24] Temporary anchorage device are nowadays used with great success in providing orthodontic traction to impacted canine.[25]

Retention of deimpacted canine must be considered as, relapse of rotation and spacing may occur after completion of the orthodontic treatment of an impacted canine occurs in 17.4% of cases in comparison to 8.7% of the control tooth.[26] To minimize or prevent relapse supracrestal fiberotomy and bonded fixed retainers are required after completion of treatment.

CONCLUSION

The management of impacted canine is a complex procedure, require a multidisciplinary treatment approach. The clinician should communicate with each other to provide the patient with proper diagnosis, idea of prognosis, and optimal treatment plan based on scientific rationale.

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Case Report

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Alloimmunization in Sickle Cell Disease with Anemia and Pregnancy: A Case Report

H K Sale[1], Vitthal J Shendage[2]

[1]Professor and Head, Department of Anaesthesiology, Noble Hospitals, Pune, Maharashtra, India, [2]Consultant, Department of Anaesthesiology, Noble Hospitals, Pune, Maharashtra, India

Abstract

Role of anesthesiologist in management of sickle cell disease in pregnancy is related to its complications such vaso-occlusive crisis with severe pain, sepsis, acute chest syndrome, stroke, priapism, avascular necrosis of hip, alloimmunization with severe hemolysis with anemia and fetal complications such as preterm, intrauterine growth restriction (IUGR), hemolysis, hyperbilirubinemia, and intrauterine device. Mainstay of treatment is symptomatic which includes analgesia, hydration, oxygenation, blood transfusion, antibiotics, folate, and hydroxyurea. Herein, we provide brief review of our patient with alloimmunization due to past blood transfusions for sickle cell anemia. We experienced severe hemolysis in our patient due to difficulty to cross match all red cell antigens in donor and antibodies against the K, E, C, Jk^b antigens in our patient. That changed our outlook toward blood transfusion in this patient which requires further red cell antigen phenotype study in donor and antibody study in patient. Furthermore, this patient had difficulty for spinal anesthesia due to decrease mobility of hip due to avascular necrosis and unbearable painful vaso-oclusive crisis requiring good pain relief. Her baby was preterm, IUGR, had hyperbilirubinemia and died on day 3 of life. Such case first time happened in our hospital and was rarely described previously in anesthesia literature to our knowledge. Though blood and hematology literature do mention about this. It is difficult to manage medicolegal aspects of such blood transfusion, where anesthesiologist is directly involved in blood transfusion in perioperative period, pain relief, oxygen, fluid-acid base, and multisystem critical care management.

Key words: Alloimmunization, Blood transfusion, Cross match, Red cell antigen phenotypes, Sickle cell disease

INTRODUCTION

Sickle cell disease (SCD) is a group of inherited single gene autosomal recessive disorders caused by the "sickle" gene, which affects hemoglobin structure.[1] Sickle cell anemia (hemoglobin S [HbS] disease) is due to the production of abnormal hemoglobin due to a single amino-acid substitution in the beta globin chain resulting in glutamic acid being replaced by valine at the 6th position and HbS is produced instead of adult hemoglobin (HbA). Someone with sickle cell trait (a carrier of SCD) will produce both HbA and HbS and is often described as HbAS.[2] Pathology and clinical presentation do not affect until 1st year of life. After that, fetal hemoglobin is replaced by (HbA and HbA2). HbA is made up of abnormal hemoglobin due to which sign-symptoms starts. The pathophysiology of SCD is a consequence of polymerization of the abnormal hemoglobin in low-oxygen conditions, which leads to the formation of rigid and fragile sickle-shaped red cells. These cells are prone to increased breakdown, which causes the hemolytic anemia, vaso-occlusion in the small blood vessels which causes most of the other clinical features including acute painful crises. Other complications of SCD include stroke, pulmonary hypertension, renal dysfunction, retinal disease, leg ulcers, cholelithiasis, and avascular necrosis (which commonly affect the femoral head and may necessitate hip replacement).[3] Sickle trait is asymptomatic, except for a possible increased risk of urinary tract infections and microscopic hematuria. SCD was previously associated with a high early mortality rate, but now the majority of children born with SCD in the UK live to reproductive age and average life expectancy is at least the mid-50s. Women with SCD appear to be susceptible to medical complications including increased infection; an increase in sickle cell related painful episodes,

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Corresponding Author: Dr. Vitthal J Shendage, Department of Anaesthesiology, Noble Hospitals, 153 Magarpatta City Road, Pune - 411 013, Maharashtra, India. E-mail: shendagevj@gmail.com

increased fetal morbidity, fetal growth restriction, preterm labor, and increased cesarean section rates.[4]

Patients often require supplementary hydration, analgesia, and oxygen. Life-threatening crises may require urgent exchange blood transfusion and management on a critical care unit. Transfusion is not without risk or burden; in particular the risk of alloimmunization (the formation of additional red cell allo-antibodies) can be significant. Patients with SCD are immunogenic and it is not uncommon for them to form antibodies that can lead to delayed hemolytic transfusion reactions, hemolytic disease of the fetus and the new born and also make future cross matching of blood difficult. Blood is routinely fully matched for to reduce this risk.[5]

CASE REPORT

A 37-year-old female, weighing 65 kg presented with severe bilateral upper limb pain and backache. She was 29 weeks pregnant ($G_3P_1L_1A_1$) and known case of SCD with anemia. 15 years back she underwent cesarean section because of sickle cell crisis and delivered a preterm baby, who is living child. She also underwent laparoscopic surgery 10 years back which was uneventful. For above reasons, she received multiple blood transfusions. She was also known case of avascular necrosis of hip and femur head with decreased mobility and painful hip joints. She has multiple episodes of painful crisis of extremity and lower back relived with hospitalization and analgesics which includes paracetamol, fentanyl, tramadol, hydration, and oxygen. In present pregnancy patient gives increased severity and frequency of above symptoms requiring frequent visits to hospital and hospitalization. The patient was admitted intensive care unit for 10 days for same reasons, after treatment she was comfortable and discharged home. However, within 12 h of discharge, she readmitted with unbearable pain in upper limb and backache which required intense care which includes fluid, oxygen, fentanyl, blood transfusion in view of anemia (Hb 7.8 g%) with pregnancy. After blood transfusion patient Hb further dropped to 6 g% and bilirubin levels reached to 10 mg% along with persistent symptoms. At this time, hematologist came into picture and thought process for alloimmunization in SCD started. Meanwhile, worsening condition of patient along with pregnancy make our team to take decision of cesarean section though she was preterm because pregnancy itself is precipitating factor for acute crisis in SCD. The patient and her family were ready for C-section with informed written consent regarding maternal and fetal complications. The patient taken for Cesarean section and spinal anesthesia given with 27 Q spinal needle in left lateral position with all aseptic precautions. We found procedure difficult due to inappropriate position in view of hip immobility and pain. After surgery, patient received two pack cells which are cross matched for different antigens in donor and antibodies in recipient considering alloimmunization due to previous blood transfusions. Post-operative day one patient Hb was 8 g% but symptoms persistent and so patient managed in critical care unit, where she received good care, hydroxyurea, warfarin, heparin along with supportive treatment, and after 3 weeks she shifted in ward and subsequently home.

DISCUSSION

There is published data to support the conclusion that the risk of alloimmunization is greater in patients receiving transfusions for SCD than in patients receiving transfusions for other chronic diseases. In a study conducted by Vichinsky *et al*. in 1990 demonstrated that alloantibodies developed in 30% and delayed transfusion reactions in 11% of patient receiving transfusions in SCD while only 5% in patients with chronic anemia receiving blood transfusion.[6] According to Vichinsky *et al*. this represent low estimate of the rate of alloimmunization, since not all antibodies are detected by standard techniques. 16% of patients have multiple antibodies which resulted in clinical complications (delayed hemolysis) and delayed transfusion therapy due to additional problems in cross matching. Red cell phenotypes most likely to cause antibodies to develop in patient with SC anemia are K, E, C, Jk^b. Activation of immune system may contribute to increased incidence of delayed transfusion reactions. Causes for increased incidence of alloimmunization in SCD are due to lack of phenotypic compatibility between donor and recipients (Giblett demonstrated that when black patient receives blood from white donor the risk of alloimmunization was higher when donor and recipients were matched for race) and racial difference(Kim *et al*., found increased incidence of alloimmunization in black patients compared to white patients).[1] The present case illustrates a problem created due to inadequate cross matching which was not done for red cell antigens which are most likely to cause antibodies in recipients' giving hemolytic reactions. After cesarean section, we read above literature and references.Then, donor's blood was cross matched with recipient for all possible red cell phenotypes in blood bank, and we transfused two packed cell volume to our patient. After 24 h, patient Hb increased with no laboratory evidence of hemolysis confirmed by bilirubin levels, liver enzymes disease etc.[7-10]

CONCLUSION

Most of anesthesiologist are aware of pathophysiology of SCD, its complications and management. Anaesthesiologist managing such cases either in operation room as anesthesiologist or as intensives in intensive care. However, awareness about alloimmunization in SCD is less amongst anaesthesiologist. This may be because this pathology is rarely seen, remain undiagnosed, unnoted or many time this management is done by hematologist as teamwork. Here, we faced difficulty in positioning due to pain and avascular necrosis of hip which was manageable. However, our nightmare was death of baby and severs hemolysis with organ dysfunction in mother who needed intensive care for more than 3 weeks and top on this economical and financial loss to prove that alloimmunization is known with SCD with previous blood transfusions. So, we recommend that all patients with SC anemia who undergo transfusion be matched with donor for the red cell antigens commonly associated with alloimmunization and transfusion reactions, aim is to avoid phenotypic incompatibility between donor and recipient.

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Case Report

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Adenomatoid Odontogenic Tumor: A Dentigerous Cyst Mimic in Maxilla

A L Hemalatha[1], S N Shobha[2], C R Raghuveer[3], Swati Sahni[3], Amita Kumari[3]

[1]Professor and Head, Department of Pathology, Adichunchanagiri Institute of Medical Sciences, Mandya, Karnataka,India, [2]Assistant Professor, Department of Pathology, Adichunchanagiri Institute of Medical Sciences, Mandya, Karnataka,India, [3]Post-graduate, Department of Pathology, Adichunchanagiri Institute of Medical Sciences, Mandya, Karnataka,India

Abstract

The adenomatoid odontogenic tumor is a rare and distinct neoplasm which is considered a slowly progressive, benign, non-neoplastic hamartomatous lesion by many. It is notoriously misdiagnosed as a dentigerous cyst. It accounts for 1-9% of odontogenic tumors. The most common site of occurrence is maxilla and it is usually associated with an unerupted, permanent tooth. It is most commonly seen in young women patients. It closely resembles ameloblastoma or dentigerous cyst. A rare case of adenomatoid tumor of maxilla mimicking a dentigerous cyst is presented here.

Key words: Adenomatoid odontogenic tumor, Dentigerous cyst, Odontogenic cyst

INTRODUCTION

The adenomatoid odontogenic tumor is a relatively uncommon tumor of odontogenic epithelium comprised of duct-like structures. It may be partly cystic and partly solid in consistency. It has been called by various names after being described for the 1st time by steensland.[1]

Drebaldt called it pseudo adenoameloblastome,[2] Harbitz "cystic adamantinoma"[3] and Ghosh "adamantinoma."[4] It was recognized as a distinctive entity by Stafne.[5] It was eventually recognized that it is not a type of ameloblastome.[6] Gorlin called it ameloblastic adenomatoid tumor while Abrams *et al.*, suggested the name ameloblastic adenomatoid tumor[7] and adopted this term in the WHO histological typing of tumor.

Clinical Summary

A 17-year-old male patient presented with progressive swelling on the left side of the face which was present since 6 months.

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Local examination revealed a diffuse swelling involving the left infraorbital and malar areas extending up to the left nasolabial fold, mid-zygomatic arch, and infraorbital margin.

Computed tomography scan findings showed an expansile radiolucent lesion with a well-defined radiosclerotic margin enwrapping a tooth within it.

A provisional clinical diagnosis of the dentigerous cyst was offered.

Enucleation was done and the specimen submitted for histopathological examination.

Gross Examination Findings

Single, globular tissue mass measuring 4 cm × 3 cm × 1.5 cm. External surface was gray brown. A tooth was embedded in the soft tissue mass (Figure 1). The cut surface was gray-white to gray-brown with firm solid areas (Figure 2).

Microscopy

A benign epithelial tumor with a round to oval tumor cells arranged in nodules, whorls, and ductular patterns was seen. The tumor cells showed scant cytoplasm and uniform nuclei with bland chromatin. The epithelial nodules were surrounded by polyhedral to spindle-shaped cells (Figure 3). Intervening areas of homogenous hyaline material and calcified deposits were seen (Figure 4).

Corresponding Author: Dr. A L Hemalatha, G-3 Sai Brindavan Apartments, 63/64 Industrial Suburb Vishwesharanagar, Mysore - 570 008, Karnataka, India. Phone: +91-8453399335. E-mail: halingappa@gmail.com

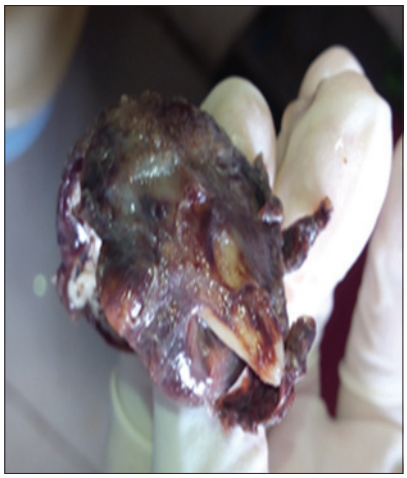

Figure 1: Globular, soft tissue mass with an embedded tooth

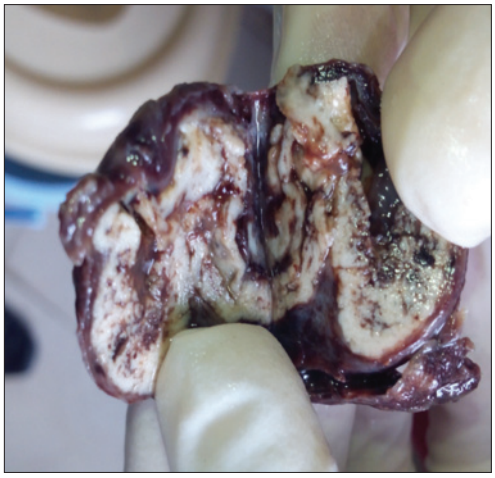

Figure 2: Cut surface - encapsulated gray - white to grey - brown tumor with firm solid areas

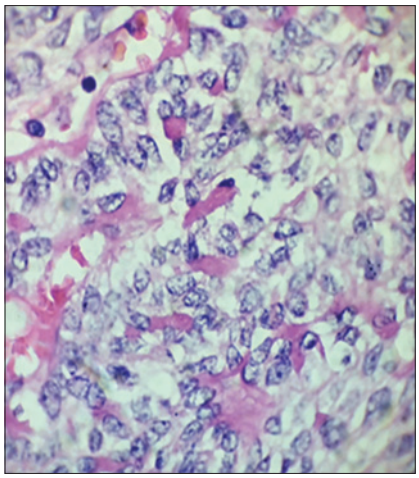

Figure 3: Epithelial nodules surrounded by polyhedral to spindle shaped cells (H and E ×45)

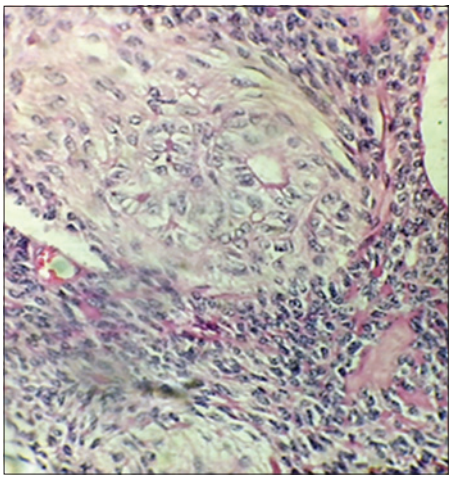

Figure 4: Tumor cells with scant cytoplasm, uniform nuclei, and bland chromatin. Intervening areas of homogenous hyaline material and calcified deposits

Final Diagnosis

Adenomatoid Odontogenic Tumor.

DISCUSSION

The adenomatoid odontogenic tumor is an uncommon neoplasm.[8] Three variants of the tumor have been described namely, intraosseous follicular, intraosseous extrafollicular and peripheral types. The extrafollicular type shows no relation with an impacted tooth which is seen in about 24% of cases as in the present case.[9] The majority of the tumors (73%) are of a follicular type and are seen in association with an unerupted tooth. The peripheral variant (3%) is seen attached to the gingival structures. The intraosseous follicular and extrafollicular types are commoner in the maxilla than in the mandible.[10,11] The tumor is a more common seen in females with a female to male ratio of 2:1.[12] The histogenesis of this tumor is debatable.[13,14] It is suspected to arise from odontogenic epithelium because it arises more commonly in the teeth bearing bones.[15] The tumors are usually small ranging from 1.5 to 3 cm.[16] Larger tumors as in the present case have also been reported.[7,17] Sometimes extensive calcification can be seen in the tumor.[7] The clinico-radiologic appearances are often mistaken for calcifying odontogenic tumor or dentigerous cyst as in the present case. The differential diagnoses include ameloblastoma, ameloblastic fibro-odontoma, and ameloblastic fibroma.[18]

Since the tumor is well-encapsulated and is known to have a benign behavior, conservative surgical enucleation is the preferred treatment of choice. It has an excellent outcome without any recurrence.[18] Our patient who underwent surgical enucleation 6 months ago is asymptomatic on follow-up.

CONCLUSION

The adenomatoid odontogenic tumor is an uncommon entity which is often clinically mistaken for the dentigerous or odontogenic cyst. Histopathology is the gold standard in its diagnosis. Conservative surgical treatment is curative.

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Case Report

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Lithopedion: A Case Report Presenting with Intestinal Obstruction and Review of Literature

Banabihari Mishra[1], Tapan Kumar Nayak[2], Kasturi Bharadwaj[3]

[1]Associate Professor, Department of Surgery, Veer Surendra Sai Medical College and Research, Burla, Odisha, India, [2]Senior Resident, Department of Surgery, Shri Ramachandra Bhanj Medical College, Cuttack, Odisha, India, [3]Post-graduate Student, Institute of Medical Sciences and SUM Hospital, Bhubaneswar, Odisha, India

Abstract

"Lithopedion" is Greek word which means "Stone Baby." Lithopedion is a calcified fetus resulting from an extra-uterine pregnancy. They constitute around 1.5-2% of all ectopic pregnancies and 0.0054% of all gestations. Only around 400 cases reported in the history. Most patients remain asymptomatic for years, but the treatment plan must be individualized according to patient's presentation and age. Complications do occur very rarely, and their management is very difficult. Here, we have described a 50-year-old lady presenting with intestinal obstruction. Diagnosis was confirmed by suggestive clinical history and X-ray abdomen. Laparotomy and retrieval of the lithopedion done. Post-operative recovery was uneventful.

Key words: Intestinal obstruction, Lithopedion, Stone baby

INTRODUCTION

"Lithopedion" is Greek word which means "Stone Baby." They constitute around 1.5-2% of all ectopic pregnancies and 0.0054% of all gestations. Patients ages vary from 20 to 100 years, from whom around two-third being over 40 years.[1] Our patient age is 50 years. The period of lithopedion retention varies from 4 to 60 years but in the history, 18 months has been reported.[1] In our case, the retention period is around 28-year. As with most cases of lithopedion, our case is completely unaware of the fetus. Complications do occur very rarely.[2] Detection of lithopedion is a harsh reminder of the antenatal care and also consideration of poor socio-economic status and cultural attitudes.[3,4] The treatment plan must be individualized and take into account the presentation, age, and symptoms of the patients.

CASE REPORT

A 50 years post-menopausal female from low economic status presented to surgery outpatient department with chief complain of intermittent dull aching pain in the right iliac fossa since 28 years. It is associated with dyspepsia, occasional vomiting, pain, and distention of abdomen since 7 days. There was no history of fever, loss of appetite, hematemesis, and malena. She was married since 36 years and blessed with 3 children. Last delivery has occurred 28 years back. Abdomen was soft, distended with visible peristalsis, no hepato-splenomegaly, a hard irregular mass (10 cm × 15 cm) palpable in the right iliac fossa, which had a nodular surface, restricted mobility, ballotable. No other mass palpable. Other systemic examinations were normal. On X-ray abdomen, a large irregular calcified mass detected at the right iliac fossa (Figure 1). Ultrasonography shows a calcified mass in the right iliac fossa without visceral involvement, could be fecal matter. Contrast-enhanced computed tomography (CT) could not done due to poverty and emergency. On laparotomy, a calcified irregular mass entrapped in omentum present in the right iliac fossa was found. On retrieval partially developed fetal structure detected wrapped in the omentum and placed in the paracecal area. There was minimal adhesion to the serosa of ascending colon and the distal part of the ileum which was the cause of obstruction. Adhesiolysis with omentectomy was done and on the removal of the omentum from the mass, the fetal appearance with skull, spine, and long bones were clearly demarcated making the diagnosis of extra-uterine intra-abdominal mummified fetus (Figures 2 and 3). Recovery was uneventful.

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Corresponding Author: Tapan Kumar Nayak, Department of General Surgery, Shri Ramachandra Bhanj Medical College, Cuttack, Odisha, India. Phone: +91-9861363474. E-mail: drtapannayak@gmail.com

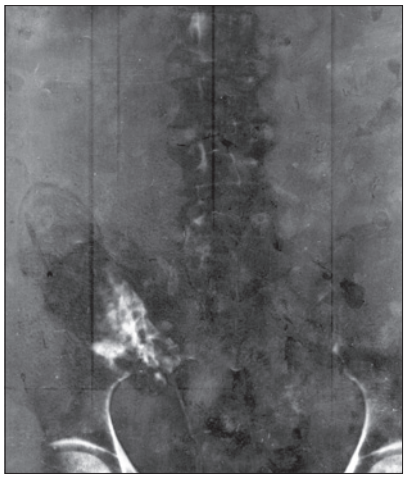

Figure 1: X-ray abdomen and pelvis (anterior-posterior-view) showing fetal shape calcification in the right iliac fossa

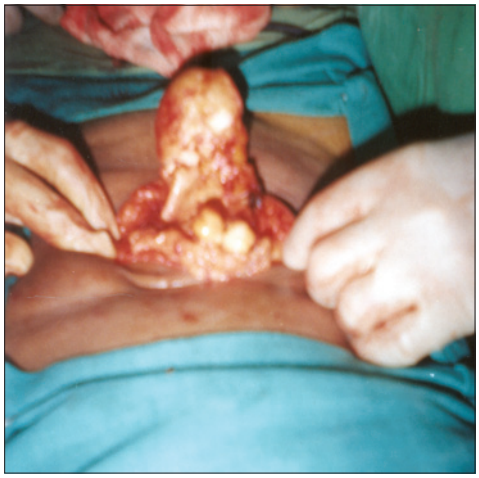

Figure 2: Fetal structure wrapped in omentum, adherent to ascending colon and distal ileum

Figure 3: The fetal appearance with skull, spine, and long bones

DISCUSSION

Until now only around 400 cases documented of Lithopedion in history.[5] Patients ages vary from 20 to 100 years.[1] About 2/3rd of all patients are over the age of 40 years. The youngest recorded patient was only 20 years old. The period of lithopedion retention varies from 4 to 60 years. The earliest period of lithopedion retention diagnosed in literature is 18 months.[1] Lithopedion typically arises in sterile dead extra-uterine fetus after 3 months of gestation period where sluggish blood circulation and local condition is conducive for calcium precipitation.[4]

It is usually enough to confirm the diagnosis from the suggestive clinical history, a palpable mass on physical examination and radiological finding by an abdominal X-ray film. Symptoms usually non-specific and chronic, e.g. vague abdominal pain and constipation. Abdominal X-ray film is an inexpensive screening tool that can confirm the diagnosis. Whenever necessary CT, magnetic resonance imaging, or barium enema can be done for planning the surgical approach.

During 1100 BC, the earliest lithopedion was found in an archeological excavation at Bering Sinkhole, on the Edwards Plateau in Kerr County, Texas.[2] In the 10th century, physician Albucasis first described lithopedion. Madame Colombe Chatri, a 68-year-old French woman, was the first reported case of lithopedion. After her death in 1982, an autopsy revealed a fully developed stone baby in her abdominal cavity for 28 years.[6] A series of 47 cases of lithopedia was reviewed by the German physician Friedrich Kuchenmeister in 1880 and identified three subgroups: (1) Lithokelyphos (only membrane is calcified), (2) lithokelyphopedion (both membrane and fetus is calcified), and (3) true lithopedion (mainly fetus is calcified, membrane minimally calcified).

Lithopedion by secondary abdominal implantation as a consequence of ruptured tubal pregnancy is very rare. Complications do occur very rarely, e.g. bladder or rectal perforation, volvulus, intestinal or urinary obstruction, extrusion of fetal parts through the abdominal wall, rectum, vagina, and abscess formation.[2,7] Our case presented with intestinal obstruction. It is very much difficult to manage a lithopedion induced complication situation, so they should undergo surgical extirpation even if asymptomatic. The treatment plan must be individualized and take into account the presentation, age, and symptoms of the patients. According to experience, surgical extirpation can be done by open or laparoscopic approach.[8]

CONCLUSION

Management of lithopedion complications is very difficult. So, whenever possible surgical extirpation should be done even if the patient is asymptomatic.

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Case Report

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Close Reduction with K-wire Fixation of Neer Type-III Fracture Surgical Neck Humerus with Multiple Valvular Heart Disease and Asthma under Interscalene Brachial Plexus Block: A Case Report

Rupak Kundu, Samit Parua, Santosh Kumar Lohar

Post-graduate Trainee, Department of Anaesthesiology and Critical Care, Gauhati Medical College and Hospital, Guwahati, Assam, India

Abstract

Regional anesthesia has always been considered as a safer alternative to general anesthesia specially in geriatric patients. The interscalene approach to the brachial plexus block is particularly well suited for operations on the shoulder, clavicle, or upper arm. The approach preferentially blocks nerves of the brachial plexus (C5-C7), with variable proximal spread to the cervical plexus (C3-C4), while usually sparing the ulnar nerve (C8-T1). We report a case of 78-year-old lady, who was prepared for close reduction with K-wire fixation of Neer Type-III fracture surgical neck humerus (right). The patient was a known asthmatic, hypertensive, with diagnosed multiple valvular heart disease (severe aortic stenosis, mild aortic regurgitation, mild tricuspid regurgitation, and mild mitral regurgitation). The patient was operated under regional anesthesia using peripheral nerve stimulator guided interscalene brachial plexus block with 30 ml of 0.5% ropivacaine. The operative procedure lasted for 1 h and throughout the procedure patients vitals, and other parameters were well maintained with the added advantage that the patient was fully conscious and oriented during the entire duration of the procedure.

Key words: Aortic stenosis, Asthmatic, Fracture humerus, Hypertensive, Interscalene block, Regional anesthesia, Valvular heart disease

INTRODUCTION

Regional anesthesia has always been used as a viable alternative to general anesthesia specially in geriatric population. There has been a dramatic rise in the elderly population with the number of people aged over 65 increasing three-fold in the last century. Consequently, this has led to a progressive increase in the number of surgical interventions in elderly people. There has been a dramatic increase in the incidence of valvular heart disease among aging population.[1] An estimate of the prevalence of moderate to severe disease valvular heart disease in patients >75 years old is 13.3%.[2] Maintenance of intraoperative hemodynamic stability in these patients can be quite challenging. Asthma is a disorder of variable intensity, typified by sentinel symptoms, airway obstruction, inflammation, and hyperresponsiveness.[3] World Wide, this condition is estimated to occur in 300 million persons and is implicated in one of every 250 deaths.[4]

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CASE REPORT

After obtaining a written informed consent, a 78-year-old American Society of Anaesthesiologists (ASA) Physical status Class III, a female patient weighing 51 kg, height 5ft 2 inch, was posted for close reduction with K-wire fixation of Neer Type-III fracture surgical neck humerus (Rt). The patient was a known case of multiple valvular heart disease (New York Heart Association Class III at present) diagnosed at the age of 51 years, other co-morbidities being hypertension for last 15 years and seasonal asthma (asymptomatic at present) since childhood. She had refused valvular heart surgery previously on

Corresponding Author: Dr. Rupak Kundu, Department of Anaesthesiology and Critical Care, Room No. 112, PG Boys Hostel No. 5, Gauhati Medical College and Hospital, Guwahati - 781 032, Assam, India. Phone: +91-7399575280. E-mail: drrupakkundusmc@gmail.com

multiple occasions. She was on the tablet amlodipine 5 mg, tablet hydrochlorothiazide 12.5 mg, tablet aspirin 75 mg, occasional use of Duolin@ metered dose inhalers for asthma. On pre-anesthetic check-up, pulse rate was 86/min, blood pressure (BP) 130/80 mmHg, respiratory rate was 18/min, and the metabolic equivalent of physical activity 4. She had Mallampati Grade was III, edentulous, absent buccal pad of fat with slight restriction of neck extension. All routine investigation results were within normal limit except pre-operative Hb being 9.3 g% after one unit whole blood transfusion and Serum creatinine being 1.7 mg/dl. ECG showed left axis deviation. Recent Transthoracic echocardiography showed severe aortic stenosis with thickened aortic valve (AVA = 0.7 cm^2, mean gradient of 58 mmHg), mild aortic regurgitation, mitral regurgitation, tricuspid regurgitation, concentric left ventricular (LV) hypertrophy, Grade-I diastolic dysfunction, and LV ejection fraction 45%. Chest X-ray showed cardiomegaly. Systemic examination revealed an ejection systolic murmur, heard loudest at the upper right sternal border and at the 2nd right intercostal space which radiated to the carotid arteries bilaterally. The patient's relatives and medical specialists decided to go ahead with surgery, in spite of her risk as she was in severe pain and to prevent immobility and infection. She was counseled on the previous day about the merits and demerits of both general anesthesia and regional anesthesia techniques and gave consent for regional anesthesia. The anesthetic plan was peripheral nerve stimulator (PNS)-guided inter scalene brachial plexus block. The patient was kept nil orally overnight prior to surgery. On the morning of surgery, she was administered 2 puff of Duolin@ inhaler about 1 h prior to surgery. On arrival to the operation theater, an intravenous line was secured with 18 G cannula and lactated ringer's solution was started. All anesthetic equipment were checked. Antibiotic as per hospital protocol was given pre-operatively. Standard ASA monitors were attached to the patient and on table vitals were recorded. With the patient in supine position and neck turned to left side, PNS-guided inter scalene brachial plexus block was performed. Contraction of the arm and shoulder was elicited at 0.9 mv stimulation current, which persisted even on reducing it to <0.5 mv, following which 30 ml of 0.5% ropivacaine was injected. 20 min post injection adequate motor block, and the sensory block was noted. Monitoring was done throughout the operation, and vitals were recorded on monitors every 3 min. The patients were kept in a state of conscious sedation with injection midazolam 1 mg IV and injection fentanyl 50 mcg IV. Oxygen was given by face mask at the rate of 3 L/min. The operation lasted for 1 h; the patient was stable intraoperatively. Estimated blood loss of around 200 ml and 800 ml Ringer lactate was given intraoperatively, and 1 units packed cell was transfused post-operatively. Intraoperative urine output was 100 ml. All intraoperative vitals were within normal limits.

DISCUSSION

Goldman first reported aortic stenosis as an independent predictor for life-threatening cardiac complications during non-cardiac surgery,[5] and this was confirmed by Detsky *et al.*[6] Aortic stenosis is often accompanied by coronary disease, heart failure, stroke, diabetes mellitus, renal failure, and hypertension. These patients have a 5-7 fold increase in mortality when subjected to the stress of non-cardiac surgery.[7,8] Perioperative mortality and nonfatal myocardial infarction were higher in patients with Aortic stenosis.[9] Post-operative cardiovascular complications were also higher in these patients following general anesthesia.[10] The Goldman cardiac risk index attempts to quantify the risk of adverse perioperative cardiac events. The index scores each of a range of various conditions including cardiac disease, age, and the nature and urgency of the proposed surgery. The total score predicts the likelihood of complications and death. For certain operations, this risk can be minimized by avoiding general anesthesia and using local anesthetic techniques. Examples include peribulbar eye blocks for cataract surgery and brachial plexus blocks for upper limb surgery. Our patient had major predictor's positive for intraoperative cardiac events, and he was to undergo an intermediate risk surgery.

We should bear in mind that "mixed" valvular lesions are more common than "pure" valvular lesions thus we need to determine which is the most severe (hemodynamically significant) lesion and/or will need to "split the difference" between management goals for multiple valve lesions.[11] In our patient, severe aortic stenosis was the predominant valvular pathology.

The incidence of aortic stenosis in elderly is 2%,[12] it being the most common valvular pathology with increasing age. Valvular sclerosis being the most commont cause. Normal aortic valve area is 2.5-4.5 cm^2, when narrowed by 25% it leads to an obstruction to the LV outflow. Aortic stenosis is classified based on valve surface area, mild is an area of 2.5-2.0 cm^2, moderate is 1.5-0.8 cm^2, and severe being <0.8 cm^2. Common symptoms include syncope, angina, and dyspnea.[13] Aortic stenosis is a fixed outlet obstruction and is dependent on sinus rhythm to maintain cardiac output. Patients may have associated concentric LV hypertrophy that may lead to diastolic dysfunction and congestion; angina may occur when the oxygen demand outstrips delivery. Aortic stenosis cases with associated LV hypertrophy have increased the rate of mortality.[14] Critical aortic stenosis, i.e. valve area of 0.7 cm^2 and gradient of 50 mmHg.[15] Our patient had severe aortic stenosis with a valve area of 0.7 cm^2, a transvalvular pressure gradient of 58 mmHg, she was symptomatic New York Heart Association stage III on medications.

Patients with concentrically LV hypertrophy do not tolerate tachycardia, atrial arrhythmias, or hypotension. Any decrease in systemic vascular resistance may precipitate coronary ischemia. They eventually cannot compensate for a fall in systemic vascular resistance which may result in severe hypotension, myocardial ischemia and a downward spiral of reduced contractility causing further falls in BP and coronary perfusion. Elevated aortic valve gradient is associated with increased risk of cardiac complications.[9] A low cardiac output state and abnormal LV function predispose these patients to higher incidence of intraoperative hypotension.[16]

Anesthetic plan in such a patient is formulated keeping in mind the above-discussed problems as these patients are in a state of low fixed cardiac output state. Hemodynamic goals in them include:

- Maintain normal heart rate
- Maintain sinus rhythm
- Adequate volume loading
- High normal systemic vascular resistance.

Anesthetic management mainly involves maintenance of sinus rhythm, systemic vascular resistance, and preload are important to avoid cardiac decompensation.[8] The selected anesthetic technique should maintain afterload and avoid tachycardia to maintain the balance between myocardial oxygen demand and supply in the presence of a hypertrophied ventricle and reduced coronary flow. Talking general anesthesia for consideration, nearly all induction agents, as well as inhalational anesthetics, cause generalized vasodilatation to a variable extent, causing decompensation, therefore, titrating dose of all inhalational and induction agents is mandatory. Maintenance of intraoperative BP at pre-induction levels prevents intraoperative cardiac ischemia. Adequate analgesia maintaining a proper plane of anesthesia intraoperatively specially during the time of intubation prevents catecholamine-induced tachycardia, hypertension, and the risk of cardiac ischemia. Direct measurement of arterial BP is helpful except for short procedures. Treating hypotension using directly acting alpha-agonists such as phenylephrine may improve systolic and diastolic LV function. Careful fluid balance is essential, specially invasive monitoring (central venous pressure, esophageal Doppler, trans-esophageal echocardiography) guided fluid therapy may be helpful. Arrhythmias must be treated promptly. In our patient, we did not use invasive monitoring as operative duration was short, no arrhythmias, episodes of ischemia, or hypotension occurred intraoperatively.

Taking into consideration the problems related with general anesthesia for such cases, performing the operation under peripheral nerve blocks with or without sedation is a good alternative to general anesthesia. It has the following advantages of offering superb hemodynamic stability in terms of maintenance of cardiac output & systemic vascular resistance, adequate sensory and motor blockade of the limb, less incidence of intraoperative tachycardia and arrhythmias, avoidance of problems related to difficult airway and intubation and decreasing the requirement of supplemental systemic analgesics. Anesthetic toxicity and intravascular injection are the main disadvantages. In our patient, we used PNS guided inter scalene brachial plexus nerve block with 0.5% ropivacaine 30 ml. Regurgitant lesions of aortic, mitral, tricuspid regurgitation can be managed by the maintenance of hemodynamic goals - high normal heart rate, adequate preloading, lowering systemic vascular resistance, lowering pulmonary vascular resistance intraoperatively. Both general and regional anesthesia can be used safely when the regurgitant lesion is the predominant one. Our patient had mild mitral, aortic, tricuspid regurgitation.

Use of regional anesthesia in this asthmatic patient also reduced the risk of perioperative respiratory complications, e.g., bronchospasm.

CONCLUSION

Intraoperative hemodynamic challenges of multiple valvular heart disease patient, perioperative pulmonary complications of an asthmatic patient, perioperative complications of a hypertensive patient, perioperative complications of an elderly patient can easily be avoided if an anesthetist prefers regional anesthesia over general anesthesia for operative management of fracture of bones of arm, forearm and hand.

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Case Report

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Pathology: Myxofibrosarcoma - An Unusual Presentation in a Young Patient

A L Hemalatha[1], Swati Sahni[2], Amita Kumari[2], Tony Joe Peechatt[2]

[1]Professor and Head, Department of Pathology, Adichunchanagiri Institute of Medical Sciences, Mandya, Karnataka, India, [2]Post-graduate, Department of Pathology, Adichunchanagiri Institute of Medical Sciences, Mandya, Karnataka India

Abstract

Myxofibrosarcoma, a low-grade malignant mesenchymal tumor is the myxoid variant of malignant fibrous histiocytoma. It is most commonly seen in the extremities. A primary myxofibrosarcoma is extremely uncommon in young adults. We report a rare case of a 35-year-old female patient with a progressively enlarging soft tissue mass in the gluteal region in whom pathological examination of the resected mass revealed the classic diagnostic features of a low-grade myxofibrosarcoma. The subsequent clinico-radiological examination did not reveal evidence of malignancy in any other location. This case is reported for its rarity of occurrence in the young patient.

Key words: Low-grade, Malignant fibrous histiocytoma, Mesenchymal tumor, Myxofibrosarcoma, Myxoid

INTRODUCTION

Myxofibrosarcoma is a myxoid variant of malignant fibrous histiocytoma (MFH) with characteristic morphological appearance inclusive of nodularity, prominent myxoid matrix, and elongated curvilinear capillaries in the extremities of the elderly.[1-3] The tumor has been categorized into low, intermediate, and high-grade categories based on the degree of cytological atypia and the presence or absence of pleomorphic MFH-like pattern within the tumor by Mentzel *et al.*[3] In their study, low-grade tumors showed mainly myxoid areas with mild cytological atypia in the cellular areas while the high-grade tumors showed a pleomorphic appearance with a high mitotic activity, multinucleated tumor giant cells, and areas of necrosis.[3] Several studies have shown that approximately 80% of these tumors occur in the extremities.[1-3] The peak incidence was observed in the 5th-7th decades with a slight female preponderance.[2,4] We report a soft tissue low-grade myxofibrosarcoma in the gluteal region of a 35-year-old female patient in view of its rarity of presentation in the young patient.

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CASE REPORT

The 35-year-old female patient presented with a painless, progressively enlarging mass in the left gluteal region. Clinical and radiological examination did not reveal any bony involvement. A provisional clinical diagnosis of a soft tissue sarcoma was made, and a wide excision of the mass was performed. The excised mass was submitted for histopathological examination.

Gross Examination Findings

Irregular, unencapsulated, poorly circumscribed, gray-white, nodular mass measuring 9 cm × 6 cm × 3 cm (Figure 1). Cut section - nodular, gray-white with multiple myxoid areas (Figure 2).

Microscopy

Showed the mesenchymal tumor composed of multiple nodules of the spindle to stellate tumor cells amidst prominent myxoid matrix (Figure 3). Individual tumor cells showed scant cytoplasm, irregular, large, and pleomorphic nuclei with prominent nucleoli. Some bi and multinucleated tumor giant cells were also seen. Occasional atypical mitoses were seen. Many curvilinear capillaries with tumor cells aligned around them were seen (Figure 4).

Corresponding Author: Dr. A L Hemalatha, G-3 Sai Brindavan Apartments, 63/64 Industrial Suburb Vishweshwara Nagar, Mysore - 570 008, Karnataka, India. Phone: +91-8453399335. E-mail: halingappa@gmail.com

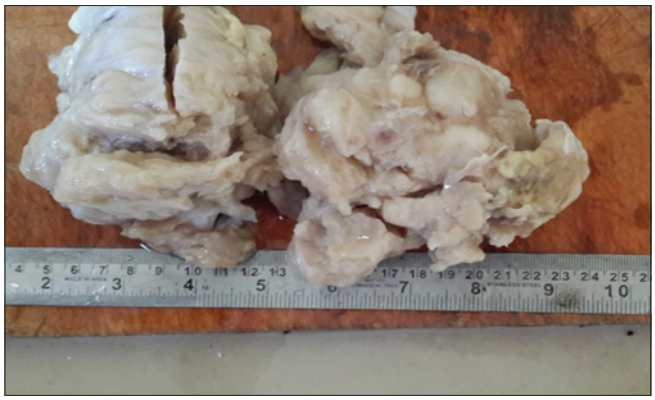

Figure 1: Irregular, unencapsulated, poorly circumscribed, gray-white, nodular mass measuring 9 cm × 6 cm × 3 cm

Figure 2: Cut section - nodular gray-white with multiple myxoid areas

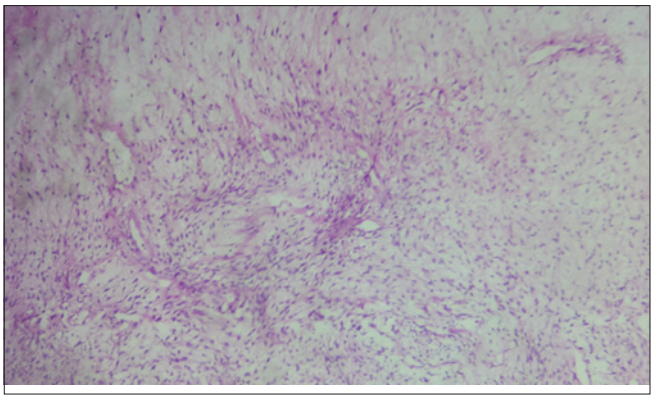

Figure 3: Mesenchymal tumor composed of multiple nodules of spindle to stellate tumor cell amidst prominent myxoid matrix (H and E - ×10)

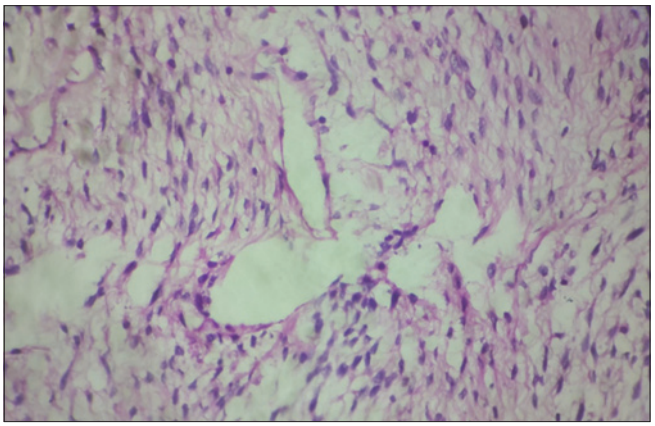

Figure 4: Many curvilinear capillaries with tumor cells aligned around them (H and E - ×45)

Final Diagnosis

Myxofibrosarcoma (low-grade myxoid MFH).

DISCUSSION

Myxofibrosarcoma is one of the frequently encountered soft tissue malignancies in elderly patients mainly seen in the extremities.[5] It belongs to the heterogeneous group of fibrohistiocytic tumors.[3,6-8] It is one of the most aggressive types of soft tissue malignancies with a high risk for local recurrence and a significantly high metastatic rate.[3] The clinical presentation is not pathognomonic thus delaying the diagnosis.

Histologically, myxofibrosarcomas show a spectrum ranging from hypocellular tumors consisting of widely spaced spindle cells amidst myxoid matrix to more cellular variants with pleomorphic nuclei and pseudo lipoblasts.[5]

The presence of curvilinear blood vessels is a consistent morphological feature. Enzinger and Weiss have classified this tumor as the myxoid variant of MFH.[2] Myxofibrosarcoma was first recognized as a distinct entity by Angervall *et al*.[1] It has been accepted as a separate entity and included in the 2002 WHO classification of tumors.[5] The prevalence of myxoid areas defines the lesion of the grade being more prominent in low-grade lesions. Grade II and III tumors have a metastatic potential and are hence recognized as truly malignant in contrast to the Grade I tumor which is just locally aggressive.[3] Metastasis usually occurs in patients with intermittent and high-grade myxofibrosarcoma.[3] However, myxoid fibrosarcoma, irrespective of the grade warrants closes surveillance.

The differential diagnoses of myxofibrosarcoma include all the other myxoid tumors. It is often difficult to distinguish them from each other since the differences are very subtle.[9] Wide resection is the treatment of choice.[3,10] Insufficient tumor-free margins make way for local recurrence and worse prognosis. Due to the high recurrence and metastatic rate in high-grade tumors, adjuvant radiotherapy is recommended. The size of the tumor (smaller than 5 cm versus >5 cm), anatomical location (distally versus proximally located tumors), and histological features (including the degree

of anaplasia and the number of mitoses) also correlate with prognosis.[3,10] A thorough follow-up is advocated to monitor eventual local recurrence.

CONCLUSION

Myxofibrosarcoma may present a diagnostic challenge to the pathologist since it is a close mimic of many other myxoid mesenchymal malignancies, and hence, caution needs to be exercised. Extensive surgical excision with adjuvant radiotherapy is the optimal therapeutic choice.

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Case Report

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Bizarre Parosteal Osteochondromatous Proliferation Arises from Proximal Femur: A Case Report

Jitendra Nath Pal[1], Amiya Kumar Bera[2], Mridul Kanti Biswas[3], Amarendra Nath Roy[2]

[1]Professor, Department of Orthopedics, Murshidabad Medical College, Murshidabad, West Bengal, India, [2]Assistant Professor, Department of Orthopedics, Murshidabad Medical College, Murshidabad, West Bengal, India, [3]Assistant Professor, Department of Pathology, Murshidabad Medical College, Murshidabad, West Bengal, India

Abstract

Bizarre parosteal osteochondromatous proliferation (BPOP) of long bones is extremely rare and often confused with osteochondroma. Careful correlations of clinical, imaging, and pathological findings give the diagnosis. A 17 years male patient presented with a progressive occasionally painful swelling over the lateral aspect of the left proximal thigh of 2 years duration without any history of trauma. The mildly tender, hard bony femoral mass was having lobulated surface. Imaging showed heterogeneously opaque bony mass without medullary canal continuity. Cartilage cap was thin with an irregular surface. During operation cortical surface of the femur was intact. It was covered with thick perichondrium, but the cartilaginous cap was thin. Histopathology demonstrates production of bluish tint cartilage with irregularly arranged chondrocytes of different stages of maturation and lamellar bone with intertrabecular spindle cells without cytological atypia. Appropriate diagnosis of BPOP can only be made when it is clinically suspected, careful radiological evaluation is made. That guides surgeon for meticulous excision to prevent recurrence. Finally, careful histopathological examination confirms the diagnosis.

Key words: Bizarre parosteal osteochondromatous proliferation, Nora's disease, Long bone

INTRODUCTION

Bizarre parosteal osteochondromatous proliferation (BPOP) also known as Nora's disease is a rare condition. It involves small bones of hands and feet.[1] Very few of them develop from long bones.[2] Florid periostitis, Turret exostosis, and BPOP are believed to be different stages of post-traumatic osteochondral proliferation.[1] However the incidence of trauma may be absent in few occasion.[3] Many a time the clinical, radiological and histopathological (HP) features are confused with that of solitary osteochondroma, parosteal osteosarcoma, chondrosarcoma and heterotrophic ossification.[1] Unless meticulously excised it has a strong tendency for recurrence.[3,4]

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This case is being reported not only because of its rarity but careful evaluation of clinical and imaging features give strong suspicion to guide surgeon for meticulous resection to prevent recurrence. Confirmation of diagnosis is obtained after careful HP study. Post-operative counseling and the need for adequate vigilance are also important issues.

CASE REPORT

A 17 years male patient presented to the Outpatient Department of our hospital in October 2013 with a progressive swelling over the lateral aspect of the left proximal thigh of two years duration. It was associated with occasional mild pain which is independent of exertion. Family history and history of trauma are non-contributory. Hard mildly tender non-indurated and lobulated swelling was found over the proximal thigh of size 7 cm and 6 cm in vertical and transverse dimensions, respectively (Figure 1a). It was attached to the bone but free from overlying structures. X-ray shows lobulated bony outgrowth from proximal femoral shaft just distal to greater trochanter and

Corresponding Author: Dr. Jitendra Nath Pal, F - 505, Maitri Apartment, 255, N S C Bose Road, Kolkata - 700 047, West Bengal, India. Phone: +91-919434053474. E-mail: jitendranathpal@gmail.com

directed laterally (Figure 1b and c). In magnetic resonance imaging, the heterogeneous surface was covered with a thick membrane which was non-continuous with shaft periosteum. It did not show any medullary continuity (Figure 2a-c). Under spinal anesthesia operation was done in the lateral position and using vertical lateral incision. After excision of the mass, the intact cortical surface under the bed of the swelling can be seen (Figure 3a). A wound was then closed in layers after achieving hemostasis. Cut surface of the excised specimen showed heterogeneous trabeculations without a medullary cavity (Figure 3b and c). The patient was allowed active movements on day one and permitted weight bearing on the third post-operative day. Stitches were removed at the 14th post-operative day.

HP demonstrates mature bone formation and plenty of spindle cells without evidence of malignancy in the intertrabecular areas with bluish tint cartilage formation with different sized irregularly arranged cartilage cells (Figure 4).

The patient was followed up at 2 weeks, 1 month, and monthly up to 6 months. X-ray at 6 months did not show any recurrence (Figure 5).

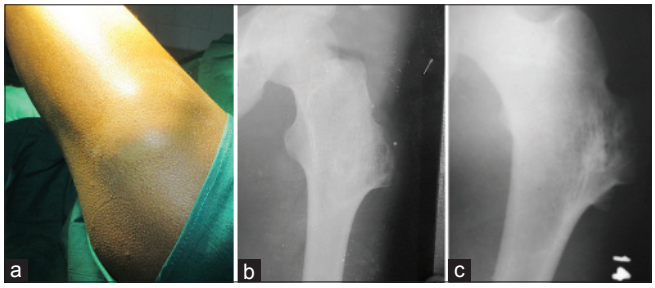

Figure 1: (a) Clinical picture of the lesion over lateral aspect of proximal thigh of left side, (b) X-ray picture in anteroposterior view, (c) X-ray picture in lateral view

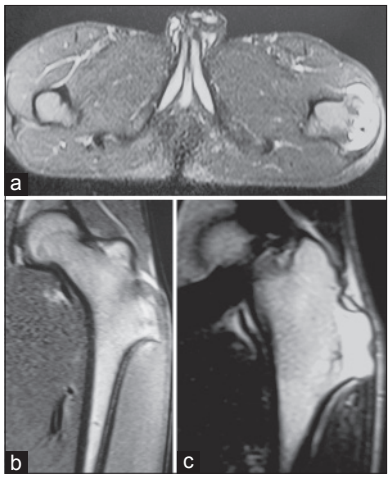

Figure 2: (a) Magnetic resonance imaging (MRI) picture in transverse section, (b) MRI picture in coronal section, (c) MRI picture in coronal section showing junction of intact cortical bone and the mass

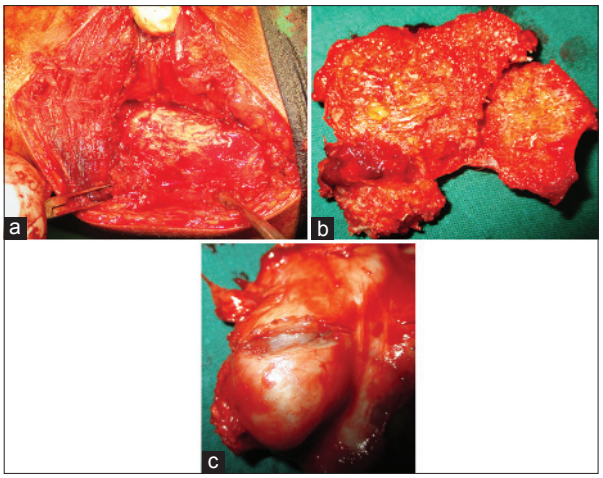

Figure 3: (a) Peroperative picture showing intact cortical surface, (b) excised specimen without medullary canal, (c) specimen showing thick perichondrium but thin cartilage cap

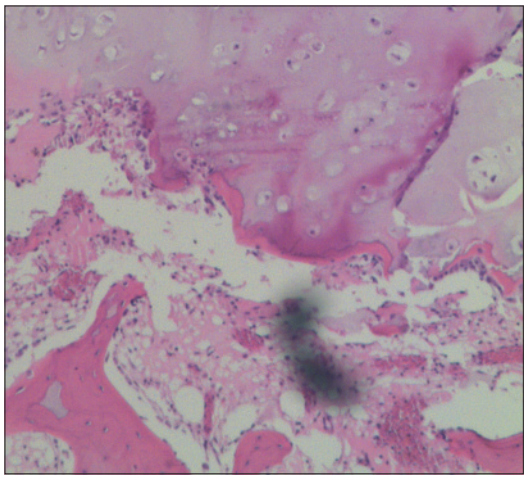

Figure 4: Pinkish bone with intertrabecular spindle cells without evidence of malignancy and cartilage formation at the interface with bluish tint and cartilage cells are irregularly arranged and of different stages of maturation

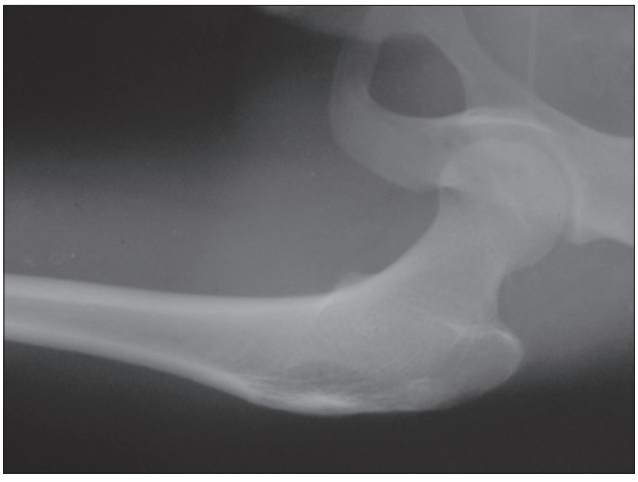

Figure 5: Follow-up X-ray after 1 year without evidence of recurrence

DISCUSSION

The diagnosis, in this case, was based on clinical, imaging, and supported by histopathology. Possibilities, in this case, are non-hereditary solitary exostosis,[5,6] BPOP,[1-4,7,8] Turret exostosis, and florid reactive periosteitis.[9] Myositis ossificans are also excluded in relation to this case.[10] Parosteal osteosarcoma, secondary chondrosarcoma are also confusing at times in histopathology findings.[1]

Non-hereditary solitary exostosis usually presents within the 3rd decade. They are directed toward diaphysis and may have medullary canal is in continuity with that of the parent bone. Metaphyseal osteochondroma is believed to stop growing with skeletal maturity. Hameetman *et al.* demonstrated mutation of tumor gene and also correlated with solitary exostosis. The traditional theory of "skeletal dysplasia" is shifting toward the theory of "cell-of-origin."[5,6] This might be the one explanation of continued growth after skeletal maturity. In this case, radiological findings and specimen examination do not show very thick cartilage cap. HP study distinctly demonstrates irregularly arranged cartilage cells at different stages of maturation which distinctly differ from exostosis.

Adler *et al.* redefined BPOP, also known as Nora's lesion, as the proliferation of bone and usually emanates from the intact cortical surface of short bones and rarely in long bones.[2] It is assigned to be reactive heterotrophic ossification. Though generally correlated with trauma, few authors denied it and genetic mutation supposing tumor genesis has been recently suggested.[3] Usual age group of the sufferer is in the 3rd or 4th decades.[7] In the early stage, cortical continuity may not be there but ultimately develops it. In some series there is some male preponderance.[4] Imaging in most occasions resembles sessile variety exostosis. BPOP apparently arises from the periosteal tissues through a process of cartilaginous metaplasia. Microscopically, it is composed of hypercellular cartilage with calcification with basophilic tintorial character and ossification with pinkish appearance.[8] Cancellous bone undergoes maturation and presence of bizarre spindle cells in the intertrabecular space creates confusion with parosteal osteosarcoma but, in this case, they are without cytologic atypia.[1] There is thinning of cartilage cap in long-standing cases. These features are similar to the present case. 50% local recurrence is reported in the literature.[3] This patient did not have recurrence in early follow-up. Secondary chondrosarcoma is not a possibility in this case as there was no primary lesion and HP features are not in its favor.

LeClere *et al.* believe Turret exostosis and florid reactive periostitis are benign osteo-cartilaginous lesions arise from reactive periosteum following relatively mild trauma.[9] Microscopically, the central area of mature bone from endochondral ossification characterized by thin hypocellular peripheral rim of cartilage and absence of periosteum over the surface. No history of trauma can be obtained in this case.

Myositis ossification develops in more peripheral from bone and ossification starts from periphery to center.[10]

CONCLUSION

As biopsy is not usually done prior to excision, a careful clinico-radiological examination creates strong suspicion for the diagnosis of BPOP for an atypical variety of bony outgrowth arising from short and ends of the long bones. This suspicion is important as BPOP has a strong tendency for recurrence, unlike solitary exostosis. Meticulous resection can minimize the chance of recurrence.

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Case Report

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Vitreomacular Traction Causing Idiopathic Full-Thickness Macular Hole Determined By Spectral-Domain Optical Coherence Tomography

Vijay Kumar Srivastava[1], M Shivakumar[2], Pratik Kataria[3], Vandana Parasar[3]

[1]Professor and Head, Department of Ophthalmology, Rajarajeswari Medical College and Hospital, Bengaluru, Karnataka, India, [2]Professor, Department of Ophthalmology, Rajarajeswari Medical College and Hospital, Bengaluru, Karnataka, India, [3]Postgraduate Student, Department of Ophthalmology, Rajarajeswari Medical College and Hospital, Bengaluru, Karnataka, India

Abstract

Macular holes commonly occur as an age-related primary idiopathic condition, not associated with other ocular problems or antecedent events. The primary mechanism for idiopathic macular hole formation is the dynamic vitreofoveal traction caused by a perifoveal posterior vitreous detachment (PVD). A 56-year-old woman presented with diminution of vision and metamorphopsia in the left eye. The anterior segment examination was normal in both eyes. A dilated fundus evaluation of the left eye showed a small full-thickness macular hole (FTMH) with cystoid foveal thickening. The optical coherence tomography (OCT) showed a stage 2 small FTMH with vitreomacular traction. Amsler grid showed a central distortion while Watzke-Allen test was positive. An FTMH is a common cause for impairment of central vision. The clinical symptoms include diminution of central vision, metamorphopsia, photopsia, and micropsia. OCT is important for the assessment of extent, progression, and resolution of macular holes. The stage 1 impending macular holes are observed, as they have a better chance for spontaneous closure. The stage 2 or greater FTMHs, with a smaller chance of spontaneous closure, are treated with pars plana vitrectomy with internal limiting membrane peeling. Recently, intravitreal injection of ocriplasmin has been used for pharmacological induction of PVD.

Key words: Fovea centralis, Macula lutea, Optical coherence tomography, Retinal diseases, Retinal perforations, Visual acuity, Vitreous body, Vitreous detachment

INTRODUCTION

The clinical spectrum of a vitreomacular interface disease includes vitreomacular adhesion (VMA), vitreomacular traction (VMT), macular epiretinal membrane (ERM), full-thickness macular hole (FTMH), lamellar macular hole, and macular pseudohole.[1]

The idiopathic macular hole was recognized as a unique clinical entity more than a century ago.[2] Macular holes commonly occur as an age-related primary idiopathic condition, not associated with other ocular problems or antecedent events.[3] The tangential traction of an attached prefoveal vitreous cortex, causing foveolar detachment and dehiscence, has been hypothesized to cause a macular hole.[4]

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The optical coherence tomography (OCT) is a decisive tool in the evaluation of the extent of VMA or traction in a case of an idiopathic macular hole, as clinical examination alone may not be sufficient.[5] This case emphasizes the importance of OCT examination in the determination of the diagnosis and the etiology of an idiopathic macular hole.

CASE REPORT

A 56-year-old woman presented with complaints of gradual, painless, progressive diminution of vision and metamorphopsia in the left eye since 5 months. On presentation, her best-corrected visual acuity was 6/60 in the left eye and 6/6 in the right eye.

Any history of trauma or ocular inflammation before the onset of symptoms was absent. No history of any systemic

Corresponding Author: Dr. Pratik Kataria, Department of Ophthalmology, Rajarajeswari Medical College and Hospital, Bengaluru, Karnataka, India. Phone: +91-9731915381. E-mail: prakat256@gmail.com

disorder was present. Gross examination of both eyes was unremarkable. Facial symmetry and ocular posture were maintained. The anterior segment examination was normal in both eyes. Intraocular pressure in both eyes was found to be within normal limits.

A dilated fundus examination of the left eye showed a small FTMH with cystoid foveal thickening (Figure 1). Rest of the fundus examination in the left eye was normal. The high-resolution spectral-domain OCT of the macula in the left eye showed a stage 2 small FTMH with VMT, along with foveal thickening and intraretinal cystic changes (Figure 2). The inner retina shows a slightly eccentric dehiscence with a centrifugal displacement of the photoreceptor layer. Amsler grid showed a central distortion while the Watzke-Allen test was positive in the left eye.

The fundus examination in the fellow eye was normal with no evidence of a vitreoretinal interface disease. A diagnosis of stage 2 FTMH with VMT in the left eye was achieved. Surgical intervention with pars plana vitrectomy and internal limiting membrane peeling was offered, but the patient elected to wait and observe for spontaneous resolution.

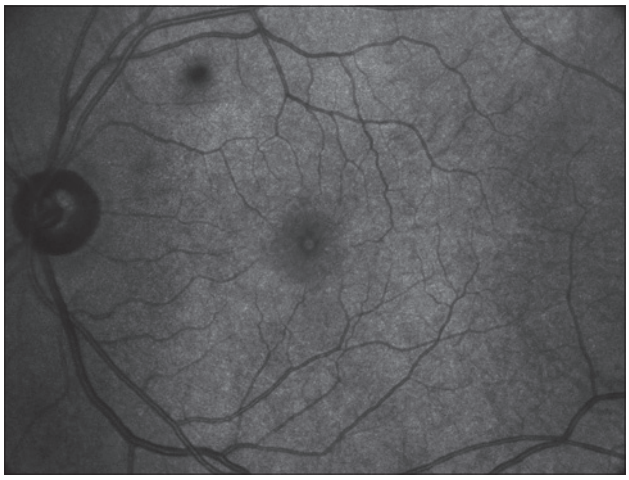

Figure 1: A red-free fundus photograph of the left eye showing a small full-thickness macular hole with cystoid foveal thickening

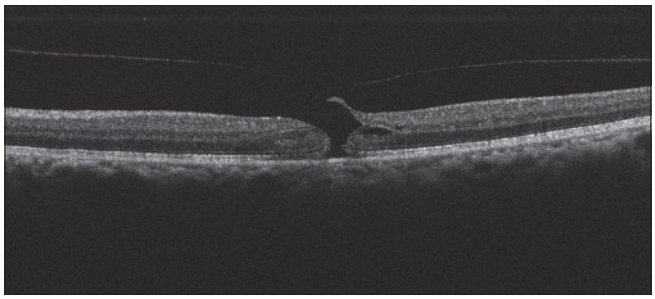

Figure 2: High resolution spectral-domain optical coherence tomography of the macula in the left eye showing a stage 2 small full-thickness macular hole with vitreomacular traction, along with foveal thickening and intraretinal cystic changes

DISCUSSION

An FTMH is a relatively common cause of impairment of central vision, most commonly occurring in females aged 60-70 years.

In eyes with accelerated vitreous liquefaction before sufficient weakening of the vitreoretinal adhesion, posterior vitreous detachment (PVD) may lead to serious complications. High-resolution imaging of the vitreoretinal interface has allowed identification of an association between PVD and the early stages of idiopathic macular hole.[6] This has led to a hypothesis that the primary mechanism for idiopathic macular hole formation is the dynamic vitreofoveal traction caused by a perifoveal PVD.[7]

Idiopathic macular hole occasionally develops in eyes with pre-existing spontaneous or surgical PVD, which may be suggestive of alternative mechanisms of macular hole formation such as primary degeneration of inner retinal layers at the central fovea.[8] However, the traction-induced foveal disruption occurring before or coincident with the vitreofoveal separation may lead to inner foveal damage with destabilization of the outer foveal layer.[7]

FTMHs are commonly classified into four stages:[4]

- Stage 0: VMA.
- Stage 1a: "Impending" macular hole with VMT.
- Stage 1b: "Occult" macular hole with VMT.
- Stage 2: "Small" FTMH ≤400 μm in diameter with VMT.
- Stage 3: "Full-size" FTMH >400 μm in diameter with VMT.
- Stage 4: Includes full-size FTMH with complete PVD.

The clinical symptoms of VMT include slowly progressive diminution of central vision, metamorphopsia, photopsia, and micropsia, which may not correlate with clinical findings.[1] The signs of VMT can be observed clinically with slit lamp biomicroscopy, ultrasonography, and OCT.[9] The spectral-domain OCT is an important tool for assessment of extent, progression, and resolution of macular holes. It yields valuable information regarding the ultrastructural changes at the vitreomacular interface and within the retinal layers.[5]

The stage 1 impending macular holes are observed and not treated surgically, as they have about a 50% chance for spontaneous closure with resolution of symptoms.[10] Spontaneous resolution with restoration of the normal foveal contour in other cases of FTMH (stage 2-4) is very rare, occurring only in 2-4% of eyes, probably secondary to ERM formation.[11] The spontaneous resolution of VMT is more likely in the eyes with less vitreous surface adhesion and without ERMs.[5]

Multiple mechanisms have been proposed for the spontaneous resolution of a macular hole, including release of traction following complete detachment of the posterior hyaloid from the foveal area, formation of a contractile ERM causing closure by shrinkage, bridging of the retinal tissue across the macular hole, and proliferation of cells at the base of the macular hole.[12]

The Müller cells may play an initial role in the spontaneous closure of an FTMH with the restoration of the outer retina as the photoreceptors themselves cannot proliferate.[2] The centripetal traction-induced by the extension and proliferation of Müller cells may facilitate adhesion of other disrupted retinal layers including the IS/OS junction.[2] The astrocytes which are present in the inner retina may also be implicated in the process of spontaneous closure, as they are also known to participate in the formation of retinal glial scars.[2]

The stage 2 or greater FTMHs, with a small chance of undergoing spontaneous closure, are treated surgically by a pars plana vitrectomy with or without internal limiting membrane (ILM) peeling.[3] Surgical intervention is usually required in eyes with a larger vitreous surface adhesion or a coexisting ERM.[13]

For many years, researchers have been investigating pharmacological tools to induce a complete PVD.[14] Recently, intravitreal injection of ocriplasmin, a recombinant form of human plasmin, has been used as a monotherapy as well as an adjunct to surgical vitrectomy.[15] It has been found to cause resolution of VMT with closure of macular hole in over 25% of the eyes, but the results are generally inferior to surgical vitrectomy.[16]

CONCLUSION

- The idiopathic macular hole represents a complication of a slowly evolving early stage of an age-related PVD.
- An OCT examination is obligatory to study both the progression and resolution of macular holes, except in straightforward cases.
- Follow-up using OCT examination enables monitoring for a spontaneous closure in early cases so that a complex surgery may be avoided. However, the risk of observation versus surgery should be explained to the patient.
- Surgical intervention with pars plana vitrectomy with ILM peeling may be considered for advanced cases, especially in cases with a larger vitreous surface adhesion or a coexisting ERM.

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Dr. Ganesh Sathyamurthy. MS, Vitreoretinal Surgeon (Consultant), Rajarajeswari Medical College and Hospital, Bengaluru, Karnataka, India.

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Case Report

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Systemic Lupus Erythematosus in Pregnancy with Secondary Anti-Phospholipid Antibody Syndrome

K Vishwanath[1], Sanjay Kulkarni[2], N G Ashwini[3], Jolly Anil John[4]

[1]Associate Professor, Department of Medicine, MS Ramaiah Medical College, Bengaluru, Karnataka, India, [2]Professor and Head, Department of Medicine, MS Ramaiah Medical College, Bengaluru, Karnataka, India, [3]Post-graduate Student, Department of Medicine, MS Ramaiah Medical College, Bengaluru, Karnataka, India, [4]Assistant Professor, Department of Medicine, MS Ramaiah Medical College, Bengaluru, Karnataka, India

Abstract

Systemic lupus erythematosus (SLE) is a multisystem autoimmune disease. The clinical spectrum of SLE ranges from benign to a very severe life-threatening illness. It is characterized by an autoantibody response to nuclear and cytoplasmic antigens. SLE can affect any organ system, but it mainly involves the skin, joints, kidneys, blood cells, and nervous systemwe are presenting this case of SLE with anti-ds DNA negative, coombs test negative with severe thrombocytopenia , with secondary APLAin a pregnant women. Thus we are presenting this case of SLEin a pregnant women with anti-ds DNA Negative, coombs test negative with severe thrombocytopenia ,with secondary APLAwhich is not usual.

Key words: Antiphospholipid antibodies syndrome, Lupus hematological flare, Pregnancy, Systemic lupus erythematosus

INTRODUCTION

Systemic lupus erythematosus (SLE) is a multisystem autoimmune disease, characterized by an autoantibody response to various nuclear and cytoplasmic antigens Systemic lupus erythematous affects women of childbearing age and is associated with higher and fetal and maternal risk compared to pregnancy in healthy women. Association of Antiphospholipid syndrome and unexplained fetal death has been explained in women who had two or more pregnancy losses.

CASE REPORT

A 19-year-old female in 23 weeks of gestation was referred to us by her obstetrician with a history of diffuse petechial rashes, easy fatigability, occasional epistaxis, with the previous history of spontaneous pregnancy losses at 6 and 8 weeks, respectively, suspecting immune thrombocytopenia. At admission, her hemoglobin was 4.3 g%, platelet count of 2000. Obstetric scan confirmed a single live intrauterine fetus with fundic placental placement.

Lab parameters showed iron deficiency and Vitamin B12 deficiency anemia (serum iron = 22, total iron binding capacity = 404, transferrin saturation = 5.4%, serum ferritin = 7. 66 Vitamin B12 = 98) with severe thrombocytopenia. Peripheral smear picture showed microcytic hypochromic anemia with a moderate degree of anisopoikilocytosis; pencil shaped and tear drop cells with normal distribution and number of white blood cells with severe thrombocytopenia. Bone marrow study revealed norm cellular bone marrow aspirate with adequate cell trait, increase in a number of megakaryocytes.

Bone marrow aspirate however showed? Hypocellular with few islands of megakaryocytic series. ANA-IF was strongly positive (+++) with a speckled pattern. ANA profile was strongly positive (+++) for SS-A native (60 k Da), Ro - 52 recombinant, and positive (+) for SS-B. APA (phospholipid) –IgM was positive(titer =13.23 MPL U/ml). Titre of ds-DNA was negative in the ANA profile. Both indirect and direct coombs test was negative.

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Corresponding Author: Dr. K Vishwanath, No 598, 2nd Main 2nd Stage E Block Rajajinagar, Bengaluru, Karnataka, India. Phone: +91-9632611288. E-mail: vishu_ani@yahoo.com

With the above presentation a diagnosis of SLE with? Secondary ANTI-PHOSPHOLIPID ANTIBODY SYNDROME, in G_3A_2 23 weeks ofpregnancy was made. Pulse therapy with high dose methylprednisolone was started. Improvement in her platelet count was seen. Immunologist opinion was sought and advised to continue methylprednisolone pulse therapy for total of 3 days.Therapy option with IV-Ig was also offered to the patient but was deferred in view of cost factor and unwillingness of the patient attenders. Rheumatologist opinion sought, advised to switch over to oral prednisolone at dose of 1 mg/kg body weight/day. A dose of 50 mg per day in 3 divided doses was started. Improvement in platelet count was maintained. Planned to taper the dose of prednisolone by 5 mg/week if target thrombocyte count above 1 lakh was maintained. Was also advised to start tab hydroxychloroquine 200 mg, po , bid dose.Low molecular weight heparin therapy was also started in view of APLA syndrome and the patient' s decision of continuation of pregnancy. Patient was discharged with advice to continue hydroxychloroquine, LWMH, prednisolone oral therapy with regular follow-up with weekly platelet count, regular ANC visits..

DISCUSSION

Systemic lupus erythematosus is an autoimmune connective-tissue disorder with a wide range of clinical features, which predominantly affects women[1] The clinical spectrum of SLE is wide and ranges from benign easily treated disease with rash, arthritis, fatigue, to a very severe life threatening illness with progressive irreversible damage. The course of the disease is variable and is characterized by flares of rampant inflammation that can threaten, in an unpredictable manner, almost any organ in the body Flare can be considered as a reappearance of clinical features which were earlier quiescent. Subtle abnormalities in hematological, cardiac and central nervous system (CNS) clinical, lab parameters and imaging occur either isolated or in combination which help to diagnose flare at an early stage Hematologic disease. In particular thrombocytopenia, is also commonduring pregnancy, with the risk ranging from 10% to 40% in different cohorts.Thrombocytopenia is a major haematological complication in patients with systemic lupus erythematosus (SLE) The pathogenesis of thrombocytopenia in SLE patients is heterogeneous, but the most common mechanism is believed to be increased platelet clearance mediated by anti-platelet autoantibodies, which is analogous to the mechanism seen in patients with idiopathic thrombocytopenic purpura (ITP). Other potential mechanisms include thrombotic thrombocytopenic purpura, disseminated intravascular coagulation, haemophagocytic syndrome, antiphospholipid syndrome and impaired thrombopoiesis3In this case as coombs test was negative, but thrombocytopenia was severe which was unusual as such severe thrombocytopenias are seen usually with lupus flare. Effect of pregnancy on SLE flares usually occur during the last half of pregnancy3 and within the first few weeks after delivery. In this case presented the hematologic manifestations of SLE occurred in first trimester and was associated with APLA positive disease. A few studies have shown decreased ds DNA levels during flare4 Even in this case anti ds DNA was negative but with coombs test negative and normal LDH a diagnosis of hematological flare was not possible.

CONCLUSION

Thus we are presenting this case of SLE in a pregnant women with anti-ds DNA NEGATIVE, coombs test negative with severe thrombocytopenia, with secondary APLA which is not usual.

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Case Pictorial

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Post-traumatic Bilateral Abducens Nerve Palsy: A Case Report

S Pallavi Reddy[1], M R Pujari[2], Vishwanath Reddy[3], Santosh Patil[4]

[1]Post-graduate Student, Department of Ophthalmology, M R Medical College, Gulbarga, Karnataka, India, [2]Professor and Head, Department of Ophthalmology, M R Medical College, Gulbarga, Karnataka, India, [3]Professor, Department of Ophthalmology, M R Medical College, Gulbarga, Karnataka, India, [4]Associate Professor, Department of Ophthalmology, M R Medical College, Gulbarga, Karnataka, India

The incidence of unilateral abducens nerve palsy has been reported to be as high as 1-2.7% of head trauma cases, bilateral abducens nerve palsy following trauma is extremely rare.[1,2] In literature, bilateral abducens nerve palsy is said to also occur by increased intracranial pressure, dural puncture, whiplash injury, hangman's fracture and halo traction. The mechanism for bilateral 6th cranial nerve palsy in this patient is controversial. Physical examination and appropriate imaging tests such as high resolution computed tomography (CT) or magnetic resonance imaging can usually identify the cause of a traumatic gaze palsy, but they did not do so in this case.[3,4]

A 50-year-old female involved in a case of road traffic accident who sustained a head injury - A 4 cm lacerated wound over the left side of the forehead which was sutured at a primary center. CT scan of the head showed fracture of the left frontal bone involving the lateral wall of the orbit and no other lesions in the brain. She complained of diplopia in primary gaze and was referred to the ophthalmology department. On examination, her visual acuity was normal. Apart from minimal sub-conjunctival hemorrhage in the left conjunctiva anterior segment of both her eyes was normal, as were the fundi. There was misalignment of the visual axis with bilateral esotropia and restriction of the ocular movement of both the eyes laterally. Bilateral trigeminal and facial nerves were found to be normal. The forced duction test was positive, and the diagnosis of bilateral abducens/sixth cranial nerve palsy was made [Figures 1-3]. She was managed conservatively and was asked to follow-up after 1 month. Her 1 and 2 months follow-ups revealed no change in the clinical picture. She was later lost to follow-up.

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Figure 1: Misalignment of visual axis on upgaze

Figure 2: Misalignment of visual axis on primary gaze

Corresponding Author: Dr. S Pallavi Reddy, Department of Ophthalmology, Basaveshwar Teaching and General Hospital, Gulbarga, Karnataka, India. Phone: +91-944036770. E-mail: pallavi_sanamreddy@hotmail.com

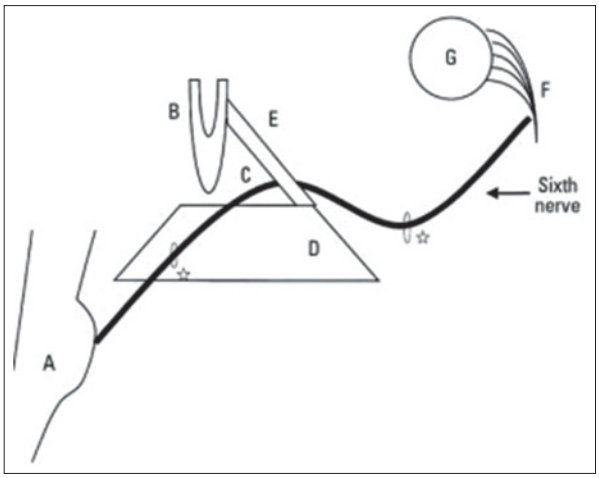

Figure 3: Schematic diagram of the course of the sixth cranial nerve from the pons (A) to the lateral rectus muscle (F). The nerve ascends over the petrous bone (D) and under Gruber's ligament (E) as it passes through Dorello's canal (C). The nerve is tethered by dura before and after the canal (stars). Injury to the peripheral nerve is thought to occur by contusion against the petrous ridge after midfrontal head impact. B: Posterior clinoidal process, G: globe

Points to Ponder

The differential diagnosis for traumatic lateral gaze palsy includes brain stem lesion such as diffuse axonal injury, peripheral nerve injury with or without basilar skull or cervical fracture, and lateral rectus muscle injury or entrapment.

- The abducens nerve is the most susceptible cranial nerve to trauma, because of its long intra cranial course. Anatomically, abducens nerve consists of intracisternal, intra cavernous and intra orbital parts.

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Case Pictorial

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Locked Acute Vertical Patellar Dislocation in Background of Ligamentous Laxity: A Rare Presentation

Kanailal Jana[1], Atanu Chatterjee[2], Dipak kumar Jha[3]

[1]Residential Surgeon, Department of Orthopaedics, Ramakrishna Mission Seva Pratisthan, Kolkata, West Bengal, India, [2]Post-Graduate Trainee, Department of Orthopaedics, Ramakrishna Mission Seva Pratisthan, Kolkata, West Bengal, India, [3]Visiting Surgeon and Professor, Department of Orthopaedics, Ramakrishna Mission Seva Pratisthan, Kolkata, West Bengal, India

When the femur rotates internally and the tibia externally with the foot fixed on the ground, the patella may dislocate almost always occurs in the lateral direction.[1] Usually, acute dislocation of patella managed with closed reduction by extension of flexed knee along with pressure applied to the lateral aspect of dislocated patella and maintained by plaster cylinder applied from groin to ankle for 4-6 weeks.[2] Cash and Hughston[3] divided acute dislocation of patella into two groups. In the first group, the patients showed anatomic predisposition to patellar instability, e.g. lateral hypermobility of patella and dysplasia of vastus medialis muscle and in the second group no predisposing factor. The stabilizing role of the medial patellafemoral ligament has been emphasized with cadaver studies demonstrating that this ligament is responsible for >50% of the lateral restraining force of the patella.[4] Vertical dislocation is termed when dislocated patellar articular surface faces lateral or medial, suggesting rotation along vertical axis.[5]

A 14-year-old girl with generalized joint laxity (Figure 1) presented with acute right patella dislocation on January 2014 at casualty in RKMSP. She had twisting injury of right knee during her bath. X-ray right patella dislocated laterally with 90° rotated (Figure 2). Reduction attempted within 4 h under spinal anesthesia but failed. Next day open reduction done. Medial patella-femoral ligament found to be torn (Figure 3). Patellar dislocation was reduced, and rotation was corrected. Small osteochondral fragments were removed. Medial soft tissue plication and

Figure 1: Generalized ligamentous laxity

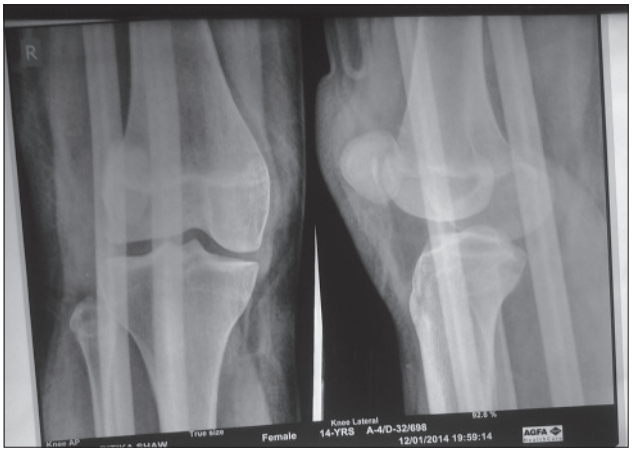

Figure 2: Radiologically dislocation of the patella showing rotational malalignment

reinforcement done with 3-0 proline sutures. Post-operative X-rays showing good alignment (Figure 4). Guarded knee movement started 3 weeks later. Now 12 months follow-up she had a good range of motion of the knee and no

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Corresponding Author: Dr. Kanailal Jana, 88 Hostel, Ramakrishna Mission Seva Pratisthan, 99 Sarat Bose Road, Kolkata - 700 026, West Bengal, India. E-mail: drkanai.jana@gmail.com

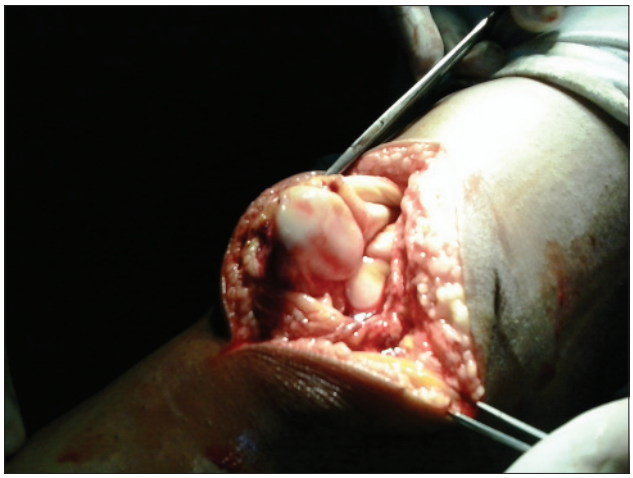

Figure 3: Operative photograph showing tear of the collateral ligament

Figure 4: Post-operative (6 months) X-ray showing good radiological reduction

recurrence of dislocation (Figure 5). She had similar left patella dislocation on May 2012 and managed by closed reduction. No history of recurrent left patellar dislocation.

Points to Ponder

1. Dislocations along with rotational components are very difficult to reduce by closed method, and they are usually associated with the osteochondral injury. Some authors recommended primary open reduction in cases where rotational components are suspected, to reduce chance of further chondral injuries during repetitive reduction maneuvers.[6]
2. Here, in this case, the patella rotates more than 90° along its vertical axis and locked in the lateral parapatellar gutter. Very limited data are available about similar presentation.

Figure 5: Post-operative photograph showing good clinical outcome at follow-up at 1 year

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Case Pictorial

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Reconstruction of the Hemi Maxillectomy Defect Using a Flexible Obturator

M Khaja Khalid Nawaz

Oral and Maxillofacial Surgeon, Department of Oral and Maxillofacial Surgery, Dr. H. Gordon Roberts Hospital, Shillong, Meghalaya, India

A male patient of 28 years reported to our dental outpatient department with difficulty in chewing, speech and oro-nasal communication. He was operated for mucoepidermoid carcinoma of left maxilla. Hemi-maxillectomy was done 1 year back. Initially, we planned for a temporary obturator without teeth for 3 months, once he got adapted to the obturator. A new impression was made again, and a flexible prosthesis with flexible clasps was constructed. The patient was called for follow-up once in 2 weeks. The prosthesis provides an excellent retention and mastication was also improved followed by no hypernasal speech and no oro-nasal communication (Figures 1-3).

A prosthesis used to close a palatal defect in a dentate or edentulous mouth is referred to as an obturator. The obturator prosthesis is used to restore masticatory function, improve speech, deglutition, and cosmetics for maxillary defect patients. Post-surgical maxillary defects predispose the patient to hypernasal speech, fluid leakage into the nasal cavity, and impaired masticator function.[1] The goals of prosthetic rehabilitation for total and partial maxillectomy patients include separation of oral and nasal cavities to allow adequate deglutition and articulation, possible support of the orbital contents to prevent enophthalmos and diplopia, support of the soft tissue to restore the midfacial contour, and acceptable aesthetic results.[2]

Lack of retention, stability and support are common prosthodontic treatment problems for patients who have had a maxillectomy.[2] The structures in the remaining maxilla amenable to providing obturator retention are limited to the remaining natural teeth and the borders of the defect. So to overcome these problems, rather than making an acrylic obturator. The best choice is to make a flexible obturator prosthesis which provides an excellent retention, support and stability.[3]

Figure 1: Maxillary defect

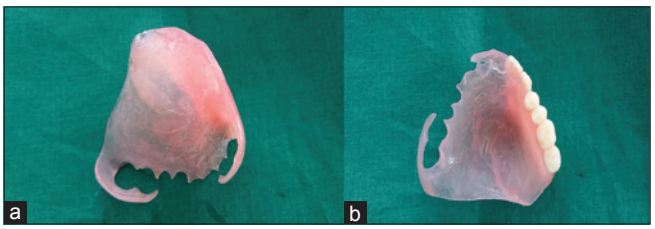

Figure 2: Flexible prosthesis with clasps. (a) Superior view. (b) Inferior view

Figure 3: Patient wearing prosthesis

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Corresponding Author: Dr. M Khaja Khalid Nawaz, Hospital Quarter's, Dr. H. Gordon Roberts Hospital, Jaiaw, Eastkhasi Hills, Shillong, Meghalaya, India. Phone: +91-9952654408/9444433030. E-mail: khalidnawazm@yahoo.com

Points to Ponder

1. Stability is the resistance to prosthesis displacement by functional forces. Flexible prosthesis provides a good retention and support in areas of the residual maxilla.
2. Depending on the location of the line of palatal resection, there will be varied degrees of undercut along this line into the nasal or paranasal cavity. The objective of prosthesis extension is to provide resistance to vertical and horizontal displacement.[4]

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Case Series

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Bull Horn Injuries in Rural Area: A Case Series

Sanjeev R Kulkarni[1], Sangeeta B Biradar[2], Basavaraj K Nagur[2], Mahesh Reddy[2], Jignesh K Savsaviya[2]

[1]Professor, Department of Surgery, Krishna Institute of Medical Science University, Karad, Maharashtra, India, [2]Resident, Department of Surgery, Krishna Institute of Medical Science University, Karad, Maharashtra, India

Abstract

Bull gore injuries are among the most common accidents in rural India, where people make their living rearing the livestock. The most common site of injury in bull gore cases is the abdomen and perineal region. The reason for perineal involvement is its anatomical configuration. Injuries involving the perineal region pose a great challenge in management due to poorly understood anatomy and difficulty in accessing the injury site. We are here presenting different series of cases of bull gore injury in the rural setup in India. Management of bull gore injury is a challenge and surgeon needs to assess the injury and take a call on the type of management. Furthermore, a surgical repair of the injury is also difficult because of the complex anatomy and the less accessibility. So needs to be taken into consideration.

Key words: Axillary injury, Penetrating injuries, Perineal injury

INTRODUCTION

Bull gore injuries are among the most common accidents in rural India, where people make their living rearing the livestock. The injuries thus sustained include the direct penetrating injuries caused by horns of the animal and blunt injuries sustained like chest and spine injuries, long bone fractures. A thorough head to toe examination is, therefore, essential in evaluating such patients. The most common site of injury in bull gore cases is the abdomen and perineal region. The reason for perineal involvement is its anatomical configuration. Injuries involving the perineal region pose a great challenge in the management due to poorly understood anatomy and difficulty in accessing the injury site. Perineal injuries are associated with delayed complications like anovaginal fistula, urethrorectal fistula, loss of sphincter function due to injury to the anal canal.

CASE SERIES

Case 1

A 65-year-old male came to the casualty with A/H/O injury to the chest by the bull gore early in the morning. The patient was conscious oriented with pulse rate (PR)-80/min and blood pressure (BP)-110/80 mmHg and on examination he had laceration over the chest about 4 cm × 2 cm and surgical emphysema with crepitus on the right side of the chest and chest X-ray was done; there were rib fractures on the right side with surgical emphysema and pneumothorax on the same side. The patient was managed with intercostal drainage tube (ICDT) insertion on the right side and strapping for rib fracture. ICDT was removed after 6 the day and patient was discharged after 2 days.

Case 2

A 35-year-old male came to casualty with A/H/O injury by bullhorn to the axillary region shown in Figure 1. While milking the cow has hit him with his horn. He presented with stab injury to the left axilla around about 2 inches deep in the axilla with no active bleeding, pulsations of the limb were normal, no vascular injury observed and the wound closed in layers with a corrugated drain. The patient was discharged after 5 days and followed up in the outpatient department wound healed well and sutures removed on 12 post-operative day.

Case 3

A 55-year-old male presented to casualty with history of trauma by a bull, while he was putting a fodder early in the morning the bull has hit him he fell down and bull walked on him, followed by this he developed pain in abdomen and shown to a local practitioner at midnight came to our hospital casualty. On examination, pt was conscious oriented with PR-88/min, BP-120/80 mmHg, P/A- tender

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Corresponding Author: Dr. Basavaraj K Nagur, Department of Surgery, Krishna Institute of Medical Science University, Karad, Maharashtra, India. Phone: +91-9404234054. E-mail: sachin.nagur@gmail.com

with guarding and BS present with no external injury, X-ray was taken which shown air under diaphragm signs of pneumoperitoneum, patient was investigated and explored, on exploration we found through and through transaction of jejunum 15 cm apart with mesenteric tear. Managed with through wash and end to end open resection anastomoses. On day 6, orally started and has been discharged on day 12.

Case 4

A 66-year-old male came to casualty with history of injury to the left iliac fossa by a bull horn with an external stab injury around about 6 cm × 2 cm shown in Figure 2. On examination, the patient was vitally stable with tenderness at the site of injury and no active bleeding. X-ray erect abdomen: WNL, ultrasound: As there was an external injury patient was explored and found a colonic sigmoid colon serosa tear through wash was given and both the wound closed. On the 6th post-operative day patient had leak from the suture site and the drain site waited for 2 days and patient was re-explored found that there was a perforation of sigmoid colon at the site of serosa tear, perforation closed sigmoid double barrel colostomy done and both the wound closed.

Orally started after 48 h. Patient has been discharged after 14 post-operative day.

Case 5

A 38-year-old female admitted to OBGY department with h/o cow horn injury to the perineal region with perineal tear, involving external genitlia and the anal region. On examination, patient was conscious oriented with PR-100/min and BP of 110/80 mmHg, with avulsion injury to the vaginal region. The patient was immediately rushed to operation theater for examination under anesthesia and further management. Through and through vaginal injury was present through wash given and reconstruction of vaginal injury done with perianal area reconstruction patient has to undergo exploratory laparotomy with transverse loop colostomy. The patient tolerated the procedure well and had been discharged 10 post-operative day with a functioning colostomy and the healthy perineal wound.

Figure 1: Injury by bull horn to the axillary region

Figure 2: injury to the left iliac fossa by a bull horn

DISCUSSION

In India, bull gore injuries are frequently observed in the rural setup were frequently people come in contact with these animals. The horn of bull is long, curved directed forward with smooth tapering ends that produce lacerations and can also penetrate the body cavities.[1,2]

But bull horn injuries of the vulva and the vagina are rare, as the perineum is ahighly protected region due to the reflex adduction of the thigh. But the rich vascular area may be easily damaged.[3] Goring is taken when the bullhorn penetrates deeply in the muscles as well as body cavities.[4] Goring is also described as a single injury which includes a mix of lacerated wound, contusion and infection by many researchers. Thus, wounds produced due to bull horn impact vary from contusions, lacerations, and penetrating wounds involving internal organs to fractures.[4]

The patterns of injuries sustained by the victim vary depending on the height of the victim, the height of the bull and position of the animal and the victim at the time of the attack by the bull. The injuries occur a more common on the abdomen and perineum.[1,2,5,6] In the abdomen, the horn first enters the skin and subcutaneous tissues and later muscles and further if the violence is more, the peritoneum is punctured with the involvement of viscera with tear.[2]

As the head of bull and the victim's abdomen is at the same level, this part of the body is most exposed to the attack. Although the surface area of abdomen is same as

that of the chest, the abdomen suffers more commonly injury with more severity than any other site. This appears dueto lack of bony shield over the abdomen permitting the horn to hook to engage and penetrate.[5] These injuries can be in the form of perforations of abdominal wall, and internally hemorrhages and perforations involving mesentery and bowels.[1,7] Visceral injuries involving spleen and more frequently liver being situated on right region of the body are commonly encountered.

Many times impact by the bull or other cattle involves the thoracic region of the body. Atri and Mehdiratta[8] in an analysis of 154 civilian chest injuries reported six cases from bullhorns with three cases of right and left side each constituting about 4%. According to other researchers and the present study chest injuries are in the form of multiple rib fractures and penetrating injuries involving lungs. Involvement of extremities is an uncommon finding in such an impact by bull.

CONCLUSION

The anatomy of the perineal region is complex, and visualization and access to various structures in the region are difficult. Hence, the repair of injury in the area needs a complete knowledge about the anatomy of the region and expert surgical skills. Usually, these injuries are associated with injury to abdominal and urological structures. In females, the anatomy of the perineum is further complicated by the presence of the uterus, vagina, and the various supporting ligaments. Most of the time when an injury is missed or when a patient undergoes primary repair the patients end up coming back to the hospital with complications like anovaginal fistula and urethrorectal fistula. Thus, causing more morbidity to the patient in terms of physical, mental, social and economic sufferings.

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