



General Information

About The Journal

International Journal of Scientific Study (IJSS) is a monthly journal publishing research articles after full peer review and aims to publish scientifically sound research articles in across all science like Medicine, Dentistry, Genetics, Pharmacy, etc.

Each article submitted to us would be undergoing review in three stages: Initial Review, Peer Review & Final Review.

All rights are reserved with journal owner. Without the prior permission from Editor, no part of the publication can be reproduced, stored or transmitted in any form or by any means.

Abstracting & Indexing Information

Index Medicus (IMSEAR), Global Index Medicus, Index Copernicus, Directory of Open Access Journals(DOAJ), Google Scholar, WorldCat, SafetyLit, WHO Hinari, Genamics Journal Seek Ulrichsweb Serials Solutions , International Committee of Medical Journal Editors(ICJME) Geneva Foundation for Medical Education & Research(GFMER), Socolar, Bielefeld Academic Search Engine(BASE) , Research Bible , Academic Journals Database, J-Gate, Jour Informatics, Directory of Research Journal Indexing(DRJI), Scientific Indexing Services(SIS) Rubriq-Beta, SHERPA RoMEO, New Jour, EIJASR), IndianScience.in, CiteFactor, Scientific Journal Impact Factor (SJIF), Journal Index.net, ROAD, Global Impact Factor(GIF) , International Society for Research Activity (ISRA), Advanced Science Index, OpenAccessArticles.com, etc

Information for Authors

The authors should follow "Instructions to Authors" which is available on website <http://www.ijss-sn.com/instructions-to-authors.html>. Authors should fill the Copyright Transfer form & Conflict of Interest

form. Manuscripts should be submitted directly to: editor@ijss-sn.com.

Publication Charges

International Journal of Scientific Study aims to encourage research among all the students, professionals, etc. But due to costs towards article processing, maintenance of paper in secured data storage system, databases and other financial constraints, authors are required to pay. However discount will be provided for the non-funding quality research work upon request. Details about publication charges are mentioned on journal website at: <http://www.ijss-sn.com/publication-charges.html>.

Advertising Policy

The journal accepts display and classified advertising. Frequency discounts and special positions are available. Inquiries about advertising should be sent to editor@ijss-sn.com.

Publishing Details

Publisher Name: International Research Organization for Life & Health Sciences (IROLHS)

Registered Office: L 214, Mega Center, Magarpatta, Pune - Solapur Road, Pune, Maharashtra, India – 411028. Contact Number: +919759370871.

Designed by: Tulyasys Technologies (www.tulyasys.com)

Disclaimer

The views and opinions published in International Journal of Scientific Study (IJSS) are those of authors and do not necessarily reflect the policy or position of publisher, editors or members of editorial board. Though the every care has been taken to ensure the accuracy and authenticity of Information, IJSS is however not responsible for damages caused by misinterpretation of information expressed and implied within the pages of this issue. No part of this publication may be reproduced without the express written permission of the publisher.



Editorial Board

Founder & Editor In Chief

Dr. Swapnil S. Bumb – India (BDS, MDS, MPH, MSc, PGDHA, PDCR)

Assistant Professor, ACPM Dental College, Dhule, Maharashtra, India

Founder Editor

Dr. Dhairya Lakhani, India

Senior Editorial Board Member

Dr. Stephen Cohen – *United States of America (MA, DDS, FACP, FICD)*

Diplomate of the American Board of Endodontics

Senior editor for nine Editions of the definitive Endodontics Textbook - Pathways of the Pulp, and a Co-editor of the renamed 10 edition Cohen's Pathways of the Pulp.

Dr. Abdel Latif Mohamed – *Australia (MBBS, FRACP, MRCPC, MPaeds, MPH, AFRACMA, MScEpi, MD)*

Professor in Neonatology, The Clinical School, Australian National University Medical School, Australia

Open Researcher and Contributor ID (ORCID): 0000-0003-4306-2933, Scopus ID: 13610882200

Dr. Bipin N. Savani – *United States of America (M.D)*

Professor of Medicine Director, Vanderbilt University Medical Center and Veterans Affairs Medical Center, Vanderbilt- Ingram Cancer Center, Nashville, TN, USA.

Associate Editor (previously co-editor) of the journal "Bone Marrow Transplantation" (official journal of the European Group for Blood and Marrow Transplantation- EBMT).

Editorial advisory board: Biology of Blood and Marrow Transplantation (official journal of the American Society of Blood and Marrow Transplantation).

Dr. Yousef Saleh Khader Al-Gaud, Jordan – *(BDS, MSc, MSPH, MHPE, FFPH, ScD)*

Professor (Full) - Department of Community Medicine

Jordan University of Science and Technology, Jordan, Irbid

Dr. P. Satyanarayana Murthy – *India (MBBS, MS, DLO)*

Professor and Head, Department of ENT and Head & Neck Surgery, Dr.Pinnamaneni Siddhartha Institute of Medical Sciences and Research Center, Chinnaautapalli, Gannavaram

Editor - Indian journal of Otolaryngology (1991),

Editorial Chairman, Indian Journal of Otolaryngology and Head & Neck Surgery 2006-2009 & 2009-2012

Editor, International Journal of Phonosurgery and Laryngology

Editor in Chief designate, International Journal of Sleep Science and Surgery

Editor in Chief Designate, Journal of Indian Academy of Otorhinolaryngology and Head & Neck Surgery

Dr. Sidakpal S. Panaich – *United States of America (M.D)*

Interventional Cardiology Fellow, Department of Cardiology, Michigan State University/Borgess Medical Center

Cardiology Fellow, Department of Internal Medicine/Cardiology, Wayne State University/Detroit Medical Center

Associate Editors

Dr. Silvana Beraj, Albania

Dr. João Malta Barbosa, United States of America

Dr. Anastasia M. Ledyeva, Russia

Dr. Asfandyar Sheikh, Pakistan

Dr. John Park, Scotland

Dr. Mohannad Saleh Kiswani, Jordan

Dr. Safalya Kadtane, India

Dr. Dorcas Naa Dedei Aryeetey, Kumasi, Ghana

Dr. Animasahun Victor Jide, Sagamu, Nigeria

Dr. Hingi Marko C., Mwanza City, Tanzania

Contents

ORIGINAL ARTICLES

- Clinical Profiles and Survival Analysis of Patients with Carcinoma Cervix at a Tertiary Care Center: A Retrospective Study
K V S Latha, T S Rahul 1
- A Study of Ophthalmological Manifestations of Rheumatoid Arthritis in Eastern India
Pampa Halder, Udbuddha Dutta, Biswadip Ghosh, Prasenjit Maiti 8
- Clinical Study on Thyroid and Insulin Hormonal Dysfunction in Patients with Chronic Obstructive Pulmonary Disease
D Nikethan 12
- Comparative Evaluation of the Effects of Two Different Local Drug Delivery Systems Incorporating Green Tea and Turmeric Extracts in the Treatment of Chronic Periodontitis: A 2-month Clinical Trial
Vishwas Madaan, Ashwini M Padhye, Himani Gupta 16
- Study on Prognostic Value of Electrophysiological Tests in Bell's Palsy
Y Kingsly Jebasingh, A Sethuram 22
- Comparison of Postmortem Analysis of Anomalous Fetuses with the Prenatal Ultrasonography Findings
P Murugalatha, M Krithiga 26
- Clinical Evaluation of Patients Undergoing Phacoemulsification for Dry Eye
R P Shamsheer 32
- Comparison of Atracurium Versus Cisatracurium Regarding Onset Time, Intubating Conditions and Haemodynamic Parameters During General Anaesthesia
Vishnu Vardhan Athaluri, M Santhi Sree, Tejesh Kumar Mallepogu 37
- Clinical and Radiological Study of Fistula in Ano in Tertiary Care Centre and Management
R Vidyasagar 44
- An Interventional Study to Enumerate the Causes of Lactation Failure, its Prevention and Management
P Murugalatha, M Krithiga 51

Clinical Study of Solitary Thyroid Nodule <i>R Vidyasagar</i>	59
A Comparable Study on Efficacy of Granisetron and Promethazine in Controlling Hyperemesis Gravidarum <i>Akriti Prasad, Mamta Singh</i>	66
Evaluation of Acceptability, Safety, and Efficacy of Intrauterine Device Insertion during the Postpartum Period: A Prospective Analysis <i>Shilpa Jain, Priyanka Priyadarshini, Hiralal Konar</i>	70
Etiological and Clinical Study of Atrial Fibrillation <i>C Mamatha Reddy, Bingi Srinivas</i>	76
Clinical Study of Diagnostic Hysteroscopy in Abnormal Uterine Bleeding and its Histopathological Correlation <i>P Padmaja, P Deepa</i>	81
A Study of Catheter Ablation versus Medical Management in Post-Myocardial Infarction Scar Ventricular Tachycardia Patients <i>C Mamatha Reddy, Bingi Srinivas</i>	86
Observational, Concurrent Study to Assess Safety and Efficacy of Glycopyrronium and Arformoterol Home Nebulization in High-risk, Symptomatic Acute Exacerbation of Chronic Obstructive Pulmonary Disease Cases: SYMPTOM Study <i>Salil Bendre, S Katiyar</i>	92
Comparison of Academic Performance of 2 nd MBBS Students Participating in Quiz Versus Nonparticipants: A Retrospective Analysis <i>Koli Paresh Girdharlal, Shetty Yashashri C, Singh Vishal</i>	98
CASE REPORTS	
A Unique Case of Acquired Capillary Hemangioma in Adult <i>Nithisha Tegginamatha, Sandhya Baskar, Neethu Narayana Rao, Remya Joseph Parappallil</i>	104
Facial Nerve Schwannoma – A Diagnostic and Surgical dilemma: A Case Report <i>T Santhi, S Vivek</i>	106
A Rare Incidence of Solitary Extramedullary Plasmacytoma of Nasal Cavity <i>Harridas Manickam, C L Tang</i>	110

Clinical Profiles and Survival Analysis of Patients with Carcinoma Cervix at a Tertiary Care Center: A Retrospective Study

K V S Latha¹, T S Rahul²

¹Associate Professor, Department of Medical Oncology, Madras Medical College, Chennai, Tamil Nadu, India, ²Senior Resident, Department of Medical Oncology, Madras Medical College, Chennai, Tamil Nadu, India

Abstract

Introduction: Cervical cancer is the fourth most frequent cancer in women with an estimated 570,000 new cases in 2018 representing 6.6% of all female malignancies. Apparently 90% of deaths from cervical cancer occurred in low- and middle-income countries; the annual death rate was more than 26,600.

Aim: This study aims to assess the clinical profiles, overall survival, and disease-free survival (DFS) of carcinoma cervix and to assess the factors that determine the treatment outcome.

Materials and Methods: A total of 298 patients who met the inclusion criteria of newly diagnosed patients with histopathologically confirmed cervical carcinoma were included in the study. The clinical profile, status of presentation, staging, compliance with treatment and follow-up, as well as the response to the treatment in terms of OS and DFS of the treated patients and its contributing factors were the outcome measures.

Results: Two hundred and forty-five (82.2%) of 298 patients of the study population completed the scheduled radical treatment. The most common presentation was Stage 2B with 125 (41.9%) patients followed by 3B with 87 (29.2%) patients and 4A with 12 (4%). The common histology was squamous cell carcinoma (90.6%). Mean duration of treatment time in concurrent chemoradiotherapy + brachy was 10.93 weeks and external beam radiotherapy + brachy was 10.63 weeks. The median follow-up duration was 4.8 years. The overall survival rate was 97.1% and the mean disease-free survival period rate was 93.4%. In the treatment group, 17 (6.9%) patients showed recurrence, 4 (1.6%) deaths of the total of 20 recurrences, and 8 deaths in the study population.

Conclusion: Similar outcome in the treatment group in terms of overall survival and DFS compared to other studies, with statistical significance in factors contributed to the recurrence. Although treatment defaulters and follow-up defaulters were reaching a good number of the study group, for which care and provision of awareness measures should be taken.

Key words: Cervical cancer, Clinical characteristics, Survival

INTRODUCTION

Cervical cancer is the fourth most frequent cancer in women with an estimated 570,000 new cases in 2018 representing 6.6% of all female malignancies. Apparently 90% of deaths from cervical cancer occurred in low- and middle-income countries; the annual death rate was more

than 26,600.^[1] The incidence of cervical cancer per 1 lakh women in India is 30.7. Incidence varies worldwide with the highest rates found in Latin America and the lowest among Jewish women in Israel. Poor nutritional status, poor self-hygiene, multiple sexual partners, first coitus in young age, early childbirth, promiscuity of the spouse, human papillomavirus infections, sexually transmitted diseases, and immune-compromised states are cited as main risk factors.^[2]

The use of cervical screening has greatly reduced the incidence of invasive cervical cancer in the western countries, but it continues to be a major cause of cancer mortality in the rest of the world because the majority of patients have locally advanced disease at presentation. In developing or less developed countries, over 80% of

Access this article online



www.ijss-sn.com

Month of Submission : 06-2019
Month of Peer Review : 07-2019
Month of Acceptance : 08-2019
Month of Publishing : 08-2019

Corresponding Author: Dr. K V S Latha, Department of Medical Oncology, Madras Medical College, Chennai, Tamil Nadu, India.

women with cervical cancer are diagnosed at an advanced stage which is associated with poor prognosis.^[3] Prognosis depends on disease stage (FIGO), tumor volume, presence of involved lymph nodes, delivered radiation dose, treatment duration, hemoglobin level, and optimum use of intra-cavitary brachytherapy.^[3] Several randomized trials in 1990 compared the effects of regimen that includes cisplatin along with radiation to radiation alone. The results of these studies showed that concurrent chemoradiation lowers the risk of recurrence and death.^[4-6] Squamous cell carcinoma accounts for 80% of all cervical cancers and adenocarcinoma constitutes approximately 20%. The standard of care for advanced carcinoma cervix is concurrent chemoradiation.

Aim

This study aims to assess the clinical profiles, treatment response, and overall and disease-free survival (DFS) of carcinoma cervix and to assess the factors that are determined the treatment outcome.

MATERIALS AND METHODS

The retrospective study of patients attended to the Institute of Obstetrics and Gynecology, Madras Medical College, Chennai, from January 2014 to December 2014, was carried out.

Inclusion Criteria

The following criteria were included in the study:

1. Newly diagnosed patients with histopathologically confirmed carcinoma cervix attending the hospital.
2. Performance status of 0–3.

Exclusion Criteria

The following criteria were excluded from the study:

1. Previously diagnosed patients and undergone treatment outside with histopathologically confirmed carcinoma cervix attending the hospital.
2. Performance status of 4.

The recorded data of thorough history and clinical examination performed including per speculum examination, per vaginal examination, digital rectal examination, and per abdominal examination, in all patients, investigations such as chest X-ray, ultrasonography abdomen, magnetic resonance imaging of abdomen and pelvis, complete blood count (CBC), renal function test, liver function test, and urinalysis will be obtained. Cystoscopy was done routinely and sigmoidoscopy was performed only in patients clinically suspicious of bowel invasion. Tumor size was examined clinically and by imaging before the treatment. DFS is analyzed from date of registration to local or distant relapse

or death or last visit. Toxicity grading was done according to the radiation therapy oncology group (RTOG) grading; it includes neutropenia and gastrointestinal symptoms like diarrhea, assessed by weekly CBC and RFT and weekly check-up.

External Beam Radiotherapy

All patients were irradiated by external beam radiation with megavoltage beams on telecobalt (Co^{60}) machine with a total dose of 45 Gy–54 Gy given in 23–28 fractions of 1.8–1.95 Gy per fraction, five fractions per week starting the 1st day of the first chemotherapy.^[7,8]

The upper border of the individualized treatment beam is at the lower margin of L4 to include distal common iliac nodes. The inferior border is 3 cm below the most inferior disease in the vagina as palpated or seen on imaging. Lateral borders are 2 cm outside the bony pelvic sidewalls. The anterior border must encompass the gross tumor volume-T (GTV-T) as well as the common iliac nodes and is usually placed through the anterior third of the symphysis pubis. The posterior border is 2 cm from the GTV-T including the posterior extension of tumor, uterosacral ligaments, and upper presacral nodes and is commonly situated 0.5 cm posterior to the anterior border of the S2/3 vertebral junction.^[7,8]

Chemotherapy

With respect to the performance status, patients were received either weekly inj. cisplatin 40 mg/m² or 3 weekly inj. cisplatin + inj. 5 FU regimen given intravenously starting on day 1 of radiation. Premedication where administered as per hospital protocol. Antiemetic prophylaxis will be continued with 5HT3 receptor

Table 1: Survival rate

DFS	n	Minimum	Maximum	Mean	Std. deviation
Disease-free survival – descriptive statistics					
DFS days	245	91	1918	1643.89	335.526
DFS weeks	245	13.00	274.00	234.8417	47.93234
Overall survival – descriptive statistics					
OS days	245	520	1918	1705.23	182.019
OS weeks	245	74.29	274.00	243.6040	26.00277
Valid N (listwise)	245				

Table 2: Comparison survival rate

Study	Number of patients	Overall survival	Disease-free survival
GOG 120 ^[16,17]	526	70% (30 months) 60% (5 years)	63% (30 months) 58% (5 years)
Donnelly <i>et al.</i> ^[8]	236	-	69% (5 years)
Kato <i>et al.</i> ^[9]	120	55.1% (5 years)	-
Present study	245	97.1% (4.8 years)	93.4% (4.8 years)

antagonist orally for 3 days after each cycle of chemotherapy.^[9,10]

Brachytherapy

After completion of the external beam therapy, all patients were advised to high-dose-rate brachytherapy, with the dosage of 7–9 Gy to Point A in two-three sittings (1 sitting/week) was given for patients with minimal residual disease after external beam radiation.^[7,8] Brachytherapy was planned 1 week after external beam radiation. The regimen was administered on admission basis. All patients were

monitored closely weekly during the course of concurrent chemoradiation for assessing the toxicity of therapy. Toxicity grading was done according to the RTOG grading.

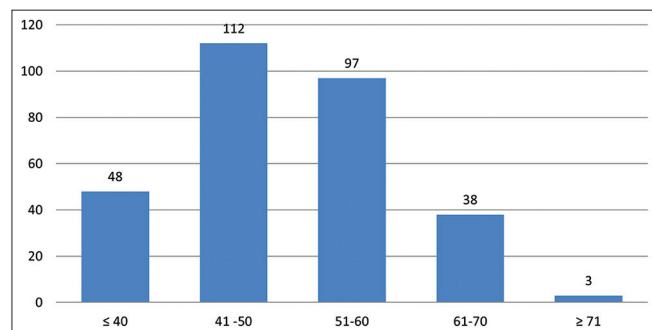


Figure 1: Age-wise distribution

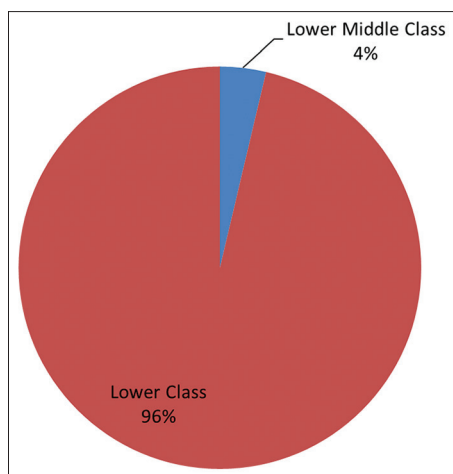


Figure 2: Socioeconomic status. #The socioeconomic status was assessed based on per capita monthly income, using Modified BG Prasad SES, revised income categories for all India (Industrial Workers) 2014

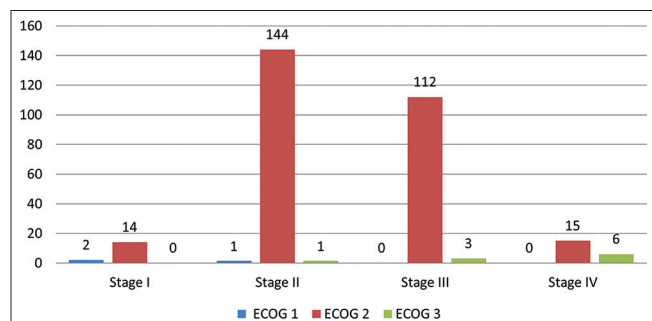


Figure 3: Stage-wise performance status

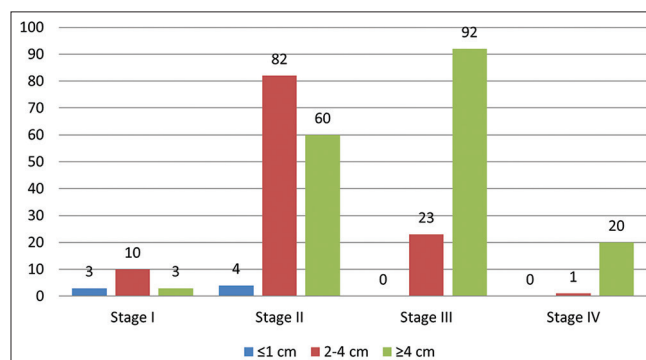


Figure 4: Size of the lesion versus stage of the disease

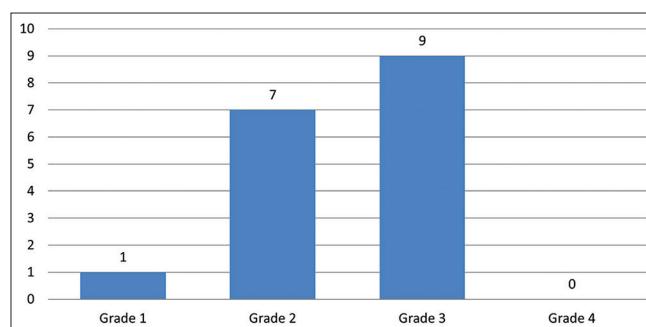


Figure 5: Grade of the tumor

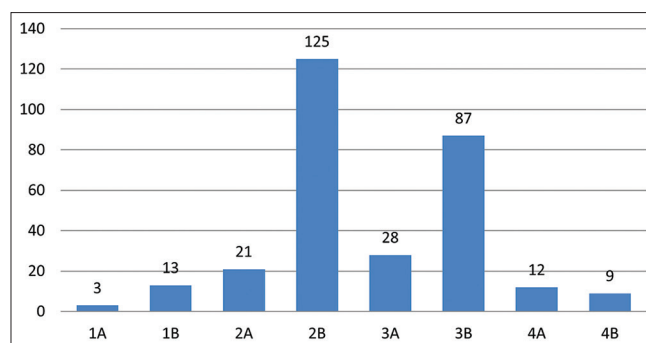


Figure 6: Stage distribution

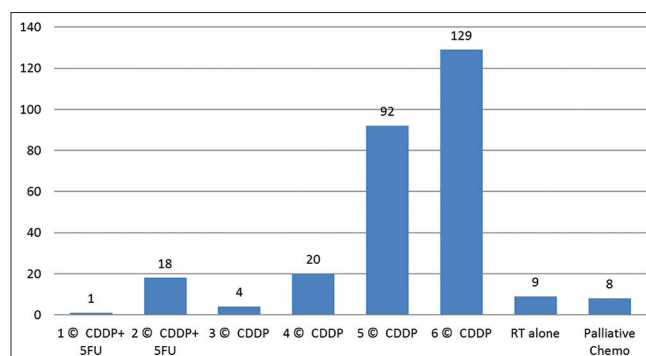


Figure 7: Number of chemotherapy/external beam radiotherapy

Treatment Monitoring and Follow-up

The patients were followed-up monthly for the first 3 months followed by 3 monthly for 3 years, then 6 monthly from completion of therapy to assess response, toxicity,

and disease status. At follow-up, patients were undergone thorough clinical examination for the detection of locoregional disease. Patients who drop out or do not complete the planned course of treatment were excluded from the study.

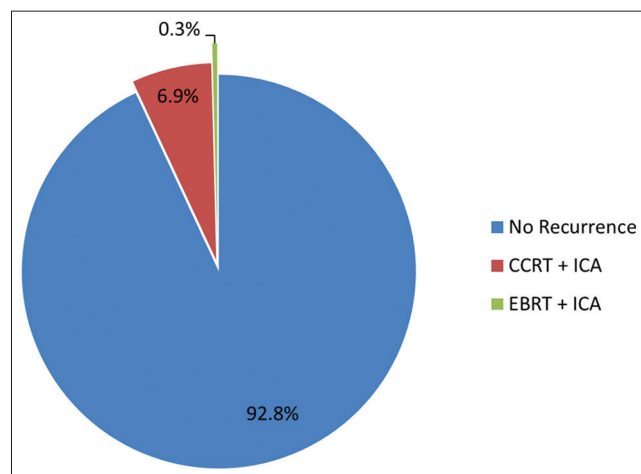


Figure 8: Treatment group recurrence

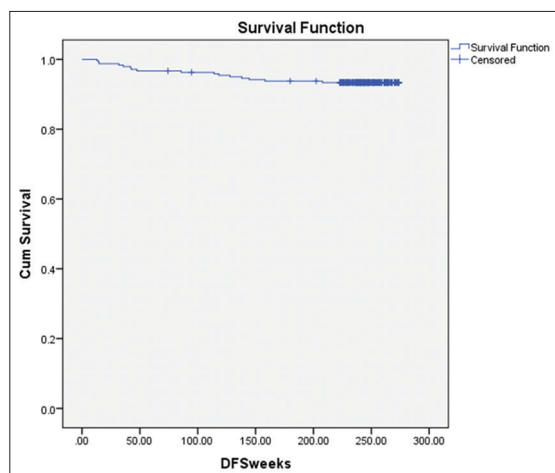


Figure 9: Disease-free survival

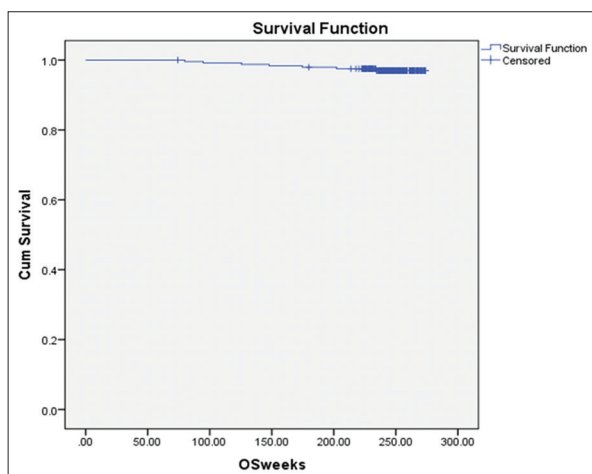


Figure 10: Overall survival

RESULTS

A total of 298 patients who fulfilled the criteria were included in the study. Of 298 patients of the study population, 245 patients completed the treatment schedule. There were 17 dropouts before the commencement of any mode of intervention; eight patients were assigned for palliative chemotherapy due to the disease burden at the time of presentation.

The mean age of this study population was 51.04 years, ranging from 30 to 80 years. Majority 37.58% of patients were in the age group of 41–50 years. Forty-eight patients (16.1%) are below the age of 40 years and 3 patients (1.02%) were the age group of above 71 years Figure 1.

The mean parity of the study population was 3.09, ranging from 0 to 11. Nulliparous being 8 patients, the majority of the population were having 3 childbirths (33.9%). Of the 298 patients, 264 (88.6%) were housewives and 34 (11.4%) were manual labors; 287 patients (96%) were lower class and 11 patients (4%) were lower middle class Figure 2.

Fifty patients had regular medication for hypertension and 65 patients were on diabetic treatments.

Bleeding PV and discharge PV were present in 57.4% and 65.4% of patients, respectively; the pain was present in 51.6% of patients. About 19.1% presented with dysperonia and 16.4% presented with postcoital bleeding and most of them were young below the age group of 50 years.

Twenty-five (8.4%) patients had habit of tobacco chewing and one had smoked, none with alcohol habit. Two hundred and eighty-five (96%) patients had ECOG 2 and 10 (3%) patients had ECOG 3, due to the locally advanced disease status Figure 3.

Two hundred and seventy-six (93%) patients had vaginal involvement, parametrial and pelvic sidewall involvement was documented in 257 and 107 patients, respectively, at the time of presentation. One hundred and seventy-five (58.7%) patients had more than 4 cm size lesion, 116 (38.9%) had 2–4 cm lesion, and 7 (2.3%) had <1 cm size lesion Figures 4 and 5.

Seventeen (5.7%) had adjacent structure involvement, in the study population.

The most common histology was squamous cell carcinoma constituting 90.6%, followed by adenocarcinoma 18% and other histological variants including clear cell, small cell, and anaplastic varieties all together 3.4% (10 patients). The most common presentation was Stage 2B with 125 (41.9%) patients followed by 3B with 87 (29.2%) patients; eight patients presented with distant metastasis before the commencement of any kind of treatment Figure 6.

Of 298 patients, 17 patients defaulted before the starting of any kind of treatment and eight patients dropped out during and in between the time of proposed external beam radiotherapy (EBRT) or concurrent chemotherapy regimen, 264 patients received concurrent chemo RT with either CDDP weekly or CDDP+5FU 3 weekly schedule, and nine patients were assigned for RT alone, for disease status either being early stage or following their surgery, or those who were not willing for chemotherapy. Eight patients were given palliative chemotherapy due to their disease burden, those who were not fit for radical intervention Figure 7.

Twenty-three (9%) developed Grade 2 neutropenia, 92 (35%) developed Grade 1 neutropenia, 149 (56%) developed Grade 0 neutropenia, and none developed Grade 3 neutropenia. Cystitis and diarrhea were noticed in 26 and 80 patients, respectively, during the concurrent chemo RT. Of 264 patients who completed concurrent chemoradiotherapy (CCRT), 28 patients failed to attend or undergo advised brachytherapy. Excluding them, the mean duration of treatment time in CCRT+ICA was 10.93 weeks and the minimum treatment duration was 8 and maximum is 15 weeks. The mean treatment duration of EBRT + ICA was similar to 10.63 weeks. Two hundred and fifty-three (92.8%) patients did not develop a recurrence of disease those who underwent any kind of treatment modality and 20 (7.2%) developed recurrence either local or distant one. Among them, 12 patients had local site, cervix, and lymph node (4.2%) recurrence and 8 (3%) developed recurrence at distant sites, being bone (7) and lung (1) metastasis. Three recurrences were reported in those 28 patients who failed to turn up for brachytherapy following the CCRT.

Sixteen patients of 236 patients developed recurrence who had undergone proposed treatment of CCRT + brachy, 220 (93.3%) patients did not develop recurrence. One patient of nine who had undergone the EBRT + brachy treatment developed local recurrence. Six patients developed metastasis in the treatment completed group (CCRT + ICA or EBRT + ICA), till their last follow-up period documented. Four deaths in the treatment group noted, one patient (at 82 years) suffered cardiac failure, one patient due to local site disease recurrence, and three patients due to distal metastasis.

Increased chances of recurrence were noted in patients with prolonged treatment duration (12.81 ± 1.291 standard deviation [SD]) compare to non-recurrent group patients (10.72 ± 1.403 SD), which is statistically significant (significant at 0.01 levels, sig. [two tailed] on *t*-test). One of 10 lower-middle-class patients developed recurrence, 16 of 235 lower-class patients developed recurrence, though statistically not significant, the recurrence was high in lower socioeconomic status patients. Tobacco consumption failed to show the significance of recurrence may be due to lesser no study population. None of four patients who had ECOG score 1 developed recurrence, 15 of 230 patients who had ECOG score 2 developed recurrence, and 2 of 11 patients who have ECOG score 3 developed recurrence. Although it failed to show the significance, the percentage-wise rise in recurrence was noted in poor performance status patients. Two of nine patients who had adjacent structure involvement developed recurrence, which was statistically significant ($P < 0.001$). Sixteen of 236 patients who had CCRT with cisplatin alone chemotherapy developed recurrence, none of 14 patients who underwent 2 cycles CDDP+5FU had not developed recurrence. Six of 26 patients who had two sittings of brachytherapy developed recurrence and 11 of 219 patients who had three sittings of brachytherapy developed recurrence which were statistically significant ($P = 0.01$) on the recurrence of disease in two sittings of the brachytherapy group. One of 14 patients in Stage I, 7 of 126 patients in Stage II, 7 of 92 patients in Stage III, and 2 of 13 patients in Stage IV were developed recurrence Figure 8.

Of 298 study population, a total of eight deaths reported include one patient who undergone palliative chemotherapy due to lung metastasis, one patient due to local site disease recurrence who denied ICA following CCRT, one patient due to distant metastasis who denied concurrent chemo, and four patients from the treatment group.

Of four patients in the treatment Group 1 patient (at 82 years) suffered cardiac failure, one patient due to local site disease recurrence, and three patients due to distal metastasis. The overall survival after a mean follow-up period of 4.8 years in the treatment group is 97.1% and the DFS in this treatment group was 93.4% [Tables 1 and 2, Figures 9 and 10].

DISCUSSION

In the early stage (FIGO Stage Ib and IIa), cervical cancers, surgery, irradiation, or combinations have been advocated, each claiming to yield higher cure rates and less morbidity. Although surgery results in accurate staging and appropriate adjuvant therapy, combined surgery and

radiation result in increased morbidity. Patients without risk factors have a 5-year survival rate of 82–92%.^[7] In the 1990s, the use of adjuvant therapy with stratified risk factors has shown benefit in survivals and is the standard of care today.^[8] However, in the 1970s–1980s, adjuvant therapy was empirical and practiced in patients with high-risk features such as pelvic nodal involvement and cut margins positive.

A combination of radiation and surgery has been used to improve therapeutic outcome. Pre-operative radiation (5000–6000 mgh, alone or combined with whole pelvis irradiation) has been administered with a rationale to render tumor biologically non-viable, decrease pelvic and distant relapses. The 5-year survival rate was 89% versus 55% for patients with negative versus positive nodes after pre-operative RT, results comparable with our series of 283 patients, in which short course hypofractionated radiation regimens had better outcome with DFS of 62% at 8 years, 6% incidence of post-operative wound infection, 1.2% intestinal obstruction/fistulae, and 2% mortality. The major criticism of these studies has been conflicting reports of higher rates of complications without significant benefit in outcome.^[9]

Since decades, radiation has played a major role in the treatment of locally advanced cervical cancer. Standard treatment has been radical radiation, with the key to success is the administration of appropriate doses to the central tumor and pelvic sidewall.^[10] In different series, 5-year survival rates of 65–75%, 35–50%, and 15–20% have been reported in patients who received radiotherapy alone for Stage IIB–IV tumors.^[11] Furthermore, the American Brachytherapy Society recommends keeping the total treatment duration to <8 weeks because prolongation of total treatment duration can adversely affect local control and survival.^[12] Modern approach to the management of cervical cancer has changed to concomitant chemoradiation in advanced cervical cancer with Level 1 evidence today with significant improvement in local control and survivals. However, hematological and gastrointestinal toxicities were significantly more with chemoradiation and no concrete data on late toxicities.^[13,14]

The study by Geara *et al.*^[15] the overall survival after 2 years was 78%. The toxicities included 19% leucopenia Grade 1–4, 12% Grade 3–4 hematological toxicities, and 37% Grade 3–4 diarrhea.

GOG 120^[16,17] study showed an overall survival of 70% (30 months) and 60% (5 years). This study also has 16.8% Grade 3–4 gastrointestinal toxicities. DFS at 30 months and 5 years was 63% and 58%, respectively.

In a study by Donnelly *et al.*,^[18] the DFS was 69% at 5 years. A study by Kato *et al.*^[19] showed overall survival 55% at 5 years.

CONCLUSION

In this study, the mean follow-up of 4.8 years, the DFS was 93.4%, and the overall survival was 97.1%, which is comparable to other published studies. The statistical significance was seen between the recurrence with treatment duration, adjacent structure involvement, and number of brachytherapies in the present retrospective study. Further studies with large sample sizes are needed to confirm the predictive factors for disease-free and overall survivals. The need for any adjuvant treatment to decrease the recurrence rate in the poor prognostic group also warrants further evaluation. Treatment defaulters and follow-up defaulters were reaching a good number of the study group, for which care and provision of awareness measures should be taken.

REFERENCES

1. Kong TW, Chang SJ, Paek J, Yoo SC, Yoon JH, Chang KH, *et al.* Comparison of concurrent chemoradiation therapy with weekly cisplatin versus monthly fluorouracil plus cisplatin in FIGO stage IIB–IVA cervical cancer. *J Gynecol Oncol* 2012;23:235–41.
2. World Health Organization. International Agency for Research on Cancer. Cervical cancer Estimated incidence, Mortality and Prevalence Worldwide in 2018. Geneva: World Health Organization; 2018.
3. Narayanan V, Bista B, Sharma S. External beam therapy in a four-field box technique with paclitaxel versus a two-field technique with cisplatin in locally advanced carcinoma cervix: A Phase II monocentric trial. *ISRN Oncol* 2012;2012:390193.
4. Denny L. Cervical cancer treatment in Africa. *Curr Opin Oncol* 2011;23:469–74.
5. Edge SE, Byrd DR, Compton CC, Fritz AG, Greene FL, Trotti A. *AJCC Cancer Staging Manual*. 7th ed. New York: Springer; 2010.
6. Jampolis S, Andras EJ, Fletcher GH. Analysis of sites and causes of failures of irradiation in invasive squamous cell carcinoma of the intact uterine cervix. *Radiology* 1975;115:681–5.
7. O'Quinn AG, Fletcher GH, Wharton JT. Guidelines for conservative hysterectomy after irradiation. *Gynecol Oncol* 1980;9:68–79.
8. Sedlis A, Bundy BN, Rotman MZ, Lentz SS, Muddersbach LI, Zaino RJ, *et al.* A randomized trial of pelvic radiation therapy versus no further therapy in selected patients with stage IB carcinoma of the cervix after radical hysterectomy and pelvic lymphadenectomy: A gynecologic oncology group study. *Gynecol Oncol* 1999;73:177–83.
9. Gerbaulet AL, Kunkler IH, Kerr GR, Haie C, Michel G, Prade M, *et al.* Combined radiotherapy and surgery: Local control and complications in early carcinoma of the uterine cervix the Villejuif experience, 1975–1984. *Radiation Oncol* 1992;23:66–73.
10. Nag S, Erickson B, Thomadsen B, Orton C, Demanes JD, Petereit D, *et al.* The American brachytherapy society recommendations for high-dose-rate brachytherapy for carcinoma of the cervix. *Int J Radiat Oncol Biol Phys* 2000;48:201–11.
11. Logsdon MD, Eifel PJ. FIGO IIB squamous cell carcinoma of the cervix: An analysis of prognostic factors emphasizing the balance between external beam and intracavitary radiation therapy. *Int J Radiat Oncol Biol Phys* 1999;43:763–75.
12. Perez CA, Grigsby PW, Castro-Vita H, Lockett MA. Carcinoma of the uterine cervix. I. Impact of prolongation of overall treatment time and

- timing of brachytherapy on outcome of radiation therapy. *Int J Radiat Oncol Biol Phys* 1995;32:1275-88.
13. Green JA, Kirwan JM, Tierney JF, Symonds P, Fresco L, Collingwood M, *et al.* Survival and recurrence after concomitant chemotherapy and radiotherapy for cancer of the uterine cervix: A systematic review and meta-analysis. *Lancet* 2001;358:781-6.
 14. Lukka H, Hirte H, Fyles A, Thomas G, Elit L, Johnston M, *et al.* Concurrent cisplatin-based chemotherapy plus radiotherapy for cervical cancer a meta-analysis. *Clin Oncol (R Coll Radiol)* 2002;14:203-12.
 15. Geara FB, Shamseddine A, Khalil A, Abboud M, Charafeddine M, Seoud M, *et al.* A phase II randomized trial comparing radiotherapy with concurrent weekly cisplatin or weekly paclitaxel in patients with advanced cervical cancer. *Radiat Oncol* 2010;5:84.
 16. Rose PG, Bundy BN, Watkins EB, Thigpen JT, Deppe G, Maiman MA, *et al.* Concurrent cisplatin-based radiotherapy and chemotherapy for locally advanced cervical cancer. *N Engl J Med* 1999;340:1144-53.
 17. Rose PG, Ali S, Watkins E, Thigpen JT, Deppe G, Clarke-Pearson DL, *et al.* Long-term follow-up of a randomized trial comparing concurrent single agent cisplatin, cisplatin-based combination chemotherapy, or hydroxyurea during pelvic irradiation for locally advanced cervical cancer: A gynecologic oncology group study. *J Clin Oncol* 2007;25:2804-10.
 18. Donnelly ED, Refaat T, Gentile M, Herskovic A, Boyle J, Helenowski I, *et al.* Evaluation of outcomes in patients with carcinoma of the cervix treated with concurrent radiation and cisplatin versus cisplatin/5-FU compared with radiation alone. *Am J Clin Oncol* 2015;38:437-41.
 19. Kato S, Ohno T, Thephamongkhon K, Chansilpa Y, Cao J, Xu X, *et al.* Long-term follow-up results of a multi-institutional phase 2 study of concurrent chemoradiation therapy for locally advanced cervical cancer in east and Southeast Asia. *Int J Radiat Oncol Biol Phys* 2013;87:100-5.

How to cite this article: Latha KVS, Rahul TS. Clinical Profiles and Survival Analysis of Patients with Carcinoma Cervix at a Tertiary Care Center: A Retrospective Study. *Int J Sci Stud* 2019;7(5):1-7.

Source of Support: Nil, **Conflict of Interest:** None declared.

A Study of Ophthalmological Manifestations of Rheumatoid Arthritis in Eastern India

Pampa Halder¹, Udbuddha Dutta², Biswadip Ghosh³, Prasenjit Maiti⁴

¹Assistant Professor, Department of Ophthalmology, R. G. Kar Medical College and Hospital, Kolkata, West Bengal, India, ²Resident, Department of Ophthalmology, R. G. Kar Medical College and Hospital, Kolkata, West Bengal, India, ³Associate Professor, Department of Rheumatology, IPGME&R and SSKM Hospital, Kolkata, West Bengal, India, ⁴Professor, Department of Ophthalmology, R. G. Kar Medical College and Hospital, Kolkata, West Bengal, India

Abstract

Introduction: Patients with rheumatoid arthritis (RA) who are positive for anti-cyclic citrullinated peptide (CCP)/rheumatoid factor (RF) have more extra-articular manifestations.

Purpose: We tried to evaluate the magnitude of ocular manifestations in RA patients and to find out whether there is any correlation of anti-CCP or RF or disease duration to ocular involvement.

Materials and Methods: A total of 288 patients diagnosed as RA with ocular symptoms were evaluated. Drug-induced effects and cataract were excluded from the study.

Results: About 18.1% were male and 81.9% were female. The minimum age was 21 and the maximum was 80 years. The average age was 45.66 years. About 36.8% of patients had ocular manifestations. They were bilateral in 66% of patients. Multiple ocular manifestations were shown in 60.4% of patients. Dry eye was observed in 30.5%, anterior uveitis in 6.25%, and episcleritis and scleritis in 7.6% each. Anti-CCP was present in 86.8% and RF in 78.5% of patients. The duration of disease was found to be statistically significant with respect to the presentation of ocular manifestations. Anti-CCP was found to be statistically significant with respect to ocular manifestations but statistically insignificant in case of RF. No statistical significance was found between gender and ocular manifestations.

Conclusion: So far, no published Indian study with such large number of patients looked at ocular manifestations of RA correlating with disease duration and impact of both anti-CCP and RF at the same time. Our study indicates that patients suffering from RA with anti-CCP positivity and long duration of disease should be evaluated ophthalmologically.

Key words: Anti-cyclic citrullinated peptide, Disease duration, Ocular, Rheumatoid arthritis, Rheumatoid factor

INTRODUCTION

Rheumatoid arthritis (RA) is a systemic disease; therefore, many patients exhibit extra-articular manifestations.^[1] Patients with RA who have high titers of rheumatoid factor (RF) or antibodies to anti-cyclic citrullinated peptide (anti-CCP) are most likely to have extra-articular manifestations of their disease, including rheumatoid vasculitis, pleuropulmonary, neurologic, digestive,

cardiovascular, cutaneous, hematologic, and ocular complications.^[2]

Common ocular manifestations of RA include keratoconjunctivitis sicca (dry eye syndrome), episcleritis, scleritis, peripheral ulcerative keratitis (PUK), retinal vasculitis, uveitis, and cataract.^[3] Inflammatory ocular diseases are associated with excess mortality.^[4]

So far, no published Indian study looked at ocular manifestations of RA correlating with disease duration and impact of both anti-CCP and RF at the same time.

Aims and Objectives

The objectives of this study were as follows:

- To evaluate the magnitude of ocular manifestations in patients suffering from RA.

Access this article online	
 www.ijss-sn.com	Month of Submission : 06-2019
	Month of Peer Review : 07-2019
	Month of Acceptance : 08-2019
	Month of Publishing : 08-2019

Corresponding Author: Dr. Biswadip Ghosh, Department of Rheumatology, IPGME&R and SSKM Hospital, Kolkata, West Bengal, India.

- To establish a relation between the duration of RA and frequency of ocular manifestations.
- To find out the statistical significance of anti-CCP/RF if any, to the presentation of ocular manifestations.

MATERIALS AND METHODS

Study Design

This was a cross-sectional observational study.

Selection of cases

Patients diagnosed with RA were evaluated after a thorough ophthalmological evaluation. These patients fulfilled the ACR/EULAR criteria for RA.^[5]

These patients were studied in the department of ophthalmology and rheumatology clinic of a tertiary care center of Eastern India between January and December 2018.

Sample size

The sample size was 288.

Inclusion Criteria

All patients diagnosed as having RA were included in the study.

Exclusion Criteria

The following criteria were excluded from the study:

- Patients with other autoimmune connective tissue disorders.
- Patients with malignancy/history of chemotherapy/history of exposure to radiation.
- Probable drug-induced ocular manifestations.
- Patients with 7.5 mg or more prednisolone equivalents per day for the past 3 months.
- Patients with a history of any ocular infection, ocular surgery, and trauma.
- Cataract, as they have multifactorial cause and itself make examination difficult.

Ophthalmological Examination

Visual acuity was tested using Snellen's chart. Color vision was recording with Ishihara's pseudoisochromatic charts. Corneal staining was done with fluorescein stain.

Schirmer's test was used to find out cases of dry eye. Normal is ≥ 15 mm wetting of the paper after 5 min. Severe dry eye is < 5 mm wetting of the paper after 5 min.

Standard ophthalmological tools such as slit-lamp biomicroscopy for anterior segment examination, applanation tonometer for IOP measurement, Goldmann two mirror gonioscope, indirect ophthalmoscopy for retina examination, and automated perimetry were used.

Table 1: Percentage of various ocular manifestations

Ocular manifestation	Number of individuals
Dry eye	88
Episcleritis	22
Scleritis	22
Anterior uveitis	18

Table 2: Prevalence of anti-CCP and rheumatoid factor in the study population

Status	Rheumatoid factor (%)	Anti-CCP (%)
Absent	21.5 (62)	13.2 (38)
Present	78.5 (226)	86.8 (250)
Total	100.0	100.0

CCP: Cyclic citrullinated peptide

Table 3: Mean duration of disease with and without ocular manifestations

Ocular manifestations	Duration of disease in years		
	Mean	Median	Std. deviation
No	3.82	3.00	2.46
Yes	6.40	6.00	2.46
P value	<0.001		
Significance	Significant		

Blood tests included complete blood count, random blood sugar, creatinine, liver function test, RF, and anti-CCP.

RESULTS AND ANALYSIS

In the present study, 288 patients were studied. Of these, 52 (18.1%) were male and 236 (81.9%) were female. A total of 576 eyes were examined.

One hundred and sixteen (40.3%) patients were in the 21–40 age group, 118 (41%) patients in the 41–60 age group, and 54 (18.8%) patients above 60 years. The minimum age was 21 and the maximum was 80 years.

The average age was 45.66 years; males 40.23 and females 46.86 years.

Ocular manifestations [Table 1] were seen in 106 (36.8%) of the study population. These manifestations were bilateral in 70 (66%) patients and unilateral in 36 (34%) patients. Multiple ocular manifestations were shown in 64 (60.4%) patients.

Dry eye was the most common ocular manifestation, observed in 88 patients (30.5%). Anterior uveitis was noticed in 18 patients (6.25%). Episcleritis and scleritis were observed in 22 patients each (7.6%).

No cases of retinal vasculitis or PUK were found.

Table 4: Significance of anti-CCP in relation to ocular manifestations

Anti-CCP	Ocular manifestations		Total	P value	Significance
	No	Yes			
Absent	32 (17.58)	6 (5.66)	38 (13.19)	0.041	Significant
Present	150 (82.42)	100 (94.34)	250 (86.81)		
Total	182 (100)	106 (100)	288 (100)		

CCP: Cyclic citrullinated peptide

Table 5: Significance of rheumatoid factor in relation to ocular manifestations

Rheumatoid factor	Ocular manifestations		Total	P value	Significance
	No	Yes			
Absent	34 (18.68)	28 (26.42)	62 (21.53)	0.276	Not significant
Present	148 (81.32)	78 (73.58)	226 (78.47)		
Total	182 (100)	106 (100)	288 (100)		

Anti-CCP [Table 2] was present in 250 patients (86.8%). RF was positive in 226 patients (78.5%). One hundred and eighty-eight (65.2%) patients had both anti-CCP and RF. Hundred patients with anti-CCP positivity and 78 patients with RF had ocular manifestations.

The duration of [Table 3] disease was found to be statistically significant ($P = 0.001$) with respect to the presentation of ocular manifestations.

Anti-CCP [Table 4] was found to be statistically significant ($P = 0.04$, odds ratio 3.55) with respect to ocular manifestations but statistically insignificant ($P = 0.276$, odds ratio 0.64) in case of RF [Table 5].

No statistical significance was found between gender and ocular manifestations ($P = 0.481$).

The statistical software SPSS version 20 has been used for the analysis.

DISCUSSION

Our study was based on a study population of 288 diagnosed with RA, having ocular complaints visiting the ophthalmology department and rheumatology clinic of our tertiary care center of Eastern India from January to December 2018. Suspected drug-induced ocular changes such as hydroxychloroquine or steroid-induced retinopathy were excluded from the study. Cases of cataract were not enumerated as it has multifactorial causes. A total of 576 eyes were examined, highest in comparison of all previous published Indian studies evaluating eyes of rheumatoid patients.

In our study, 52 patients (18.1%) were male and 236 (81.9%) were female. This is comparable to the study by Vignesh

and Srinivasan^[6] who had 77% of females and 23% of males.

Ocular manifestations were seen in 106 (36.8%) of the study population. These manifestations were bilateral in 70 (66%) patients and unilateral in 36 (34%) patients. Multiple ocular manifestations were shown in 64 (60.4%) patients. These findings are compatible with a study by Vignesh and Srinivasan^[6] who had 39% of patients with ocular manifestations. However, in his study, 85% of patients had bilateral findings and 80% of patients had multiple findings. Reddy *et al.*^[7] also had 39% of patients with ocular findings. About 65% of patients had bilateral findings. The prevalence of ocular lesions was 27.2% reported by Zlatanović *et al.*^[8]. It seems that Indian rheumatoid patients have more ocular involvement, probably due to less than adequate treatment of this autoimmune disease.

Dry eye was the most common ocular manifestation observed in 88 patients (30.5%). Episcleritis and scleritis were observed in 22 patients each (7.6%). Anterior uveitis was noticed in 18 patients (6.25%). Zlatanović *et al.*⁸ carried out a study, in which dry eye was appreciated in 17.65% of patients and episcleritis and scleritis in 5.06% and 2.06% of patients, respectively.

Anti-CCP was present in 250 patients (86.8%). RF was present in 226 patients (78.5%). Kaur *et al.*^[9] had ocular signs in 38% of rheumatoid patients with 83% anti-CCP positivity and 77% RF positivity. We found positive correlation of anti-CCP with ocular manifestations, compatible with Vignesh *et al.* On the other hand, there was no significant relation between ocular involvement and RF. Same result was reported by Markovitz *et al.*^[10]

The mean duration of disease was found to be 6.40 ± 2.46 years in patients with ocular manifestations

and 3.82 ± 2.46 years in patients without ocular manifestations. The duration of disease was found to be statistically significant ($P = 0.001$) with respect to the presentation of ocular manifestations. This is comparable to the study by Vignesh and Srinivasan^[6] who found it to be 5.4 ± 2.7 years and 2.1 ± 1.6 years, respectively. In our study, we also found that the duration of disease was found to be statistically significant ($P = 0.016$) with respect to unilateral/bilateral presentation of ocular manifestations.

Although Zlatanović *et al.*^[8] reported more female susceptibility, we did not find any correlation between gender and ocular involvement.

CONCLUSION

We emphasize the need to ask the patients suffering from RA whether they have any eye symptoms and if affirmative then examination of both eyes in detail. Particular attention is to be given to those rheumatoid patients who have long disease duration and anti-CCP positivity. Please note that inflammatory ocular diseases are associated with excess mortality.^[4]

Limitations

- Only those patients who have ocular symptoms were evaluated. If all patients with RA were examined irrespective of symptoms, data would have been more robust.

- The study group was conducted purely on Indian (mostly Bengali) ethnic background.
- This was a single-center study.

REFERENCES

- Moreland LW, Curtis JR. Systemic nonarticular manifestations of rheumatoid arthritis: Focus on inflammatory mechanisms. *Semin Arthritis Rheum* 2009;39:132-43.
- Hochberg MC, Johnston SS, John AK. The incidence and prevalence of extra-articular and systemic manifestations in a cohort of newly-diagnosed patients with rheumatoid arthritis between 1999 and 2006. *Curr Med Res Opin* 2008;24:469-80.
- Aboud SA, Abd Elkhalek MO, Aly NH, Abd Elaleem EA. Ocular involvement and its manifestations in rheumatoid arthritis patients. *Delta J Ophthalmol* 2017;18:57-62.
- Artifoni M, Rothschild PR, Brézin A, Guillemin L, Puéchal X. Ocular inflammatory diseases associated with rheumatoid arthritis. *Nat Rev Rheumatol* 2014;10:108-16.
- Aletaha D, Neogi T, Silman AJ, Funovits J, Felson DT, Bingham CO 3rd, *et al* 2010 rheumatoid arthritis classification criteria: An American college of rheumatology/European league against rheumatism collaborative initiative. *Ann Rheum Dis* 2010;69:1580-8.
- Vignesh AP, Srinivasan R. Ocular manifestations of rheumatoid arthritis and their correlation with anti-cyclic citrullinated peptide antibodies. *Clin Ophthalmol* 2015;9:393-7.
- Reddy SC, Gupta SD, Jain IS, Deodhar SD. Ocular manifestations of rheumatoid arthritis. *Indian J Ophthalmol* 1977;25:20-6.
- Zlatanović G, Veselinović D, Cekić S, Zivković M, Dorđević-Jocić J, Zlatanović M, *et al*. Ocular manifestation of rheumatoid arthritis-different forms and frequency. *Bosn J Basic Med Sci* 2010;10:323-7.
- Kaur P, Bal BS, Singh B, Duggal A, Kaur I. To study the prevalence of ocular manifestations in rheumatoid arthritis and their correlation with anti cyclic citrullinated peptide antibodies and rheumatoid factor. *IOSR J Dent Med Sci* 2016;15:58-63.
- Markovitz E, Perry ZH, Tsumi E, Abu-Shakra M. Ocular involvement and its' manifestations in rheumatoid arthritis patients. *Harefuah* 2011;150:713-8,751.

How to cite this article: Halder Pampa, Dutta Udbuddha, Ghosh Biswadip, Maiti Prasenjit. A Study of Ophthalmological Manifestations of Rheumatoid Arthritis in Eastern India. *Int J Sci Stud* 2019;7(5):8-11.

Source of Support: Nil, **Conflict of Interest:** None declared.

Clinical Study on Thyroid and Insulin Hormonal Dysfunction in Patients with Chronic Obstructive Pulmonary Disease

D Nikethan

Assistant Professor, Department of Medicine, Viswabharathi Medical College, Kurnool, Andhra Pradesh, India

Abstract

Background: Many systemic changes take place in patients with chronic obstructive pulmonary disease (COPD) cause hormonal imbalance which, in turn, affects the severity of the disease. The systemic manifestations of COPD include a number of endocrine disorders such as those involving the pituitary, the thyroid, the gonads, the adrenals, and the pancreas. The fluctuating severity of hypoxia in COPD patients results in alterations in thyroid function tests and insulin-like growth factor-1 (IGF-1) levels.

Aim of the Study: This study aims to evaluate the thyroid function tests, insulin, and IGF-1 levels in patients with chronic COPD disease and analyze the data.

Materials and Methods: Sixty-four COPD patients and 32 normal subjects as control group were included in this study. The COPD group was diagnosed and classified according to Global Initiative for Chronic Obstructive Lung Disease criteria. All were subjected to thorough clinical history, examination, and chest X-ray and spirometry. Hormonal levels of thyroxine hormone (total triiodothyronine [TT3], total thyroxine, free triiodothyronine, and free thyroxine) and IGF-1 and insulin were measured.

Observations and Results: There was a statistically significant difference between patients with COPD and controls in regard with mean values of total T3, but there was no statistically significant difference in regard with mean values of total T4, thyroid-stimulating hormone, free T3 and T4, or insulin levels in this study. Hormonal levels according to the stages of COPD showed no statistical difference between Stage I COPD patients and controls, but there was statistically significant difference in regard to other stages of COPD and control groups, i.e., in the present study, the hormonal level of TT3 was normal in all COPD patients; however, in Stages III and IV, there was a reduction in the hormone level in these stages than control subject and in comparison to Stage I and II.

Conclusion: There were significant differences between some hormonal levels in COPD and in controls. There were demonstrable thyroid hormonal changes and insulin levels in patients of severe degree COPD patients which could be attributed to as systemic manifestation resulting in cachexia, muscle wasting.

Key words: Chronic obstructive pulmonary disease, Insulin-like growth hormone, Thyroid dysfunction

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a very common and major cause of chronic morbidity and mortality throughout the world. It was ranked as sixth as the cause of death in 1990, especially in industrialized

areas. It was also presumed that it would become the third leading cause of death worldwide by 2020.^[1] The disease is no longer considered to affect not only the lungs and airways but also results in systemic changes in the body. The systemic manifestations of COPD include endocrine disorders involving the pituitary, the thyroid, etc. The thyroid hormone regulates the metabolism of proteins, lipids, and carbohydrates, and controls the activity of membrane-bound enzymes.^[2,3] The thyroid hormone enhances mitochondrial oxidation and thus augments metabolic rate.^[4] This effect on metabolic rate is probably responsible for the association between the thyroid hormone and respiratory drive.^[5] Limited data on the prevalence of thyroid diseases among

Access this article online



www.ijss-sn.com

Month of Submission : 06-2019
Month of Peer Review : 07-2019
Month of Acceptance : 08-2019
Month of Publishing : 08-2019

Corresponding Author: Dr. D Nikethan, Department of Medicine, Viswabharathi Medical College, RT Nagar, Penchikalapadu, Kurnool, Andhra Pradesh, India

patients with COPD are available.^[6,7] There is a potential possibility of increase in developing hypothyroidism and hyperthyroidism in COPD patients and the severity of airway obstruction in these patients affects the rate of survival.^[8] It is associated with impairment of thyroid gland function.^[9] There was every possibility of differences in hormone levels during stable and exacerbation phases in comparison to healthy controls. Some authors found a decrease in growth hormone or IGF-1, others an increase in growth hormone or IGF-1. An increase of growth hormone might reflect a non-specific response of the body to stress (for instance, hypoxemia). Before growth hormone supplementation can be advised as part of the treatment in COPD, further controlled studies must be performed to investigate its functional efficacy.^[10] In this study, hormonal assays including thyroid hormones, IGF-1, and insulin were done to observe and analyze their changes in patients with COPD and a healthy control group.

MATERIALS AND METHODS

In this study, the subjects were divided into two groups. Group A consisted of 64 patients who were diagnosed as COPD and attending the Department of Medicine, Viswabharathi Medical College, RT Nagar, Panchikalapadu, Kurnool, Andhra Pradesh. An institutional ethical committee clearance was obtained before the commencement of the study. A committee approved consent form was used for the study.

Inclusion Criteria

(1) Patients with COPD belonging to the age group of 35–75 years were included in the study. (2) Patients with COPD and classified according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2009 criteria were

included in the study. (3) 32 healthy non-smoking volunteers were included in the study. (4) Patients with symptoms of chronic bronchitis, evidence of airway obstruction according to GOLD study 2009, and no improvement in forced vital capacity 1 (FEV1) of more than 10% after inhalation of 200 mg of salbutamol were included in the study.

Exclusion Criteria

(1) Patients who are on oral glucocorticoids or with any other drug known to affect thyroid function tests such as amiodarone or iodine-containing contrast media were excluded from the study. (2) Patients aged below 35 years and above 75 years were excluded from the study. (3) Patients with clinical evidence of thyroid disease or coexistence of other diseases altering thyroid function tests were excluded from the study. (4) Patients with fasting hyperglycemia were excluded from the study. (5) Patients with positive urine glucose or renal failure were excluded from the study. All the patients were subjected to clinical examination, chest X-ray, spirometry, complete blood picture, fasting, and 2 h postprandial blood glucose. Hormonal assay using enzyme-linked immunosorbent assay technique measuring the following hormonal levels: (a) Total thyroxine (TT4), (b) total triiodothyronine [TT3], (c) thyroid-stimulating hormone (TSH), (d) free thyroxine, (e) free triiodothyronine, (f) fasting serum insulin hormone level, and (g) insulin growth factor range (insulin-like growth factor-1 [IGF-1]).

OBSERVATIONS AND RESULTS

The clinical and laboratory parameters of the two groups are summarized in Table 1. It was observed that there was a statistically significant reduction in FEV1, FEV1/FVC, paO_2 , and paCO_2 values when compared between patients with COPD ($n = 64$) and controls ($n = 32$).

Table 1: The clinical and laboratory parameters in both the groups (Group A – 64 and Group B – 32)

Characteristics	Chronic obstructive pulmonary disease patients ($n=64$)	Control ($n=32$)	P-value
Age range	35–75	40–65	0.081
Mean age	52.75±8.9	47.16±7.10	0.734
Sex	All male	All male	---
BMI	20.2–33.9	21.7–29.3	0.89
Mean BMI	23.9±2.4	25.8±1.18	
Stage of the disease			
Stage I	16 (25%)	--	
Stage II	21 (32.8%)	--	
Stage III	13 (20.31%)	--	
Stage IV	14 (21.87%)	--	
Spirometry			
FEV1%	61.3±15.2	109.1±7.7	0.001
FEV1/FVC	58.5±12.6	98.8±7.45	0.001
Arterial blood gases	pH 7.4±0.02	7.41±0.02	0.001
	paO_2 74±9.33	82.8±4.5	
	paCO_2 44.6±6.54	38.6±1.3	
Fasting blood sugar	87.72±13.4	83.6±11.1	0.36
2 h postprandial	115.3±26.1	99.9±22.82	0.04

BMI: Body mass index, FEV1: Forced vital capacity 1

There was a statistically significant difference between patients with COPD and controls in regard with mean values of total T3, but there was no statistically significant difference in regard with mean values of total T4, TSH, free T3 and T4, or insulin levels in this study [Table 2].

Hormonal levels according to the stages of COPD showed no statistically significant difference between Stage I COPD patients and controls, but there was a statistically significant difference in regard to other stages of COPD and control groups [Table 3].

It was observed in this study that the calculated TT3 and TT4 ratio did not correlate with paO_2 levels in Stage I and Stage II of COPD group; however, there was a strong positive correlation between TT3 and TT4 ratio and paO_2 in Stage III and Stage IV of COPD. The IGF1 level in chronic obstructive lung disease was: In mild stage (Stage I) 2/10 (20%) of patients in Group A, the hormone levels were reduced, while in the remaining 8/64 (80%) of patients, the hormone levels were within normal limits. In moderate stage

(Stage II), 11/18 (61.11%) of patients, the hormone levels were reduced, while in 7 (36.88%) of patients, the hormone levels were within normal limits. In severe stage (Stage III), 12/20 (60%) of patients, the hormone levels were reduced, while in 40% of patients, the hormone levels were within normal limits. In very severe stage (Stage IV), 9/16 (56.25%) of patients, the hormone levels were reduced, while in 7/16 (43.75%) of patients, the hormone levels were within normal limits.

DISCUSSION

The severity of the COPD disease produces systemic response in patients such as hormonal imbalance which, in turn, affects the homeostasis. Hormonal imbalance in thyroid function tests and IGF-1 levels varies with the degree of hypoxia in COPD patients.^[5] The present study was conducted to observe the hormonal levels of TT3, TT4, free T3, free T4, TSH, IGF-1, and insulin in severe stages of COPD patients. The patients with COPD presenting a spectrum in disease severity were included in the study as indicated by the various degrees of airway obstruction and hypoxia. There was a statistically significant difference between patients with COPD and controls in regard with mean values of total T3, but there was no statistically significant difference in regard with mean values of total T4, TSH, free T3 and T4, or insulin levels in this study. Hormonal levels according to the stages of COPD showed no statistically significant difference between Stage I COPD patients and controls, but there was a statistically significant difference in regard to other stages of COPD and control groups, i.e., in the present study, the hormonal level of total triiodothyronine (TT3) was normal in all COPD patients; however, in Stages III and IV, there was a reduction in the hormone level in these stages than control subject and in comparison to Stages I and II. Similar results were observed with other studies.^[6,7] However, few authors found that TT3 is reduced in all COPD patients, especially those with hypoxemia than control subjects.^[8] The calculated TT3–TT4 ratio was used, as this ratio has been proven to be a useful tool in studying the peripheral conversion of thyroxine to triiodothyronine

Table 2: The range and mean values of different hormonal levels between COPD patients and controls (Group A – 63 and Group B – 32)

Hormones	COPD patients Group A	Controls Group B	P-value
Total T3 (ng %)			
Range	78–176	198–224	0.023
Mean	140.4±25.7	155.6±23.65	0.012
Total T4 (μg)			
Range	5.2–11.7	6.1–11.3	0.16
Mean	8.1±1.24	8.9±1.0	
TSH (μIU/dl)			
Range	0.3–3.8	0.08–4.5	0.24
Mean	1.7±0.98	1.15±1.16	0.06
Free T3 (pg/ml)			
Range	1.2–37	1.7–4.2	0.21
Mean	2.6±0.4	2.8±0.6	
Free T4			
Range	0.68–1.9	0.07–1.8	0.22
Mean	1.07±0.25	1.09±0.39	
Insulin			
Range	6.1–24.3	9.90–19.02	0.4
Mean	14.90±3.9	14.7±2.35	

COPD: Chronic obstructive pulmonary disease

Table 3: The different hormonal level in relation to disease stages of COPD in comparison to control group (Group A – 64 and Group B – 32)

Hormonal level	Stage I (10)	Stage II (18)	Stage III (20)	Stage IV (16)
Total triiodothyronine mean+SD	162.9±20.6	142.6±17.9	127±21.5	120.6±28.1
Total thyroxine mean+SD	0.82±1.4	0.82±1.6	0.81±1.8	0.84±1.8
Thyroid-stimulating hormone mean+SD	2.1±0.8	1.6±0.7	1.9±1.4	2.01±0.8
Free triiodothyronine mean+SD	2.7±0.4	2.7±0.3	2.6±0.4	2.6±0.6
Free thyroxine mean+SD	1.2±0.2	1.2±0.1	1.2±0.3	1.2±0.3
Insulin mean+SD	14.4±5.4	16.3±1.7	16.2±5.4	16±1.5
P-value	0.12	0.049	0.004	0.02

SD: Standard deviation

in various disease states.^[9] In the present study also, there was reduction in TT3/TT4 ratio in Stage III and Stage IV COPD patients and there was a strong positive correlation between TT3/TT4 ratio and PaO₂ in Stage III and Stage IV ($r = 0.475$ and $P = 0.040$), this agrees with the results in other studies.^[6,8] Such pattern of hormonal changes suggests that hypoxemia acts not only at the central levels of hypothalamic pituitary thyroid but also interferes with the peripheral metabolism and turnover of thyroid hormone. The free T3 and T4 levels were normal in the present study in all stages of COPD in comparison to the controls; this was the results in other researches.^[7,10] Review of literature showed that free T3 and T4 were higher in COPD than the control and the authors could not explain their observation.^[7,9] The TSH and insulin levels in this study were normal in all COPD patients, and this agrees with other studies also.^[6,9] It could be concluded that thyroid dysfunction may be ascribed to chronic COPD as a confounding factor and related to hypoxemia or hypercapnia. However, there needs to be further investigation done before concluding that there is definite evidence of thyroid dysfunction in COPD patients. Circulating IGF-1 level was used as a marker of growth hormone (GH) action because IGF-1 has a longer half-life than GH, and its concentration integrates the pulsatile release of GH.^[11] In this study, it was observed that there was reduction in IGF-1 level in different stages of COPD. Little information is available regarding circulating growth hormone or IGF-1 levels in COPD in literature.^[6] However, the data that exist suggest that IGF-1 levels in stable COPD patients tend to be low, consistent with the impression that the growth hormone axis is suppressed by chronic disease.^[11] The mechanisms by which COPD alters endocrine function are incompletely understood but likely involve hypoxemia, hypercapnia, and systemic inflammation. Altered endocrine function can worsen the clinical manifestations of COPD through several mechanisms.

CONCLUSION

There were demonstrable thyroid hormonal changes and insulin levels in patients of severe degree COPD patients which could be attributed to as systemic manifestation resulting in cachexia, muscle wasting. However, more sophisticated investigation should be done, especially to evaluate the role of hormonal replacement therapy.

REFERENCES

1. Roberto R, Antonio A, Jean B, Gershon AS, Warner L, Cascagnette P, Victor JC, *et al.* Pocket Guide to COPD Diagnosis, Management and Prevention: Global Initiative for Chronic Obstructive Lung Disease (GOLD); 2010.
2. Yen PM. Genomic and nongenomic actions of thyroid hormones. In: Braverman LE, Utiger RD, editors. *The Thyroid. A Fundamental and Clinical Text.* 9th ed. Philadelphia, PA: Lippincott Williams and Wilkins; 2005. p. 135-50.
3. Silva JE. Intermediary metabolism and the sympathoadrenal system in hypothyroidism. In: Braverman LE, Utiger RD, editors. *The Thyroid. A Fundamental and Clinical Text.* 9th ed. Philadelphia, PA: Lippincott Williams and Wilkins; 2005. p. 817-23.
4. Silva JE. Thermogenesis and sympathoadrenal system in thyrotoxicosis. In: Braverman LE, Utiger RD, editors. *The Thyroid. A Fundamental and Clinical Text.* 9th ed. Philadelphia, PA: Lippincott Williams and Wilkins; 2005. p. 607-20.
5. Saaresranta T, Polo O. Hormones and breathing. *Chest* 2002;122:2165-82.
6. Karadag F, Ozcan H, Karul AB, Yilmaz M, Cildag O. Correlates of non-thyroidal illness syndrome in chronic obstructive pulmonary disease. *Respir Med* 2007;101:1439-46.
7. Dimopoulou I, Ilias I, Mastorakos G, Mantzos E, Roussos C, Kouras DA, *et al.* Effects of severity of chronic obstructive pulmonary disease on thyroid function. *Metabolism* 2001;50:1397-401.
8. Beers MH, Berkow R. *The Merck Manual.* 17th ed. Whitehouse Station: Merck; 1999. p. 575.
9. Gow SM, Seth J, Beckett GJ, Douglas G. Thyroid function and endocrine abnormalities in elderly patients with severe chronic obstructive lung disease. *Thorax* 1987;42:520-5.
10. Coşkun F, Ege E, Uzaslan E, Ediger D, Karadağ M, Gözü O, *et al.* Evaluation of thyroid hormone levels and somatomedin-C (IGF-1) in patients with chronic obstructive pulmonary disease (COPD) and relation with the severity of the disease. *Tuberk Toraks* 2009;57:369-75.
11. Olivieri O, Girelli D, Stanzial AM, Rossi L, Bassi A, Corrocher R, *et al.* Selenium, zinc, and thyroid hormones in healthy subjects: Low T3/T4 ratio in the elderly is related to impaired selenium status. *Biol Trace Elem Res* 1996;51:31-41.

How to cite this article: Nikethan D. Clinical Study on Thyroid and Insulin Hormonal Dysfunction in Patients with Chronic Obstructive Pulmonary Disease. *Int J Sci Stud* 2019;7(5):12-15.

Source of Support: Nil, **Conflict of Interest:** None declared.

Comparative Evaluation of the Effects of Two Different Local Drug Delivery Systems Incorporating Green Tea and Turmeric Extracts in the Treatment of Chronic Periodontitis: A 2-month Clinical Trial

Vishwas Madaan¹, Ashwini M Padhye², Himani Gupta³

¹Director, Ivory Dental and Physiotherapy Centre, Seawoods, Navi Mumbai, Maharashtra, India, ²Professor and Head, Department of Periodontics, MGM Dental College and Hospital, Kamothe, Mumbai, Maharashtra, India, ³Senior Lecturer, Department of Periodontics, MGM Dental College and Hospital, Kamothe, Mumbai, Maharashtra, India

Abstract

Aim: This randomized, triple-blinded parallel study was aimed to evaluate the effects of two different local drug delivery (LDD) systems incorporating green tea and turmeric extracts as an adjunct to scaling and root planing (SRP) in the treatment of chronic periodontitis (CP).

Materials and Methods: Thirty-four subjects randomized to receive either Gel A or Gel B containing green tea or turmeric extract were included in the study. Following SRP, probing pocket depth (PPD), relative attachment level, gingival margin position (GMP), bleeding on probing, gingival index, and periodontal inflammatory surface area were recorded at baseline and 8 weeks after treatment with Gel A or Gel B.

Results: Mean PPD reduction from baseline to 8 weeks was -24.57% for Gel A while for Gel B, it was -22.99%. On comparison of GMP values for Gel A and Gel B at baseline (3.03 ± 1.10 and 2.80 ± 1.06) and at the end of 8 weeks (3.27 ± 1.41 and 3.27 ± 1.14), a statistically significant difference was noted. However, the percentage change was positive (7.69% and 16.67%) in both groups.

Conclusion: Both LDD gel systems were equally beneficial and showed a noteworthy reduction in the clinical parameters recorded when used as an adjunct to SRP in the treatment of CP.

Key words: Chronic periodontitis, Drug delivery systems, Green tea extract, Turmeric extract

INTRODUCTION

The cornerstone of periodontal treatment is non-surgical mechanical therapy. The beneficial effects of scaling and root planing (SRP) are based on achieving a reduced mass of bacteria in the periodontal pockets^[1] and an ecologic shift toward a less pathogenic microflora.^[2] Nonetheless, mechanical debridement alone may fail to eradicate

pathogenic organism from niches such as subepithelial gingival tissues, radicular dentinal tubuli, altered cementum, or furcation and other inaccessible areas difficult for adequate instrumentation.^[3] Effects of combining SRP with local or systemic antimicrobial agents have been evaluated for additional improvements in clinical results.^[4] Systemic antibiotics enter the periodontal tissues and counter the microorganisms beyond the reach of conventional mechanical debridement.^[5] However, they are administered at a higher dose to achieve necessary concentration at the target site and may lead to the development of hypersensitivity reactions, drug toxicity, resistant bacteria, etc. This has led to the invention of the local drug delivery (LDD) system.^[6]

Goodson in 1979 developed the concept of controlled release-LDD. This limits the drug to its target site,

Access this article online



www.ijss-sn.com

Month of Submission : 06-2019
Month of Peer Review : 07-2019
Month of Acceptance : 08-2019
Month of Publishing : 08-2019

Corresponding Author: Dr. Vishwas Madaan, Ivory Dental and Physiotherapy Centre, Seawoods, Navi Mumbai, Maharashtra, India.

therefore, yielding higher concentrations. Various LDD systems incorporating an antimicrobial agent for use in the periodontal pocket include fibers, films, injectable systems, gels, strips and compacts, vesicular, and microparticle and nanoparticle systems. Of these, the injectable systems are particularly attractive due to the ease of application, the reduced cost of the therapy, and the ability of the gel to completely fill the periodontal pocket.^[7]

An LDD gel comprises an active agent dispersed in a vehicle. Osmotically reactive thermosetting gels are widely used as porous solids that adhere on application of pressure. They configure as swollen networks possessing both the cohesive properties of solids and the diffusive transport characteristics of liquids. Poloxamer 407 is one such gel that remains stable in its native state and also harbors a hydrogel character that allows it to provide a time-dependent drug release making it suitable for subgingival use as a vehicle for sustained drug delivery.^[8]

Side effects of various antimicrobials, tested subgingivally, have led the researchers in the field of phytosciences, to harness antimicrobial activity of herbs and to utilize their medicinal aspects. Globally, plant extracts such as allicin, proanthocyanides, terpenes, alkaloids, catechol, and flavonoids^[9] have been employed for their anti-inflammatory, antibacterial, antifungal, and antiviral activities.^[10] *Camellia sinensis*, commonly known as tea, contains a number of bioactive chemicals and is particularly rich in flavonoids including catechins^[11] that are strong antioxidants and possesses bactericidal effects that alleviate symptoms of periodontal disease. Turmeric, a rhizome of *Curcuma longa* which is a common antiseptic containing curcuminoids, acts as potent scavengers of oxidant radicals.^[12]

Green tea extracts (GTEs)^[13] and turmeric extracts^[14] in LDD systems have been used in the treatment of periodontitis. However, there is no reported literature comparing the clinical effects of these two extracts in a novel Pluronic polymer-based LDD system. Hence, this study was designed as a randomized, triple-blinded, parallel trial that aimed to evaluate and compare the effects of two different LDD systems incorporating GTE and turmeric extracts as an adjunct to SRP in the treatment of chronic periodontitis (CP).

MATERIALS AND METHODS

Injectable biodegradable LDD gel systems with two different herbal extracts were prepared according to the cold method.^[15] Poloxamer 407 (20% concentration) gave the best handling characteristics with regard to

film thickness and viscosity and was used as a vehicle in our study.^[16] About 20 g of Poloxamer 407 added to 100 ml of distilled water cooled at 2–8°C, agitated with a magnetic stirrer, and yielded a gel with 20% critical micellar concentration (CMC); and for this CMC, the sol–gel transition temperature was found to be 35–38°C. Each herbal extract along with 1.5% weight/volume of carbopol 934 was added separately to 20% Poloxamer 407 so as to yield two different gels with a drug concentration of 1 mg/ml as determined by ultraviolet spectrophotometer at 765 nm (UV-1800, Shimadzu, Japan). These gels were sterilized using gamma irradiation at 2.5 Mrad and supplied in 2 ml syringes covered and labeled as Gel “A” or Gel “B” by the pharmacist from C.U. Shah College of Pharmacy, Mumbai, India, fitted with a blunt cannula bent at 45° having a diameter of 0.9 mm. The LDD syringes were stored in a refrigerator at 2–8°C until further use.

Experimental Design and Treatment Protocols

The study protocol was previously approved by the institutional ethics committee and the study was conducted in accordance with the Declaration of Helsinki, 7th revision in 2013. The study population included 34 subjects (21 males and 13 females), 30–55 years of age, referred to the outpatient section, Department of Periodontics, MGM Dental College and Hospital, Navi Mumbai, India (First patient enrollment – September 5, 2014; last patient follow-up – October 6, 2015). The study aims together with any potential benefits or detrimental effects, and alternatives were discussed with the subjects, and a written, signed, and informed consent to participate in the study was obtained. To calculate the sample size^[17] at 80% power, the level of significance was set at 0.05, to detect a standard deviation (SD) in relative attachment level (RAL) at 0.21.^[18] This data when analyzed by MedCalc Statistical Software version 15.8 (MedCalc Software bvba, Ostend, Belgium; <http://www.medcalc.org>; 2015) yielded a sample size of 34 per group. Hence, it was decided to select 34 subjects with CP amounting to a total of 68 sites to be evaluated.

All systematically healthy subjects diagnosed with CP willing to participate and maintain regular appointments were considered for the study. The sites were selected based on the following criteria: local factors, two non-adjacent sites with probing pocket depth of 5–7 mm and interproximal attachment loss of ≥3mm measured using North Carolina-15 probe with radiographic evidence of alveolar bone loss. Exclusion criteria included subjects with/who have a known history of allergic reactions to turmeric and/or green tea, presence of three or more adjacent periodontal pockets on the same potential test teeth, received any form of periodontal therapy, surgical or non-surgical within the past 6 months, received antibiotic/anti-inflammatory therapy within the past 6 months,

presence of pulpal or periapical involvement on qualifying teeth, pregnant and lactating women, and smokers.

Initially, a full-mouth periodontal examination was performed and subjects fulfilling inclusion criteria underwent SRP. On recall after 1 week, which was considered as the baseline visit, two test sites with maximum PPD were selected to receive the gels. PPD, RAL, gingival margin position (GMP), bleeding on probing (BOP),^[19] gingival index (GI),^[20] and periodontal inflammatory surface area (PISA) score^[21] were recorded at baseline and at the end of 8 weeks. The probing site measurements were standardized using a custom-made acrylic stent, considering the apical margin of stent as a fixed reference point for RAL and GMP measurements. BOP, GI, and PISA were also recorded at this visit. All measurements were performed by a single investigator. After isolation with cotton rolls, the two selected sites were randomized by coin toss method to receive either Gel A or Gel B, starting from apical end of the pocket and moving coronally till the pocket just overfilled. Both test sites were covered with a eugenol-free periodontal dressing (Coe-Pak™ GC America Inc., Alsip IL, USA). Subjects were advised to discontinue tooth brushing at the test sites for 7 days and refrain from any other unassigned means of oral hygiene practices during the tenure of this study. Subjects were recalled, after 7 days of gel application, for the removal of the periodontal dressing and home care instructions were reinforced to include brushing at the test sites as well. All subjects were instructed to report any untoward event. The contents of Gel A or Gel B were kept masked from the investigator; the patient and the statistician (triple-blind randomized parallel trial design) were revealed only after the completion of the study. Reduction in PPD, 0–8 weeks, was defined as the primary outcome variable while change in RAL, GMP, BOP, GI, and PISA was set as secondary outcome variables.

Statistical Analyses

Data collected at baseline and at the end of 8 weeks were analyzed using Windows PC-based software – MedCalc Statistical Software, version 15.8 at alpha 0.05 with 95% confidence limits. PISA was calculated based on 6-point PPD and BOP values from an Excel sheet freely available at www.parsprototo.in for the test teeth. Values were averaged (mean \pm SD) for each parameter. The distributions of all variables were checked for normality using the D'Agostino-Pearson test which gave a statistically significant ($P < 0.05$). As all the distributions violated assumption of normality, a decision was taken to use non-parametric tests. Pair-wise comparison of means of all parameters between the two groups was done using Mann–Whitney U-test, to ascertain pairs that deviated considerably at $P < 0.05$.

Wilcoxon signed-rank test was used to compare within group the means of all parameters at baseline and at the end of 8 weeks. Spearman's rank correlation coefficient analysis was done to identify any association between the parameters.

RESULTS

The present study was a triple-blind, prospective cohort, and randomized trial with a sample size of 34 subjects diagnosed with CP. Four subjects were excluded from the study: Two reported using mouthwashes and two reported back with dislodged periodontal dressings; making the effective sample size as 60 sites in 30 subjects. During the course of the study, no untoward consequences were reported.

Table 1 represents mean \pm SD for all parameters recorded at baseline and at the end of 8 weeks. Mean baseline PPD for Gel A and Gel B was 5.83 ± 0.79 and 5.80 ± 0.55 while at the end of 8 weeks; it was 4.40 ± 0.67 and 4.47 ± 0.57 , respectively. PPD reduction [Graph 1] from baseline to 8 weeks for Gel A was -24.57% while for Gel B reduction was -22.99% which was statistically significant for both groups ($P < 0.0001$). Mean RAL reduction for Gel A from baseline (8.90 ± 1.42) to 8 weeks (7.50 ± 1.33) and similarly for Gel B (baseline 8.60 ± 1.07 to 8 weeks 7.57 ± 1.10) was statistically significant for both groups ($P < 0.0001$) [Table 2].

On comparing the GMP values at baseline (3.03 ± 1.10 and 2.80 ± 1.06) and at the end of 8 weeks (3.27 ± 1.41 and 3.27 ± 1.14) for Gel A and Gel B, a statistically significant difference was noted ($P = 0.0313$ and $P = 0.010$,

Table 1: Results of Mann–Whitney “U”-test carried out at 5% level of significance to test the difference between the mean of the two test gels with respect to PPD, RAL, GMP, BOP, GI, and PISA

Parameters	Timeline	Gel A mean \pm SD	Gel B mean \pm SD	P-value
PPD (mm)	Baseline	5.83 \pm 0.79	5.80 \pm 0.55	0.850
	8 weeks	4.40 \pm 0.67	4.47 \pm 0.57	0.681
RAL (mm)	Baseline	8.90 \pm 1.42	8.60 \pm 1.07	0.360
	8 weeks	7.50 \pm 1.33	7.57 \pm 1.10	0.834
GMP (mm)	Baseline	3.03 \pm 1.10	2.80 \pm 1.06	0.407
	8 weeks	3.27 \pm 1.41	3.27 \pm 1.14	1.000
BOP (%)	Baseline	74.17 \pm 16.72	72.50 \pm 16.54	0.699
	8 weeks	38.33 \pm 14.28	35.83 \pm 12.60	0.475
GI score	Baseline	1.63 \pm 0.22	1.58 \pm 0.23	0.313
	8 weeks	1.23 \pm 0.16	1.23 \pm 0.15	0.837
PISA (mm ²)	Baseline	52.62 \pm 19.16	47.91 \pm 19.64	0.351
	8 weeks	21.45 \pm 7.05	18.93 \pm 8.54	0.218

PPD: Probing pocket depth, RAL: Relative attachment level, GMP: Gingival margin position, BOP: Bleeding on probing, GI: Gingival index PISA: Periodontal inflammatory surface area, SD: Standard deviation

respectively). However, the percentage change was positive (7.69% and 16.67%) in both groups [Table 2 and Graph 1].

BOP was present at baseline in most sites (74.17% and 72.50% for Gel A and Gel B, respectively); however, the proportions dropped significantly at week 8 (38.33% and 35.83%; $P < 0.0001$). These proportions were not statistically significant between the two groups at any of these time points. On comparison of GI scores at baseline (1.63 ± 0.22 and 1.58 ± 0.23) and at week 8 (1.23 ± 0.16 and

1.23 ± 0.15) for both groups, a statistically significant result was obtained ($P < 0.0001$). Similarly, statistically significant PISA score reduction was seen between baseline (52.62 ± 19.16 and 47.91 ± 19.64) and at week 8 (21.45 ± 7.05 and 18.93 ± 8.54) ($P < 0.0001$). However, the differences between the groups for all parameters were not statistically significant ($P > 0.05$).

Spearman's rank correlation coefficient analysis [Table 3] demonstrated a positive correlation between PPD and RAL and PPD and BOP for Gel A at the end of 8 weeks. GMP and RAL exhibited a strong positive correlation. PISA and BOP also exhibited a strong positive correlation. The results for Gel B after 2 months showed a strong positive correlation between GMP and RAL.

Table 2: Result of Wilcoxon signed-rank test was done to compare the changes in the mean PPD, RAL, GMP, BOP, GI, and PISA at baseline and after 8 weeks within the two test gels

Groups	PPD	RAL	GMP	BOP	GI	PISA
Gel A	<0.0001*	<0.0001*	0.0313*	<0.0001*	<0.0001*	<0.0001*
Gel B	<0.0001*	<0.0001*	0.010*	<0.0001*	<0.0001*	<0.0001*

* $P < 0.05$ – Statistically significant. PPD: Probing pocket depth, RAL: Relative attachment level, GMP: Gingival margin position, BOP: Bleeding on probing, GI: Gingival index PISA: Periodontal inflammatory surface area

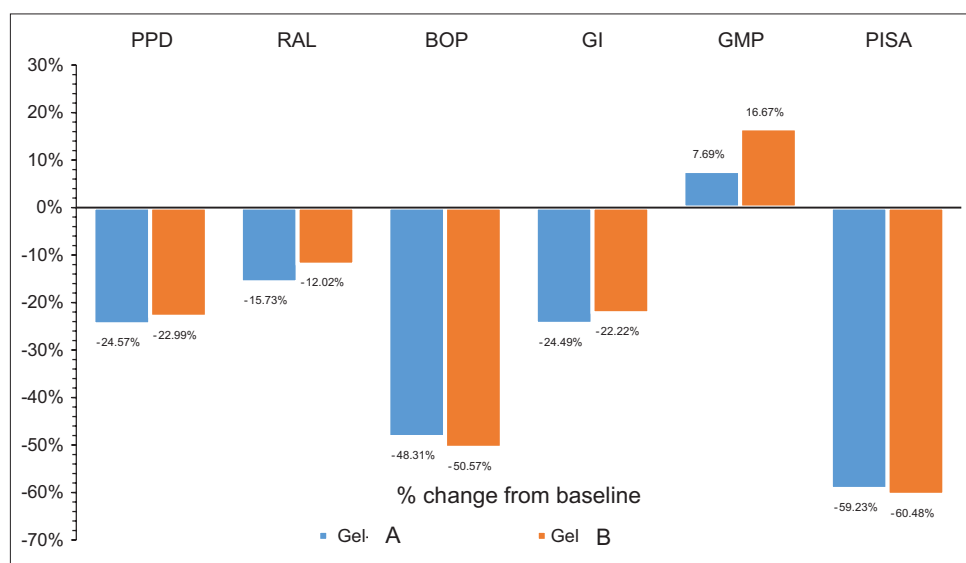
DISCUSSION

LDD systems have been developed with the aim of overcoming the limitations of conventional therapy and

Table 3: Spearman's rank correlation coefficient analysis was done to observe for any correlation between the PPD, RAL, GMP, BOP, GI, and PISA values

Gel A							Gel B						
	PPD	RAL	BOP	GI	GMP	PISA		PPD	RAL	BOP	GI	GMP	PISA
PPD	1.000	0.432*	0.432*	0.151	-0.099	0.147	PPD	1.000	0.042	0.221	0.049	-0.447*	-0.102
RAL	-	1.000	0.211	0.075	0.788**	-0.304	RAL	-	1.000	-0.127	-0.041	0.681**	0.222
BOP	-	-	1.000	0.355	-0.059	0.469**	BOP	-	-	1.000	0.359	-0.117	0.307
GI	-	-	-	1.000	0.082	0.248	GI	-	-	-	1.000	-0.006	0.059
GMP	-	-	-	-	1.000	-0.409*	GMP	-	-	-	-	1.000	0.164
PISA	-	-	-	-	-	1.000	PISA	-	-	-	-	-	1.000

If the r value is -1, there is a perfect negative correlation, If the r value falls between -1 and -0.5, there is a strong negative correlation, If the r value falls between -0.5 and 0, there is a weak negative correlation, If the r value is 0, there is no correlation, *If the r value falls between 0 and 0.5, there is a weak positive correlation, **If the r value falls between 0.5 and 1, there is a strong positive correlation, If the r value is 1, there is a perfect correlation. PPD: Probing pocket depth, RAL: Relative attachment level, GMP: Gingival margin position, BOP: Bleeding on probing, GI: Gingival index. PISA: Periodontal inflammatory surface area



Graph 1: Percentage change in probing pocket depth, relative attachment level, gingival margin position, bleeding on probing, gingival index, and periodontal inflammatory surface area from baseline to 8 weeks

providing highly concentrated drugs at the target site, improved patient compliance with reduced propensity for the development of bacterial resistance.^[22] The currently available LDD systems are often expensive and difficult to procure in developing nations like India.^[7]

Green tea catechins (GTCs) are bactericidal against a variety of periodontopathogens such as *Porphyromonas gingivalis* (Pg),^[23] *Prevotella intermedia* (Pi),^[24] and *Aggregatibacter actinomycetemcomitans*.^[25] They are known inhibitors of cysteine proteinases of Pg and protein tyrosine phosphatase in Pi,^[26] along with inhibition of collagenase activity. Hirsawa *et al.* (2002) found that GTC showed a bactericidal effect against Pg and Pi with a minimum inhibitory concentration of 1.0 mg/ml. Turmeric has been employed traditionally in Indian medicine for several decades due to its proven properties as a potent anti-inflammatory, antioxidant, antimicrobial, and antimutagenic agent.^[27] It exerts its anti-inflammatory action by inhibition of nuclear factor-kappa beta ligand activation^[28] and downregulation of pro-inflammatory enzyme cyclooxygenase-2^[29] by reducing the inflammatory mediators generated through arachidonic acid pathway.^[30]

Poloxamer 407 has unique thermoreversible characteristics as it behaves like a mobile viscous liquids at 2–8°C, which is transformed into a semisolid gel at body temperature (37°C).^[31] As an LDD vehicle, it possesses a surfactant ability that accounts for its higher biocompatibility and bioadhesivity, allowing adhesion to the periodontal pocket and, finally, it can be rapidly eliminated through normal catabolic pathways, with a half-life of 25 h,^[32] decreasing the risk of irritative or allergic host reactions.^[33]

GTE and turmeric extracts were relatively easy and inexpensive to prepare when compared to other herbal formulations such as garlic, pomegranate, and cranberry, which require extensive extraction process and specialized reagents to stabilize the extracts. To date, no study has compared the effects of GTEs with that of turmeric extracts in an LDD system in the treatment of CP. Hence, the main purpose of this study was to assess and compare the clinical efficacy of two different herbal agents, i.e., GTE and turmeric extract in a novel gel-based LDD system, consisting of Poloxamer 407 as vehicle, as an adjunct to SRP in the treatment of CP.

Clinical parameters such as PPD, RAL, BOP, and GI were recorded at baseline and after 8 weeks. PISA quantifies the inflammatory burden posed by periodontitis as it reflects the surface area of bleeding pocket epithelium in square millimeters. It was calculated using conventional parameters of periodontal assessment, such as PPD and

BOP measurements. GMP was measured along with PPD and RAL to account for probing depth reduction due to gingival recession.

In the present study, PPD significantly decreased from the baseline to 8 weeks for both the test gels (PPD reduction for Gel A 1.43 and for Gel B 1.33) with a significant gain in RAL (baseline – 8.90 ± 1.42 and 8.60 ± 1.07; 8 weeks – 7.50 ± 1.33 and 7.57 ± 1.10), but there was no statistically significant difference between the two groups (PPD baseline $P = 0.850$ and 8 weeks $P = 0.681$ and RAL baseline $P = 0.360$ and 8 weeks $P = 0.834$), indicating that green tea and turmeric were both equally beneficial for reducing the PPD and obtaining gain in RAL. PPD and RAL results for Gel A consisting of GTE are in accordance with a study by Chava and Vedula^[18] and with findings of a meta-analysis done by Kalsi *et al.*^[4] PPD and RAL results of Gel B containing turmeric extract are similar to those presented by Bhatia *et al.*^[34] (PPD reduction of 1.60) and Behal *et al.*^[35] (PPD reduction of 1.40). The significant gain in RAL of Gel B has been attributed to curcumin that enhances wound healing by causing an increase in fibronectin and promotes migration of epithelial cells to wounded sites by promoting localization of TGF-β1, thus helping reepithelization.^[36]

A statistically significant reduction in the percentage of sites with BOP ($P < 0.0001$) and GI ($P < 0.0001$) was seen in both the test groups. Similar results were obtained by Awadal^[37] and Sarin *et al.*^[38] with GTE and Jaswal *et al.*^[39] and Mali *et al.*^[40] with turmeric extract.

The values of GMP for Gel A ($P = 0.0313$) and Gel B ($P = 0.010$), though minor, showed a statistically significant increase after 8 weeks when compared to baseline. This observation indicates that PPD reduction could also be attributed to gingival recession. Consequently, the Spearman's correlation coefficient test at 8 weeks shows a weak correlation between GMP and PPD ($r = 0.447$) in Gel B; however, no such correlation was found between GMP and PPD in Gel A. This confirms the observation that Gel B containing turmeric extract caused more recession.

The LDD agents used in this study prove to be equally effective when used as an adjunct to SRP in the treatment of CP. However, it should be noted that both the test gels were used as an adjunct to SRP and no attempt was made to evaluate the gels as a monotherapy agent. Additional long-term studies are recommended to evaluate the microbiologic and biochemical effects of GTE and turmeric extract LDD systems. Furthermore, the effective therapeutic concentrations achieved in gingival crevicular fluid need to be elucidated.

CONCLUSION

This study is first of its kind that has compared the efficacy of GTE and turmeric extract in a poloxamer gel when used as an LDD agent, as an adjunct to SRP in the treatment of CP. Both the LDD agents were equally beneficial and showed a reduction in the clinical parameters which were statistically significant. Hence, they prove as a safe and cost-effective treatment modality.

REFERENCES

- Bollen CM, Quirynen M. Microbiological response to mechanical treatment in combination with adjunctive therapy. A review of the literature. *J Periodontol* 1996;67:1143-58.
- Cugini MA, Haffajee AD, Smith C, Kent RL Jr, Socransky SS. The effect of scaling and root planing on the clinical and microbiological parameters of periodontal diseases: 12-month results. *J Clin Periodontol* 2000;27:30-6.
- Gontiya G, Galgali SR. Effect of hyaluronan on periodontitis: A clinical and histological study. *J Indian Soc Periodontol* 2012;16:184-92.
- Kalsi R, Vandana KL, Prakash S. Effect of local drug delivery in chronic periodontitis patients: A meta-analysis. *J Indian Soc Periodontol* 2011;15:304-9.
- Genco RJ. Antibiotics in the treatment of periodontal diseases. *J Periodontol* 1981;52:545-85.
- Walker CB, Pappas JD, Tyler KZ, Cohen S, Gordon JM. Antibiotic susceptibilities of periodontal bacteria. *In vitro* susceptibilities to eight antimicrobial agents. *J Periodontol* 1985;56 Suppl 11:67-74.
- Kaplish V, Walia MK, Kumar SL. Local drug delivery systems in the treatment of periodontitis: A review. *Pharmacophore* 2013;4:39-49.
- Escobar-Chávez JJ, López-Cervantes M, Naik A, Kalia YN, Quintanar-Guerrero D, Ganem-Quintanar A, *et al.* Applications of thermo-reversible pluronic F-127 gels in pharmaceutical formulations. *J Pharm Pharm Sci* 2006;9:339-58.
- Palombo EA. Traditional medicinal plant extracts and natural products with activity against oral bacteria: Potential application in the prevention and treatment of oral diseases. *Evid Based Complement Altern Med* 2009;2011:15.
- Aibinu I. Medicinal plants as antimicrobials. In: Odugbemi T, editor. *Outline and Pictures of Medicinal Plants from Nigeria*. 1st ed. Lagos: University of Lagos press; 2006. p. 53-64.
- Cabrera C, Artacho R, Giménez R. Beneficial effects of green tea a review. *J Am Coll Nutr* 2006;25:79-99.
- Mathur V, Tijare M, Desai A, Gupta S, Kallianpur S. Curcumin oral cure from the Indian curry. *Int J Pharmacother* 2014;4:137-40.
- Rattanasuwan K, Rassameemasmaung S, Sangalungkarn V, Komoltri C. Clinical effect of locally delivered gel containing green tea extract as an adjunct to non-surgical periodontal treatment. *Odontology* 2016;104:89-97.
- Nagpal M, Sood S. Role of curcumin in systemic and oral health: An overview. *J Nat Sci Biol Med* 2013;4:3-7.
- Schmolka IR. Artificial skin. I. Preparation and properties of pluronic F-127 gels for treatment of burns. *J Biomed Mater Res* 1972;6:571-82.
- Galgatte A, Chaudhari E. Preformulation study of poloxamer 407 gels: Effect of additives. *Int J Pharm Sci* 2014;6:130-3.
- Hulley SB, Cummings SR, Browner WS, Grady D, Newman TB. *Designing Clinical Research: An Epidemiologic Approach*. 4th ed. Philadelphia, PA: Lippincott Williams and Wilkins; 2013. p. 73.
- Chava VK, Vedula BD. Thermo-reversible green tea catechin gel for local application in chronic periodontitis: A 4-week clinical trial. *J Periodontol* 2013;84:1290-6.
- Ainamo J, Bay I. Problems and proposals for recording gingivitis and plaque. *Int Dent J* 1975;25:229-35.
- Loe H, Silness J. Periodontal disease in pregnancy. I. prevalence and severity. *Acta Odontol Scand* 1963;21:533-51.
- Nesse W, Abbas F, van der Ploeg I, Spijkervet FK, Dijkstra PU, Vissink A, *et al.* Periodontal inflamed surface area: Quantifying inflammatory burden. *J Clin Periodontol* 2008;35:668-73.
- Wilson TJ, Kornman KS. *Fundamentals on Periodontics*. 2nd ed. Chicago: Quintessence Publishing; 2003.
- Khan R, Islam B, Akram M, Shakil S, Ahmad A, Ali SM, *et al.* Antimicrobial activity of five herbal extracts against multi drug resistant (MDR) strains of bacteria and fungus of clinical origin. *Molecules* 2009;14:586-97.
- Hirasawa M, Takada K, Makimura M, Otake S. Improvement of periodontal status by green tea catechin using a local delivery system: A clinical pilot study. *J Periodontol Res* 2002;37:433-8.
- Nakanishi T, Mukai K, Yumoto H, Hirao K, Hosokawa Y, Matsuo T, *et al.* Anti-inflammatory effect of catechin on cultured human dental pulp cells affected by bacteria-derived factors. *Eur J Oral Sci* 2010;118:145-50.
- Makimura M, Hirasawa M, Kobayashi K, Indo J, Sakanaka S, Taguchi T, *et al.* Inhibitory effect of tea catechins on collagenase activity. *J Periodontol* 1993;64:630-6.
- Banerjee A, Nigam SS. Antimicrobial efficacy of the essential oil of *Curcuma longa*. *Indian J Med Res* 1978;68:864-6.
- Plummer SM, Holloway KA, Manson MM, Munks RJ, Kaptein A, Farrow S, *et al.* Inhibition of cyclo-oxygenase 2 expression in colon cells by the chemopreventive agent curcumin involves inhibition of NF-kappaB activation via the NIK/IKK signalling complex. *Oncogene* 1999;18:6013-20.
- Chen H, Zhang ZS, Zhang YL, Zhou DY. Curcumin inhibits cell proliferation by interfering with the cell cycle and inducing apoptosis in colon carcinoma cells. *Anticancer Res* 1999;19:3675-80.
- Sajithal GB. Effect of curcumin on products of arachidonic acid metabolism for anti-arthritis therapy. *Biochem Pharmacol* 1998;56:1607-14.
- Singh K, Kumar SL. Injectable *in-situ* gelling controlled release drug delivery system. *Int J Drug Dev Res* 2012;4:56-69.
- Boodhwani M, Feng J, Mieno S, Ramlawi B, Sodha N, Clements R, *et al.* Effects of purified poloxamer 407 gel on vascular occlusion and the coronary endothelium. *Eur J Cardiothorac Surg* 2006;29:736-41.
- Madan M, Bajaj A, Lewis S, Udupa N, Baig JA. *In situ* forming polymeric drug delivery systems. *Indian J Pharm Sci* 2009;71:242-51.
- Bhatia M, Urolagin SS, Pentyala KB, Urolagin SB, K B M, Bhoi S, *et al.* Novel therapeutic approach for the treatment of periodontitis by curcumin. *J Clin Diagn Res* 2014;8:ZC65-9.
- Behal R, Mali AM, Gilda SS, Paradkar AR. Evaluation of local drug-delivery system containing 2% whole turmeric gel used as an adjunct to scaling and root planing in chronic periodontitis: A clinical and microbiological study. *J Indian Soc Periodontol* 2011;15:35-8.
- Sidhu GS, Singh AK, Thalloor D, Banaudha KK, Patnaik GK, Srimal RC, *et al.* Enhancement of wound healing by curcumin in animals. *Wound Repair Regen* 1998;6:167-77.
- Awadalla H. Green tea use on oral health. *Int J Dent Hyg* 2011;9:110-6.
- Sarin S, Marya C, Nagpal R, Oberoi SS, Rekhi A. Preliminary clinical evidence of the antiplaque, antigingivitis efficacy of a mouthwash containing 2% green tea a randomised clinical trial. *Oral Health Prev Dent* 2015;13:197-203.
- Jaswal R, Dhawan S, Grover V, Malhotra R. Comparative evaluation of single application of 2% whole turmeric gel versus 1% chlorhexidine gel in chronic periodontitis patients: A pilot study. *J Indian Soc Periodontol* 2014;18:575-80.
- Mali AM, Behal R, Gilda SS. Comparative evaluation of 0.1% turmeric mouthwash with 0.2% chlorhexidine gluconate in prevention of plaque and gingivitis: A clinical and microbiological study. *J Indian Soc Periodontol* 2012;16:386-91.

How to cite this article: Madaan V, Padhye AM, Gupta H. Comparative Evaluation of the Effects of Two Different Local Drug Delivery Systems Incorporating Green Tea and Turmeric Extracts in the Treatment of Chronic Periodontitis: A 2-month Clinical Trial. *Int J Sci Stud* 2019;7(5):16-21.

Source of Support: Nil, **Conflict of Interest:** None declared.

Study on Prognostic Value of Electrophysiological Tests in Bell's Palsy

Y Kingsly Jebasingh¹, A Sethuram²

¹Professor, Department of Neurology, Kanyakumari Government Medical College, Kanyakumari, Tamil Nadu, India, ²Associate Professor, Department of Neurology, Kanyakumari Government Medical College, Kanyakumari, Tamil Nadu, India

Abstract

Introduction: Bell's palsy is an idiopathic peripheral disease of the seventh cranial nerve. More than 70% of patients attain complete clinical recovery, with no noticeable residua. Electrophysiological tests may offer valuable information in defining the severity of nerve injury and a possible subsequent dysfunction.

Aim: This study aims to assess the prognostic value of electrophysiological tests in the management of Bell's palsy.

Materials and Methods: All the patients with Bell's palsy and without clinical evidence of other cranial nerve damage or central nervous system diseases were included in the study. Nerve conduction study was performed on the 14th day or on the first visit of the patient to the hospital.

Results: In 101 patients, majority of patients come under Grade IV (43.6%) and next comes Grade V (31.7%). Eighty-two patients (81.2%) had normal latency, among these, 73 cases recovered within 6 months. Of 17 who had prolonged latency, seven patients recovered fully.

Conclusions: Electrophysiological studies can predict the duration of the clinical recovery and the outcome of the illness. The amplitude ratio of compound muscle action potential is the most reliable parameter in assessing the prognosis.

Key words: Bell's Palsy, Electromyography, Nerve conduction study

INTRODUCTION

Bell's palsy is an idiopathic peripheral disease of the seventh cranial nerve. This is the most frequent cranial mononeuropathy with an annual incidence of 10–40 cases per 100,000 population with geographical variations.^[1,2] It can occur at any age, but mostly in the third and fourth decade of life. The disease was described as a distinct entity by Sir Charles Bell in 1893, and since then, it has commonly been referred to as Bell's palsy. It is seen as often in men as in women. Those at high risk include pregnant women and people with diabetes mellitus. About 10% of those with Bell's palsy have a family history of the condition. More than 70%

of patients attain complete clinical recovery, with no noticeable residua.^[1] Persistent sequelae are usually noted in cases with profound axonal loss. Electrophysiological tests may offer valuable information in defining the severity of nerve injury and a possible residual dysfunction.^[3]

Electrophysiological tests may offer valuable information in defining the severity of nerve injury and possible subsequent dysfunction. Previous electrophysiological investigations point to a special prognostic value of the amplitude of compound muscle action potential (CMAP) in Bell's palsy since the CMAP amplitude depends on the number of excitable axons. The degree of degeneration of nerve fibers is directly proportional to the decrease in the CMAP amplitude.^[4-7]

Aims

This study aims to assess the prognostic value of electrophysiological tests in Bell's palsy.

Access this article online



www.ijss-sn.com

Month of Submission : 06-2019
Month of Peer Review : 07-2019
Month of Acceptance : 08-2019
Month of Publishing : 08-2019

Corresponding Author: Dr. A Sethuram, Department of Neurology, Kanyakumari Government Medical College, Kanyakumari, Tamil Nadu, India.

MATERIALS AND METHODS

This prospective study was done on 101 patients with clinical signs of Bell's palsy, of both sexes, in various age groups who attended the Neurology Outpatient Department, Institute of Neurology, Madras Medical College and Government General Hospital, Chennai. All the patients underwent neurological and ENT evaluation.

Inclusion Criteria

All the patients with Bell's palsy and without clinical evidence of other cranial nerve damage or central nervous system diseases were included in the study.

Exclusion Criteria

Patients with middle ear disease or posterior cranial fossa disease and chronic illness such as diabetes mellitus, hypertension, and malignancy were excluded from the study.

Grading was done on the first visit and on the 14th day, 1st, 2nd, 3rd, 6th, 9th, and 12th months to assess the improvement, response to treatment.

Nerve conduction study was performed on the 14th day or on the first visit of the patient to the hospital.

For the CMAP examination, supramaximal stimulation was applied for 0.2 ms duration over the trunk of the facial nerve, using the bipolar stimulating electrode with the anode between the ramus of the mandible and the mastoid and the cathode in front of the tragus of the ear. The CMAP was recorded with a plate electrode in the target muscles, orbicularis oculi, and orbicularis oris. The amplitude and the latency of the CMAP were analyzed.

The mean amplitudes on the affected side were computed as the percentage ratio of the normal amplitudes on the healthy side (taken as 100%). The patients were grouped according to the ratio into three groups:

1. A (30–100%)
2. B (10–30 %)
3. C (<10% or not stimulatable).

The latency of the CMAP was also recorded in the same muscles on both the healthy and affected side. The corresponding mean value was computed, and the patients were grouped according to the latency recorded into three groups.

- 1) A (<4 ms)
- 2) B (More than 4 ms) and
- 3) C with no CMAP recorded.

To estimate prognostic values, the electrophysiological parameters, of amplitude and latency of the CMAPs, were correlated with the duration of clinical recovery.

RESULTS

One hundred and one patients with signs of the Bell's palsy were included in this study. Most of the cases belong to the age group of 31–40. Only 2.9% of patients belonged to the age group of 61–70. In the present study, sex ratio was almost even. Forty-seven were female (46.6%) and 54 were male (53.4%). Majority of patients come under Grade IV (43.6%) and next comes Grade V (31.7%), III (19.8%), and the least in Grade VI (4.9%).

Of 26 patients in Group A, 23 patients had complete recovery. Of eight patients in Group B, three patients recovered and the one patient in Group C had recovered within 6 months.

All the patients in Group A had complete recovery. Ten patients showed complete improvement in Group B and of 10 cases in Group C, only one recovered Table 1 and 2.

During the 1st week, the CMAP latency was within normal limits and of the 35 patients, 10 had an incomplete recovery Table 3.

Eighty-two patients (81.2%) had normal latency, among these, 73 cases recovered within 6 months. Of 17 who had prolonged latency, seven patients recovered fully and two patients in Group C did not show any improvement Table 4.

DISCUSSION

Matthews in his study observed that older age could badly influence the course of the illness.^[8] Heath *et al.*^[9] presented the results of their research showing that the average age of patients who had a rapid and complete recovery was 35.8 ± 15.9 years, while patients with an incomplete recovery were 55.4 ± 18.8 years old. The results of this study had not shown the existence of a correlation between the age and the duration, degree of clinical recovery. However, it is necessary to point out that older individuals had poor recovery when compared to younger individuals. However, in these individuals, the other factors responsible for poor recovery such as severe degree of weakness and very low CMAP amplitude were present.

Djordjević and Djurić have shown in their clinical research that in a certain number of patients had a changing neurological deficit, during the first 2 weeks of the illness. They were suggesting that the prognosis based on the degree of the motor deficit was significantly limited in the early stage of the illness.^[10]

The poor correlation between the degree of the paresis in the early stage of the illness, and duration and degree of recovery was observed in the present series also.

It was noted by May *et al.*^[11] and Hauser *et al.*^[12] that majority of patients with signs of incomplete facial paralysis of the third and fourth degree, on the 14th day of the illness, had a rapid and complete recovery.

The present study shows that patients with signs of incomplete facial paralysis of the third and fourth degree, on the 14th day of the illness, had a rapid and complete recovery.

These results showed that an incomplete facial paralysis had a complete clinical recovery, while a complete paralysis indicated bad prognosis, which is consistent with literature data.^[11,12] An absolute bad prognostic sign was the lack of any movement of the mimic musculature during the first 4 weeks.

CMAP Amplitude 1st week

Analyzing the CMAP recorded in the 2nd week of the illness in the above 35 patients, all the patients in Group A had complete recovery. Of 11 patients in Group B, 10 patients showed complete improvement and of 10 cases in Group C, only one recovered. This observation showed that CMAP recorded in the 2nd week was very helpful in assessing the prognosis of the disease.^[10] This observation correlates with Esslen's reports^[13] who showed that the CMAP amplitude decrease is recorded from the 3rd to the 10th day, while Tojima *et al.*^[14] in their results showed that this decrease occurred in the first 7 days and remained stable thereafter.

The results observed on the 14th day of the illness showed a strong positive correlation between the rate of recovery and CMAP amplitude. The more the amplitude is decreased, the slower was the recovery. Most of the patients whose amplitude was more than 30% of the normal side recovered completely during the first 2 months, suggesting mild damage of the nerve (neuropraxia). The patients whose amplitude values were between 10% and 30% recovered within 6 months which corresponded to the second type of nerve damage (axonotmesis). The distinct amplitude decreases to 0–10% pointed to severe nerve damage (neurotmesis) and an incomplete clinical recovery. The above observation correlated well with the observations made by others.^[10]

In this study, there was a decrease of CMAP amplitude in seven patients in the clinically normal side which did not show any motor deficit. Among the seven cases, five cases showed this abnormality in the 1st week and the other two cases on the 9th and 11th days, respectively, depicting subclinical involvement on the other side also. Since electrophysiological studies were done only in 35 patients in the 1st week, this may be an underestimation. If electrophysiological studies were done in the 1st week in all cases, the identification of the subclinical cases might be high. A similar observation was made by Natarajan and

Table 1: Analysis of compound muscle action potential recorded in the 1st week in 35 patients and recovery

Amp ratio	Recovery in months			In complete recovery in 12 months	Total
	<2	2–6	>6		
A	15	8	0	3	26
B	0	3	0	5	8
C	0	1	0	0	1
Total	15	12	0	8	35

Table 2: Analysis of compound muscle action potential recorded after 2 weeks in same 35 patients and recovery

Amp ratio	Recovery in months			In complete recovery in 12 months	Total
	<2	2–6	>6		
A	13	1	0	0	14
B	1	9	0	1	11
C	0	1	0	9	10
Total	14	11	0	10	35

Table 3: Analysis of compound muscle action potential latency recorded in during 1 week and rate of recovery

Latency	Recovery in months			In complete recovery in 12 months	Total
	<2	2–6	>6		
A	17	8	0	10	35
B	0	0	0	0	0
C	0	0	0	0	0
Total	0	0	0	0	35

Table 4: Analysis of compound muscle action potential latency recorded in after 2 weeks and rate of recovery

Latency	Recovery in months			In complete recovery in 12 months	Total
	<2	2–6	>6		
A	49	24	0	9	82
B	3	2	2	10	17
C	-	-	-	2	2
Total	52	26	2	21	101

Dhas^[15] who had documented 20% of subclinical cases in their study.

CMAP Latency

The role of the CMAP latency in the early diagnosis and prognosis of Bell's palsy is uncertain. Although some researchers showed that abnormal latency could point to a bad prognosis, it is believed that this factor has a limited significance. Since the latency reflects the function of the

fastest fibers, it can stay within normal values for a long time even in cases of a distinct axonal loss. Gilliat and Taylor^[16] reported that latency stays within normal values until the M potential is lost. However, some studies have demonstrated that abnormal latency can be suggestive of a bad prognosis. Langworth and Taverner^[17] emphasized that the electrical stimulation in facial palsy it is argued that the pathological process is probably ischaemia secondary to compression of the nerve in the facial canal. Danielides *et al.* have provided the results of their study made in 1994 and 1996^[18] which showed that the latency extension results in a bad prognosis of the illness. They also claim that the reliability of this feature was less important than CMAP amplitude for the prognosis. This observation showed that even though latency measurement as an independent factor is not much helpful in assessing the prognosis, if combined with the amplitude predicts the prognosis.

CONCLUSIONS

Electrophysiological studies can predict the duration of the clinical recovery and the outcome of the illness. The amplitude ratio of CMAP is the most reliable parameter in assessing the prognosis. Latency measurement as an independent factor is not much helpful in assessing the prognosis, however, when combined with the amplitude ratio predicts the prognosis. Simultaneous subclinical facial nerve involvement does occur on the contralateral side in 16% of the cases. Bell's palsy patients with incomplete facial paralysis have excellent outcomes.

REFERENCES

1. Roob G, Fazekas F, Hartung HP. Peripheral facial palsy: Etiology, diagnosis and treatment. *Eur Neurol* 1999;41:3-9.
2. Bongiovanni LG, Bertolasi L, Polo A, Zanette GP, Zanolli L, Teatini F. Motor unit firing rates in orbicularis oculi muscle after Bell's palsy. *Electroencephalogr Clin Neurophysiol* 1995;95:46P.
3. Dumitru D, Walsh NE, Porter LD. Electrophysiologic evaluation of the facial nerve in Bell's palsy. A review. *Am J Phys Med Rehabil* 1988;67:137-044.
4. Kimura J. *Electrodiagnosis in Diseases of Nerve and Muscles*. 2nd ed. Philadelphia, PA: FA Davis Co.; 1989.
5. May M, Blumenthal F, Klein SR. Acute Bell's palsy: Prognostic value of evoked electromyography, maximal stimulation, and other electrical tests. *Am J Otol* 1983;5:1-7.
6. Fish U. Total facial nerve decompression and electroneurography. In: Silverstein H, Norrell H, editors. *Neurological Surgery of the Ear*. Birmingham: Aesculapius; 1997. p. 21-33.
7. Danielides V, Skevas A, Kastanioudakis I, Assimakopoulos D. Comparative study of evoked electromyography and facialnerve latency test in the prognosis of idiopathic facial nervepalsy in childhood. *Childs Nerv Syst* 1994;10:122-5.
8. Matthews WB. Prognosis in Bell's palsy. *Br Med J* 1961;2:215-7.
9. Heath JP, Cull RE, Smith IM, Murray JA. The neurophysiological investigation of Bell's palsy and the predictive value of the blink reflex. *Clin Otolaryngol Allied Sci* 1988;13:85-92.
10. Djordjević G, Djurić S. Early prognostic value of electrophysiological tests in Bell's palsy estimating the duration of clinical recovery. *Med Biol* 2005;12:47-54.
11. May M, Wette R, Hardin WB Jr, Sullivan J. The use of steroids in Bell's palsy: A prospective controlled study. *Laryngoscope* 1976;86:1111-22.
12. Hauser WA, Karnes WE, Annis J, Kurland LT. Incidence and prognosis of bell's palsy in the population of Rochester, Minnesota. *Mayo Clin Proc* 1971;46:258-64.
13. Esslen E. Electromyography and Electroneurography. In: Fisch U, editor. *Facial Nerve Surgery*. Amstelveen: Kugler Publications; 1997. p. 93-100.
14. Tojima H, Aoyagi M, Inamura H, Koike Y. Clinical advantages of electroneurography in patients with bell's palsy within two weeks after onset. *Acta Otolaryngol Suppl* 1994;511:147-9.
15. Natarajan V, Dhas GA. *Electrophysiological Studies in Fifty Cases*. Sorrento, Italy: 7th Congress of Electromyography and Related Clinical Neurophysiology; 1987.
16. Gilliat RW, Taylor JC. Electrical changes following section of the facial nerve. *Proc R Soc Med* 1959;52:1080-3.
17. Langworth EP, Taverner D. The prognosis in facial palsy. *Brain* 1963;86:465-80.
18. Danielides V, Skevas A, Van Cauwenberge P. A comparison of electroneuronography with facial nerve latency testing for prognostic accuracy in patients with Bell's palsy. *Eur Arch Otorhinolaryngol* 1996;253:35-8.

How to cite this article: Jebasingh YK, Sethuram A. Study on Prognostic Value of Electrophysiological Tests in Bell's Palsy. *Int J Sci Stud* 2019;7(5):22-25.

Source of Support: Nil, **Conflict of Interest:** None declared.

Comparison of Postmortem Analysis of Anomalous Fetuses with the Prenatal Ultrasonography Findings

P Murugalatha¹, M Krithiga²

¹Associate Professor, Department of Pediatrics, Theni Government Medical College and Hospital, Theni, Tamil Nadu, India, ²Assistant Professor, Department of Pediatrics, Theni Government Medical College and Hospital, Theni, Tamil Nadu, India

Abstract

Background: Congenital anomalies cause around 10–15% of perinatal deaths in India. At present, these fetal deaths are only evaluated with ultrasonography (USG) findings. With this study, we aimed to do the postmortem analysis of these anomalous fetuses and compare the findings with antenatal ultrasound findings.

Materials and Methods: A descriptive study carried out with 43 anomalous fetuses over 1½ years period in a tertiary care institute by comparing the postmortem analysis of anomalous fetuses with the prenatal USG findings.

Results: Among the 43 cases, 41 had antenatal USG taken. In 11 cases, autopsy confirmed the USG findings and autopsy showed extra findings in 16 cases. Antenatal USG was normal in 12 cases, but autopsy only identified anomalies. In two cases, autopsy detected no anomalies. Among 41 cases, 12 cases with normal antenatal USG had significant findings and 11 cases with abnormal USG had new findings after physical examination and X-ray evaluation.

Conclusion: Fetal autopsy helps in identifying many external and internal malformations which were undetected by antenatal USG. Fetal autopsy can be useful in 95% of cases – it can either confirm or add findings. Limited fetal autopsy can benefit in 56% of cases. The study shows that in majority of cases, the limited fetal autopsy itself will detect many anomalies undetected by the USG.

Key words: Anomalous fetuses, Autopsy, Ultrasonogram, X-ray

INTRODUCTION

Congenital anomalies cause around 10–15% of perinatal deaths in India.^[1,2] Over the past several decades, research has dramatically improved our insight into genetic and environmental causes of many isolated birth defects, multiple congenital anomaly syndromes, and other genetic conditions. Anomalies can be malformations, deformations, dysplasia, or disruptions.^[3]

When there is a fetal loss associated with anomalies, there will be an added psychological and social trauma for parents. There can be worries regarding the recurrence of these anomalies. Hence, there should be adequate evaluation of

these fetuses. The risk factors and probable etiology of these anomalies should be searched for and analyzed. Thus, the evaluation of congenital anomaly starts from antenatal period, assessing the maternal factors, familial risk factors, and ultrasonogram evaluation. In the postnatal period, we can do a morphological, radiological, and histopathological evaluation with investigations for infectious, genetic, chromosomal, or metabolic causes if needed.^[4]

At present, PM analysis is not being done in majority of the institutions. Decisions are made based only on the ultrasonography (USG) findings. Although some anomalies can be detected by USG, these findings can be proved right or wrong and modified with new findings after fetal autopsy. In some cases, the anomalies detected can be put together and concluded as some association, sequence, or syndrome. If necessary and feasible, confirmatory tests like karyotyping can be done for these cases. Proper genetic counseling can be done for the patients if a definite etiology is identified.

At present, these fetal deaths are only evaluated with USG findings. With this study, we aimed to do the postmortem

Access this article online



www.ijss-sn.com

Month of Submission : 06-2019

Month of Peer Review : 07-2019

Month of Acceptance : 08-2019

Month of Publishing : 08-2019

Corresponding Author: Dr. M Krithiga, Plot No: 419, K.K Nagar, Madurai, Tamil Nadu, India

analysis of these anomalous fetuses and compare the findings with antenatal ultrasound findings.

Objectives

The objectives of this study were as follows:

1. Postmortem analysis of anomalous fetuses delivered at a tertiary care institute using
 - Relevant obstetric, medical, and family history
 - Morphological assessment
 - Radiological assessment using X-ray
 - Fetal autopsy with histopathological assessment
 - Karyotyping.
2. Asses the utility of fetal autopsy in detecting the anomalies compared to antenatal ultrasonogram
3. Asses the utility of limited fetal autopsy (physical and radiological examination).

MATERIALS AND METHODS

Study Design

This was a descriptive study.

Period of Study

The study duration was from January 2018 to June 2019.

Study Setting

Labour room, neonatal intensive care unit and pathology laboratory at a tertiary care institute.

Subjects

Definition – any anomalous fetus following termination on anomaly detection, intrauterine death, or early neonatal death (first 7 days).

Inclusion Criteria

The following criteria were included in the study:

1. Anomalous fetuses who died following the second-trimester abortion, intrauterine death, or early neonatal death (first 7 days)
2. Parents giving an informed written consent
3. Anomalies diagnosed by USG or during physical examination; minor or major; internal or external; and hydrops fetalis.

Method

The obstetricians helped in counseling the parents regarding the autopsy and informing the investigator regarding the subjects. Pathological autopsy was done at the department of pathology.

After counseling the parents and getting the consent, the importance of karyotyping was informed. If they were willing, a cardiac blood sample was taken for karyotyping. A thorough physical examination was done and looked for

any anomalies. The X-ray whole body of subject was taken and the body was immersed in formalin for doing autopsy.

Observations

A total of 43 fetuses/neonates with anomalies were analyzed [Figure 1].

Of 43 cases, 19 were male, 21 were female, and 3 ambiguous [Figure 2].

Majority belonged to 21–24 gestational weeks (23.2%) [Table 1].

Twenty-five of 43 cases were small for gestation age [Figure 3]. Majority of the mothers belonged to 21–34 years [Table 2] group and were primigravida. Four mothers had

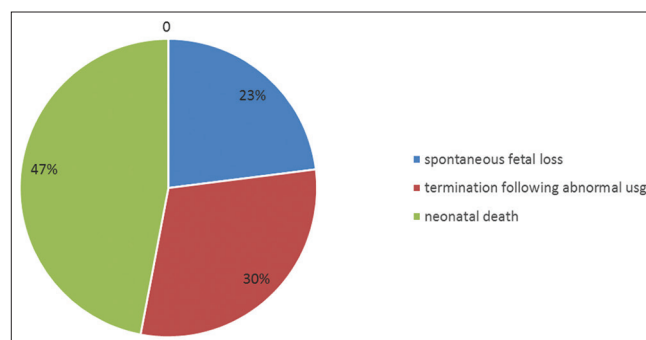


Figure 1: Subject groups

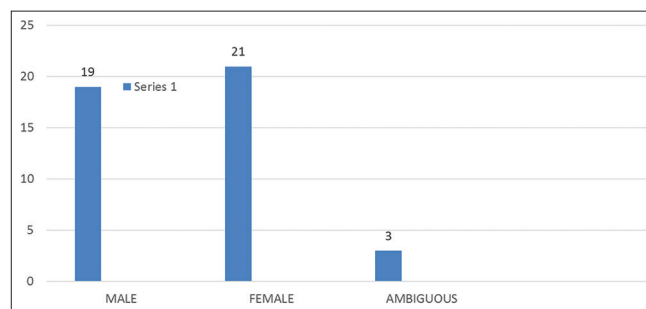


Figure 2: Sex distribution

Table 1: Gestational age

Gestational age	<20 weeks	21–24 weeks	25–28 weeks	29–32 weeks	33–36 weeks	Term
Number of cases	5	10	8	4	7	9
Percentage	11.6	23.2	18.6	9.3	16.2	20.9

Table 2: Maternal age

Maternal age	Number	Percentage
<20	6	14.3
21–34	35	83.3
>35	1	2.3

a history of stillbirths in the past and two of them were congenital anomalies [Figure 4]. Only a very few had any significant medical history. They include congenital heart disease – atrial septal defect, diabetes, hypothyroidism, and infertility treatment.

Details of ultrasonogram were available in 41 subjects. No anomalies were detected in 10 subjects. Many non-specific findings such as intrauterine growth restriction, oligohydramnios, and polyhydramnios were also taken into account [Table 3].

Among the 43 cases, 41 had antenatal USG taken. In 11 cases, autopsy confirmed the USG findings and autopsy showed extra findings in 16 cases. Antenatal USG was normal in 12 cases, but autopsy only identified anomalies. In two cases, autopsy detected no anomalies [Figure 5].

Among 41 cases, 12 cases with normal antenatal USG had significant findings and 11 cases with abnormal USG had new findings after physical examination and X-ray evaluation [Figure 6].

DISCUSSION

Congenital anomalies are associated with a major proportion of fetal losses and early neonatal deaths. Parental anxiety can be further aggravated by the association of anomalies in fetal loss. Their major concern

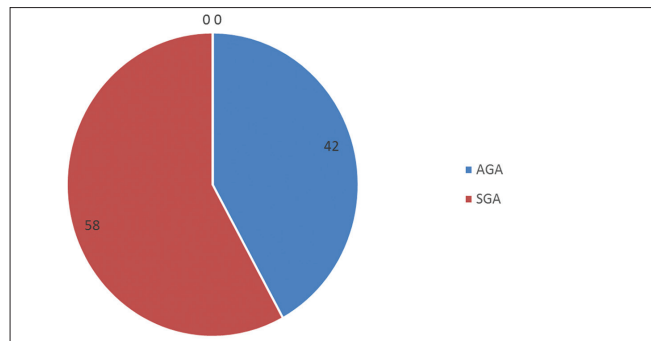


Figure 3: Weight

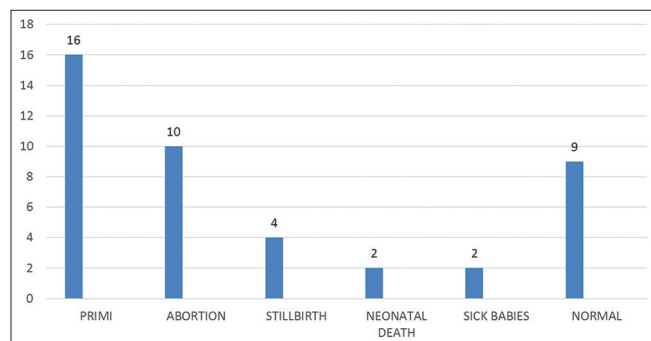


Figure 4: Obstetric history

will be of the chances of recurrence of these anomalies. Before embarking on this study, the anomalous fetuses were analyzed solely based on the findings of antenatal ultrasonogram.

We studied 43 cases with anomalies which included pregnancy terminated after detecting anomalies in antenatal ultrasonogram, stillbirths, and early neonatal deaths; the study intends to reiterate the importance of postmortem analysis of fetuses [Table 4].

Postmortem analysis included relevant history regarding family, medical illness of mother, past and present obstetric history, antenatal ultrasonogram findings, and natal and postnatal events in neonatal deaths; chromosomal analysis, physical examination, radiological evaluation [Table 5], and internal examination with histopathological evaluation. In this study, we performed the above measured in all cases except chromosomal analysis which was done in three cases due to unavailability and the cost factor of the procedure. Other investigations required were those for infections and metabolic causes.

Table 3: Anomalies found in ultrasonography

Finding	Number of cases	Percentage
No anomalies	10	24.3
IUGR	25	60.9
Oligohydramnios	7	17
Polyhydramnios	4	9.7
Hydrops fetalis	4	9.7
Renal anomalies	8	19.5
Renal agenesis	3	
Echogenic kidney	2	
Hydronephrosis	1	
Renal cyst	1	
Renal dysplasia	1	
Head, neck, and spine	16	39
Hydrocephalus	3	
Encephalocele	1	
Meningocele	1	
Anencephaly	1	
Brain malformation	1	
Arnold Chiari malformation	1	
Spina bifida	1	
Hemivertebrae	1	
Cleft palate	1	
Cystic hygroma	1	
Occipital swelling	1	
Curved spine	2	
Thoracoabdominal	12	27.9
Lung hypoplasia	2	
Cardiomegaly	2	
Endocardial cushion defect	1	
Cardiac hypoplasia	1	
Cystic mass in abdomen	1	
Thoracoomphalophagus	1	
Duodenal atresia	1	
Diaphragmatic hernia	1	
Omphalocele	2	
Limb anomaly	4	9.7

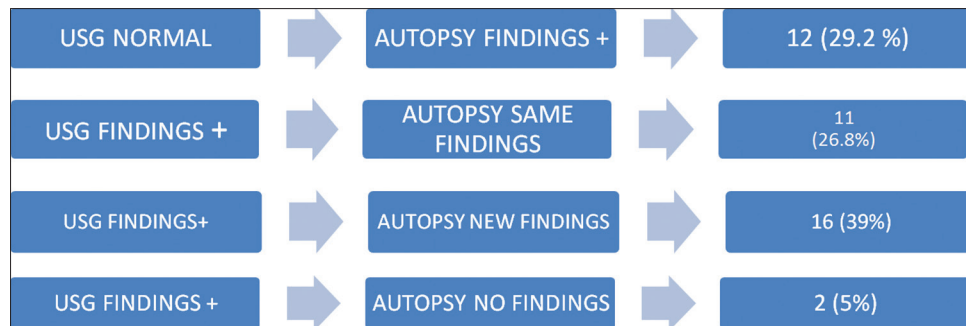


Figure 5: Correlation between ultrasonography and autopsy findings

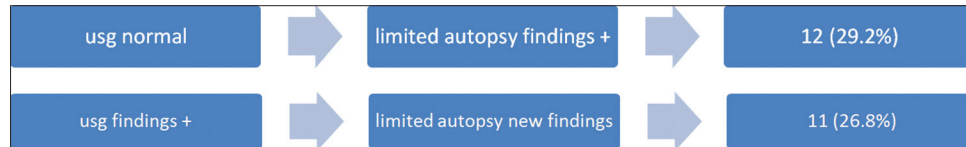


Figure 6: Correlation between ultrasonography and limited autopsy

Table 4: Physical examination finding (n=43) (one subject can have more than one anomaly)

Findings	Number of cases	Percentage
No anomalies	6	13.9
Hydrops fetalis	8	18.6
Head and neck	22	51.1
Anencephaly	1	
Cleft lip	3	
Cleft palate	5	
Facial dysmorphism	4	
Anophthalmia	2	
Anotia	2	
Coloboma iris	1	
Swelling neck	2	
Aplasia cutis	1	
Hemangioma	1	
Thoracoabdominal	17	39.5
Congenital heart disease	2	
Diaphragmatic hernia	1	
Meningomyelocele	1	
Thoracopagus	1	
Kyphoscoliosis	1	
Ambiguous genitalia	3	
Imperforate anus	2	
Single umbilical artery	3	
Omphalocele	2	
Gastroschisis	1	
Limb anomalies	10	23.2
Syndactyly	3	
Polydactyly	1	
Talipes equinovarus	2	
Joint dislocation	1	
Bowing of legs	1	
Absent fingers	1	
Ectrodactyly	1	

Unlike other similar studies, this was a prospective study. There were eight cases of non-immune hydrops fetalis, of which four had some internal malformations.

Table 5: X-ray findings (n=43) (one subject can have more than one finding)

Finding	Number of cases	Percentage
No skeletal anomaly	26	60.4
Thorax	9	20.9
Skull and spine	5	11.6
Limbs	6	16.2
Lungs	7	16.2
Congenital lobar emphysema	3	
Congenital cystic adenomatoid malformation	1	
Hypoplastic lungs	2	
Lung cyst	1	
Renal	7	16.2
Renal agenesis	4	
Renal cyst	1	
Infantile polycystic disease	1	
Dilated urinary bladder with megaureters	1	
Brain	4	9.3
Hydrocephalus	2	
Arnold Chiari malformation	1	
Dandy-Walker malformation	1	
Cardiac anomalies	5	11.6
Single atria and ventricle	1	
Myocardial hypertrophy	4	
Abdominal	6	13.9
Intestinal stenosis	3	
Liver cyst	1	
Diaphragmatic hernia	1	
Rudimentary liver	1	
Others	4	9.3
Spinal hemangiomas	1	
Scalp hemangioma	1	
Lymphangioma	1	
Storage disorder – liver and heart	1	
Hydrops fetalis – unknown cause	4	9.3
Internal organs	14	32.5

The fetal autopsy helped detecting additional findings in 39% of cases. In 29.2% of cases, antenatal USG was normal

Table 6: Efficacy of ultrasound examination – detection rate of different types of anomalies

Types of anomaly	Anomalies detected		Percentage of anomalies detected with USG
	With USG	After autopsy	
Intracranial	4	4	100
Hydrops	5	8	62.5
Limb	4	10	40
Renal	2	7	28.5
Lung	2	7	28.5
Cleft palate	1	5	20
Cleft lip	1	3	33.3
Intestinal atresia/stenosis	Nil	3	0
Cardiac	Nil	5	0

and fetal autopsy detected some anomalies. In 26.8% of cases, fetal autopsy confirmed the ultrasonogram findings. About 5% of cases had no anomalies after autopsy.

It was also found that certain ultrasonogram findings were either found absent or modified after autopsy, especially renal anomalies [Table 6]. After assessing the detection rate of different types of anomalies by USG, it was found that intracranial anomalies were detected in all cases, and cardiac and gastrointestinal anomalies were completely missed by antenatal USG.

With limited fetal autopsy, 29.2% of cases had some anomalies in spite of normal USG and 26.8% had new anomalies in addition to USG findings.

In a retrospective study done by Sankar and Phadke,^[5] fetal autopsy detected additional findings in 58% of cases and confirmed the USG findings in 42% of cases. They were able to reach a final diagnosis in 59% of cases.

In another retrospective study by Phadke and Gupta, fetal autopsy provided a definite diagnosis in 72/91 (79.1) of the cases. Fetal autopsy confirmed the sonographic findings in 89 of 91 cases. About 97.8% autopsy helped in redefining the diagnosis and the risk of recurrence in 30 of 91 (33%) cases.

The similar previous studies all had confirmed the utility of fetal autopsy. Many studies have compared its utility with antenatal USG.^[6-10]

The difference in the results of the above-mentioned studies from this may be due to the lack of experience and lack of infrastructure.

Fetal autopsies were done only rarely in our institution. With this study, we observed the practical difficulties of doing fetal autopsy as a routine for fetal loss. The study needs a coordinated involvement of three departments – obstetrics, pediatrics, and pathology. The participant of nursing staffs and paramedical staffs also is necessary.

Although the number of fetal losses during the study period was very high, there were many factors that made the parents unwilling for the study. They include certain religious beliefs which will not allow any intervention over body after death, emotional factors, especially in neonatal death, delay in getting the body after the postmortem analysis, and unawareness of labor room staff regarding the importance of postmortem analysis.

Limitations

The sample size was small.

We could not do complete evaluation in majority of cases.

Karyotyping was done only if the parents were interested after counseling, due to the financial factors and transplantation problems. It could be done only in three subjects, of which two samples became lysed and the other one was normal.

The recurrence risk could not be analyzed.

The ultrasonogram was done by different personnel and their can be interobserver variation.

CONCLUSION

This study done on 43 anomalous fetuses/newborns at tertiary institute shows the utility of fetal autopsy and limited fetal autopsy.

Fetal autopsy helps in identifying many external and internal malformations which were undetected by antenatal ultrasonogram.

Fetal autopsy can be useful in 95% of cases – it can either confirm or add findings.

It is possible to diagnose 53% of cases with fetal autopsy.

Limited fetal autopsy can benefit in 56% of cases – it can either confirm or add findings.

Although some of the anomalies cannot be characterized as any known disease, autopsy helps to describe the individual anomalies.

The study shows that in majority of cases, the limited fetal autopsy itself will detect many anomalies undetected by the ultrasonogram.

Hence, in cases, where the parents are not willing for autopsy, a limited autopsy can be done which includes physical examination and radiological examination.

Suggestions

Fetal autopsy should be made a hospital policy for all fetal loss, as this could have avoid the logistical constraints.

In cases, where the parents are not willing for autopsy, a limited autopsy can be done – which includes physical examination, photography, and radiological examination. Further, reading and consultation with experts later may yield the definite diagnosis.

For complete evacuation, other investigative modalities such as karyotyping, metabolic screening, and immunoassay need to be present in concerned hospital or nearby center.

Parents need a lot of counseling and motivation, especially in the setting of religious beliefs against autopsy and neonatal deaths.

The labor room staff needs to be aware of the significance and the different steps of fetal autopsy.

Proper communication between obstetricians, pediatricians, and pathologist is needed.

REFERENCES

1. Pradhan R. Perinatal autopsy; a study from India. *J Indian Acad Forensic Med* 2013;35:10-3.
2. Isaksen CV, Eik-Nes SH, Blaas HG, Torp SH. Comparison of prenatal ultrasound and postmortem findings in fetuses and infants with central nervous system anomalies. *Ultrasound Obstet Gynecol* 1998;11:246-53.
3. Vimercati A, Grasso S, Abruzzese M, Chincoli A, de Gennaro A, Miccolis A, *et al.* Correlation between ultrasound diagnosis and autopsy findings of fetal malformations. *J Prenat Med* 2012;6:13-7.
4. Boyd TK, Redline RW. Pathology of the placenta. In: Gilbert-barness E, Kapur RP, Oligny LL, Siebert JR, editors. *Potter's Pathology of the Fetus, Infant and Child*. 2nd ed. Philadelphia, PA: Mosby Elsevier; 2007. p. 645-93.
5. Sankar VH, Phadke SR. Clinical utility of fetal autopsy and comparison with prenatal ultrasound findings. *J Perinatol* 2006;26:224-9.
6. Phadke SR, Gupta A. Comparison of prenatal ultrasound findings and autopsy findings in fetuses terminated after prenatal diagnosis of malformations: An experience of a clinical genetics center. *J Clin Ultrasound* 2010;38:244-9.
7. Saller DN Jr., Lesser KB, Harrel U, Rogers BB, Oyer CE. The clinical utility of the perinatal autopsy. *JAMA* 1995;273:663-5.
8. Hauerberg L, Skibsted L, Graem N, Maroun LL. Correlation between prenatal diagnosis by ultrasound and fetal autopsy findings in second-trimester abortions. *Acta Obstet Gynecol Scand* 2012;91:386-90.
9. Boyd PA, Tondi F, Hicks NR, Chamberlain PF. Autopsy after termination of pregnancy for fetal anomaly: Retrospective cohort study. *BMJ* 2004;328:137.
10. Kaasen A, Tuveng J, Heiberg A, Scott H, Haugen G. Correlation between prenatal ultrasound and autopsy findings: A study of second-trimester abortions. *Ultrasound Obstet Gynecol* 2006;28:925-33.

How to cite this article: Murugalatha P, Krithiga M. Comparison of Postmortem Analysis of Anomalous Fetuses with the Prenatal Ultrasonography Findings. *Int J Sci Stud* 2019;7(5):26-31.

Source of Support: Nil, **Conflict of Interest:** None declared.

Clinical Evaluation of Patients Undergoing Phacoemulsification for Dry Eye

R P Shamsheer

Assistant Professor, Department of ENT, KMCT, Kozhikode, Kerala, India

Abstract

Background: “Dry eye” is a multifactorial disease of tears and ocular surface that can be result from aqueous deficiency or may be evaporative in nature. Dry eye affects individuals worldwide. Long-term epidemiological studies have shown that the incidence rates among the population between ages 43 and 86 years at 5 and 10 years of follow-up to be 13.3% and 21.6%, respectively.

Aim of the Study: The aim of the study was to assess the incidence and severity pattern of dry eye among patients who have undergone phacoemulsification.

Materials and Methods: A total of 152 patients undergoing phacoemulsification for matured cataracts in the Department of Ophthalmology of KMCT Hospital were included in this study. The incidence of dry eye on day 7 after phacoemulsification was assessed using the ocular surface disease index (OSDI) questionnaire. Tear breakup time (TBUT), fluorescein staining with Oxford Schema, and Schirmer I test without anesthesia were performed after the questionnaire. The TBUT measures the interval between the last complete blink and the first appearance of a dry spot or disruption of the tear film.

Observations and Results: Among 152 subjects, there were 97 male patients (63.81%) and 55 (36.18%) female patients with a male to female ratio 1.76:1. The mean age was 57.13 ± 9.50 years. The eldest patient was aged 78 years. On day 7 postoperatively, the mean scores of OSDI questionnaire (preoperatively vs. postoperatively was 12.57 vs. 35.10, respectively), TBUT (preoperatively vs. postoperatively was 15.85 ± 1.25 s vs. 13.9 ± 0.70 s), Oxford Schema (preoperatively vs. postoperatively was Grades 1 vs. 2), and Schirmer I without anesthesia (preoperatively vs. postoperatively was 22.10 ± 5.44 mm at 5 min [15–35 mm] vs. 7.50 ± 2.20 in 55.30% [6.10–9.05], respectively) showed a trend toward dry eye syndrome during the 1st week.

Conclusions: Dry eye symptoms can develop immediately after phacoemulsification and the severity can peak on day 7. Both symptoms and signs of dry eye can improve over time. However, it is important that ophthalmologists assess dry eye before and after phacoemulsification to ensure proper treatment, quality of vision, and quality of life for their patients.

Key words: Cataract and OSDI questionnaire, Dry eye, Phaco-emulsification

INTRODUCTION

“Dry eye” is a disease of the pre-corneal tear film with varied etiology and ocular symptoms such as ocular discomfort, visual disturbance, and tears film instability, with potential damage to the ocular surface.^[1] When the disease is severe it affects the patient’s ocular and general health, well-being, and quality of life.^[2,3] Epidemiology

of the disease studied worldwide showed that aging, connective tissue disease, history of allergy or diabetes, and use of antihistamines and refractive surgery are some of the risk factors for the dry eye syndrome.^[4-8] One among the various causes producing dry eye is cataract surgery, the most common procedure performed in ophthalmic departments. Dry eye is complained as a symptom of irritation after cataract surgery. It can occur after an extracapsular cataract extraction because a large incision is created in the eye during the procedure that sometimes damages the cornea.^[9] Phacoemulsification is another method of commonly performed methods of cataract surgery worldwide where a smaller incision is given, and ultrasonic-driven oscillating tips are used to emulsify or fragment the crystalline lens. However, there are fewer reports of dry eye syndrome, which are focused

Access this article online



www.ijss-sn.com

Month of Submission : 06-2019
Month of Peer Review : 07-2019
Month of Acceptance : 08-2019
Month of Publishing : 08-2019

Corresponding Author: Dr. R P Shamsheer, Department of ENT, KMCT, Kozhikode, Kerala, India

on patients who had undergone phacoemulsification and subsequently developed dry eye.^[1] Review of literature shows that factors responsible for dry eye after cataract surgeries are prolong use of antibiotic-steroid eye drops, decrease tear film breakup time due to surface irregularity at the site of the incision, decrease mucin production from the conjunctiva secondary to incision placement, decrease corneal sensation due to surgical incision which disrupts the cornea-lacrimal gland loop leading to reduced tear secretion, poor tear film production and stability due to surgically induced ocular inflammation, and exposure to light from the operating microscope.^[10-12] In the present study, various measurements to assess the incidence and severity pattern of dry eye syndrome among patients who have undergone phacoemulsification was undertaken.

Type of the Study

This was a cross-sectional, prospective analytical study.

Duration of the Study

The study was from April 2015 to March 2017.

Institute of the Study

This study was conducted at KMCT Medical College, Manassery, Kozhikode, Kerala.

MATERIALS AND METHODS

A total of 152 patients undergoing phacoemulsification for matured cataracts in the Department of Ophthalmology of KMCT Medical College Hospital, Manassery, Kozhikode, Kerala, were included in this study. An Ethical Committee Clearance was obtained before commencing the study. An Ethical Committee cleared consent form was used for the study.

Inclusion Criteria

- (1) Patients aged above 38 years were included in this study.
- (2) Patients with a cataract without dry eye as assessed by the ocular surface disease index (OSDI) questionnaire (OSDI scores of 25 or less) were included in this study.

Exclusion Criteria

- (1) Patients below 38 years were excluded from this study.
- (2) Patients who received concomitant medications causing dry eye such as antihistamines, antidepressants, birth control pills, decongestants, medications in the accutane, gabapentin, sildenafil citrate, and anticholinergic drugs and who had autoimmune diseases were excluded from the study.
- (3) Patients developing other complications following phacoemulsification were excluded from the study. After the surgery, the incidence of dry eye in all the patients was assessed using the OSDI questionnaire. The

severity of the dry eye was assessed and calculated from the average of the OSDI scores, tear breakup time (TBUT), the Schirmer I test without anesthesia, and the Oxford Schema. The patients' pre-operative and post-operative characteristics were observed and analyzed. The incidence of dry eye on day 7 after phacoemulsification was assessed using the OSDI questionnaire,^[13] a 12-item questionnaire used worldwide to accurately assess symptoms of ocular irritation related to dry eye, and vision was modified by omitting items four and five which assess the presence of blurred and poor vision because it is difficult to differentiate the change of these symptoms caused by cataract surgery alone or combined with visual symptoms due to cataract surgery-induced dry eye conditions. The total OSDI score was calculated by using the formula: OSDI score = (sum of all answered questions) × 100/total number of answered questions) × 4. The OSDI scores range from 0 to 100. Scores from 0 to 25 are considered normal; scores exceeding 25 indicate the presence of dry eye symptoms. TBUT, fluorescein staining with Oxford Schema, and Schirmer I test without anesthesia were performed after the questionnaire. The TBUT^[1] measures the interval between the last complete blink and the first appearance of a dry spot or disruption of the tear film. Three TBUT scores were averaged to determine whether the patient had dry eye. An average score of 10 s or more was classified as normal; a TBUT shorter than 10 s indicated the presence of dry eye. Conjunctival and corneal fluorescein staining were graded using the Oxford Schema^[1] with 0–I indicating normal and II–V indicating dry eye. For the Schirmer I test^[1] without anesthesia, Schirmer paper strips were inserted over the lower lid margin, midway between the middle and outer third of the lid. The wetness on the strip was measured 5 min after application. A wet area that measured 10 mm or less was diagnosed as dry eye. The OSDI questionnaire and the three clinical tests were administered on day 0 (baseline), after week 1 and after 1st and 3rd months after phacoemulsification. Cataract surgeries were performed under topical anesthesia induced with 0.5% tetracaine hydrochloride. Before surgery, the eye was prepared and draped using sterile techniques. Phacoemulsification was performed with a 2.75-mm temporal clear corneal incision and a side port of about 1 mm 90° incision away from the main incision. The range of phacoemulsification time was 5–10 min and foldable intraocular lens was inserted thereafter. There was no intraoperative complication in all cases. After surgery, all patients instilled tobramycin with dexamethasone ophthalmic eye drops 4 times daily for 1 month. All the data were analyzed using standard statistical methods. The associations between age, sex, underlying disease, and dry eye postoperatively were analyzed by Fisher's exact test.

OBSERVATIONS AND RESULTS

A total of 152 patients undergoing phacoemulsification in the Department of Ophthalmology of a tertiary teaching Hospital of Kerala were included in this study. Totally 152 eyes were assessed for evidence of dry eye by the methods described in materials and methods. The demographic data was tabulated and shown in Table 1. There were 97 male patients (63.81%) and 55 (36.18%) female patients with a male to female ratio 1.76:1. The mean age was 57.13 ± 9.50 years. The eldest patient was aged 78 years.

The data of subjects preoperatively and on days 7, 30, and 90 postoperatively for the OSDI questionnaire and three clinical tests were made available in Table 2 from 152 patients. On day 7 postoperatively, the mean scores of OSDI questionnaire (preoperatively vs. postoperatively was 12.57 vs. 35.10, respectively), TBUT (preoperatively vs. postoperatively was 15.85 ± 1.25 s vs. 13.9 ± 0.70 s), Oxford Schema (preoperatively vs. postoperatively was Grades 1 vs. 2), and Schirmer I without anesthesia (preoperatively vs. postoperatively was 22.10 ± 5.44 mm at 5 min [15–35 mm] vs. 7.50 ± 2.20 in 55.30% [6.10–9.05], respectively) showed a trend toward dry eye syndrome during the 1st week. The agreement between the three

clinical tests and the OSDI questionnaire in various combinations was analyzed by Kappa analysis and showed no agreement with each other except for the OSDI questionnaire with the Oxford Schema and the TBUT with the Oxford Schema. Poor agreement was detected between the OSDI questionnaire and the Oxford Schema (agreement 47.2%, kappa 9.8%, $P = 0.03$) and the TBUT and the Oxford Schema (agreement 73.0%, kappa 39.9%, $P < 0.001$) showed fair agreement. The cataract surgery was performed using phacoemulsification in all the eyes. The mean duration of surgery was 27.5 min (± 10.1 , range 10–50 min). The total microscope light exposure time was little longer (mean, 31.1 ± 10.5 min) than the duration of actual surgery. The length of main incision in the phacoemulsification group was 2.8 mm.

DISCUSSION

The basic principle in the causation of the dry eye is either presence of aqueous production deficiency or excessive evaporation of the tears. This syndrome affects individuals worldwide. Long-term population-based studies have shown the incidence rates of dry eye among the population between ages 43 and 86 years at 5 and 10 years of follow-up to be 13.3% and 21.6%, respectively.^[4,5] Dry eye can occur following ophthalmic surgeries such as photorefractive keratectomy and laser-assisted *in situ* keratomileusis (LASIK). The incidence rates of dry eye, assessed by corneal fluorescein staining after 1st week postoperatively for either nasal- or superior-hinge LASIK, were 47.06% and 52.94%, respectively.^[6] After LASIK surgery, dry eye can persist up to 6 months or more with an incidence of 20%,^[7] whereas in patients who have undergone blepharoplasty, dry eye can last up to 2 weeks or more with an incidence of 10.9%.^[12] As it is difficult to assess the dry eye by a single test, different diagnostic tools with different sensitivities and specificities are used to diagnose dry eye.^[13] In the present study OSDI questionnaire was used to assess the severity, natural history, and effects of dry eye. The OSDI questionnaire was having a sensitivity of 60% and specificity of 79% in the present study. One explanation for TBUT and Oxford Schema indicating more cases of dry eye postoperatively when compared to

Table 1: The demographic data of the study group (n=152)

Demographic observation	Male-97	Female-55
Mean age	59.35 \pm 2.70	56.10 \pm 3.05
Socioeconomic status		
High	24 (15.78%)	14 (9.21%)
Middle	38 (25%)	20 (13.15%)
Low	35 (23.02%)	21 (13.81%)
Educational status		
Uneducated	34 (22.36%)	16 (10.52%)
Vocational courses	43 (28.28%)	31 (20.39%)
Graduation	20 (13.51%)	18 (11.84%)
Smoking	52 (16.44%)	04 (02.63%)
Hypertension	42 (27.63%)	19 (12.5%)
Diabetes mellitus	30 (19.73%)	10 (06.57%)
Dyslipidemia	15 (09.86%)	11 (07.23%)
Heart disease	35 (23.02%)	21 (13.81%)
Glaucoma	11 (%)	09 (%)
Parkinsonism	06 (%)	00
Prostate hypertrophy	16 (%)	--

Table 2: The pre-operative and post-operative OSDI score and test results (n=152)

Dry eye assessment tests	Pre-operative Assessment (95% CI)	Day 7 Mean, incidence (95% CI)	Day 30 Mean, incidence (95% CI)	Day 90 Mean, incidence (95% CI)
OSDI questionnaire score	11.64 (07.10–16.35)	35.10 (31.0–42.50)	19.40 (17.65–23.15)	15.30 (13.45–19.40)
TBUT	15.85 \pm 1.25 s	13.9 \pm 0.70 s	14.7 \pm 0.31 s	15.15 \pm 1.10 s
Oxford Schema	Grade 1-100%	Grade 3-62.25%	Grade 2-81.45%	Grade 1-96%
Schirmer I without anesthesia	22.10 \pm 5.44 mm at 5 min (15–35 mm)	7.50 \pm 2.20-55.30% (6.10–9.05)	14.60 \pm 1.20-69.25% (12.70–18.30)	18.30 \pm 3.50-88.30% (16.25–19.80)

OSDI: Ocular surface disease index, CI: Confidence interval, TBUT: Tear breakup time

the Schirmer I test without anesthesia [Table 2] was that these tests could easily detect tear film instability and ocular surface inflammation respectively. Abnormal TBUT and Oxford Schema could have resulted from microscopic light exposure, toxic substances from inflammatory cytokines, medications, or preservatives. Only mild injected bulbar conjunctiva and without anterior segment, inflammation was found postoperatively in patients who developed abnormal TBUT and Oxford Schema results. Phacoemulsification can affect or interrupt the neurogenic response of the ocular surface and decrease tear secretion.^[13] However, the small number of cases with an abnormal Schirmer I test without anesthesia indicated that phacoemulsification affects the tear film stability and ocular surface inflammation more than tear secretion. Similar to other studies, this study also reported that dry eye can develop after cataract surgery.^[9,12,14,15] In particular, Li *et al.*^[12] reported high percentages of patients who developed dry eye following phacoemulsification; lower tear meniscus height, decreased TBUT scores, decreased Schirmer I test scores, and serious squamous metaplasia detected by impression cytology. Liu *et al.*^[14] reported worsening of the tear film pattern, height of the tear meniscus, and scores detected by the TBUT, Schirmer I test, and corneal fluorescein staining after phacoemulsification. Whereas Ram *et al.*^[9] reported no difference in the eye between before and after phacoemulsification in 23 of their patients. The reason for the discrepancy may be due to its small sample size and retrospective study design. There was no evidence of late reaction of dryness such as filamentary keratopathy, superior limbic keratoconjunctivitis, or persistent epithelial defect in this study. Ofloxacin eye drops 4 times daily for 2 weeks, prednisolone acetate ophthalmic suspension 1% 4 times daily for 1 week, and pranopulin eye drops 1% 4 times daily for 1 month were used during the post-operative period in this study. Review of literature shows that one of the factors causing dry eye was the delay in recovery process of the corneal nerves. Cornea is one of the most highly innervated organs with about 44 corneal nerve bundles entering the cornea around the limbus centripetally^[15] and larger nerve fibers that run from the 9 o'clock to the 3 o'clock position and bifurcate to achieve a homogenous distribution over the entire cornea;^[16] it is vulnerable to any damage within that region. Temporal corneal incisions created during phacoemulsification can reduce the corneal sensitivity in the surgical area and other areas far from the incision site.^[17,18] The damage to the corneal nerves may expand when longer phacoemulsification time is needed to break up a dense cataract.^[19] Disruption of the normal corneal innervations or lacrimal functional unit feedback can reduce the tear flow and blink rate and cause instability of the tear hyperosmolarity and tear film.^[1] As the corneal healing progresses postoperatively, new neurite

cells emerge, and after 25 days, the neural growth factor is released to regenerate the subepithelial corneal axon.^[20] Thus, the recovery of the corneal nerves may explain why the dry eye was seen early after surgery and improved thereafter. In the present study also delayed innervations might seem to be played a role in the occurrence of dry eye. Examination of the opposite eye in all the patients in this study did not reveal any significant dryness developing after surgery. Commonly used preservatives like benzalkonium in the local anesthetic eye drops can cause dry eye after phacoemulsification.^[9,11,12,21] Vigorous irrigation of the tear film and manipulation of the ocular surface during surgery is another factor that may reduce the goblet cell density and result in shortened TBUT postoperatively.^[12] It was observed in this study that use of light filters, decreased exposure time, appropriate irrigation, and gentle handling of the ocular surface tissue may decrease the postoperative complications. Benzalkonium chloride also can induce tear instability and decrease the number of mucin-expressing cells.^[12,22,23] Excessive and incorrect use of preserved eye drops is important factors that contribute to the development of dry eye after phacoemulsification and corneal toxicity.^[23] Minor factors associated with dry eye are elderly age, female gender, and diabetes.^[1,4,12] However, in the present study dry eye was not associated with those factors, which may have been due to the small sample size in other studies. In some individuals spontaneous appearance of dry eye may also occur hence further studies should be conducted to compare postoperative patients with subjects without operation who serve as control. Pre-operative assessment of the eye for vision as well as presence of dry eye is essential as dry eye may interfere with vision not in mild cases but certainly in moderate and severe cases. Hardten^[24] suggested using the ocular surface stress test, which takes about 30–60 min to perform and can be done after routine ocular examinations such as the slit-lamp examination and pupil dilatation. If an abnormal ocular surface is detected, the patients are at high risk of developing dry eye postoperatively. Other clinical tests such as the TBUT and fluorescein staining can be used to screen for dry eye. If dry eye is detected preoperatively, artificial tears or topical cyclosporine A can be prescribed postoperatively.^[21]

CONCLUSIONS

Dry eye symptoms can develop immediately after phacoemulsification and the severity can peak on day 7. Both symptoms and signs of dry eye can improve over time. However, it is important that ophthalmologists assess dry eye before and after phacoemulsification to ensure proper treatment, quality of vision, and quality of life for their patients.

REFERENCES

1. The definition and classification of dry eye disease: Report of the definition and classification subcommittee of the international dry eye workshop (2007). *Ocul Surf* 2007;5:75-92.
2. Mertzani P, Abetz L, Rajagopalan K, Espindle D, Chalmers R, Snyder C, *et al*. The relative burden of dry eye in patients' lives: Comparisons to a U.S. normative sample. *Invest Ophthalmol Vis Sci* 2005;46:46-50.
3. García-Catalán MR, Jerez-Olivera E, Benítez-Del-Castillo-Sánchez JM. Dry eye and quality of life. *Arch Soc Esp Oftalmol* 2009;84:451-8.
4. Moss SE, Klein R, Klein BE. Incidence of dry eye in an older population. *Arch Ophthalmol* 2004;122:369-73.
5. Moss SE, Klein R, Klein BE. Long-term incidence of dry eye in an older population. *Optom Vis Sci* 2008;85:668-74.
6. De Paiva CS, Chen Z, Koch DD, Hamill MB, Manuel FK, Hassan SS, *et al*. The incidence and risk factors for developing dry eye after myopic laser. *Am J Ophthalmol* 2006;141:438-45.
7. Shojia MR, Besharati MR. Dry eye after laser for myopia: Incidence and risk factors. *Eur J Ophthalmol* 2007;17:1-6.
8. Schaumberg DA, Dana R, Buring JE, Sullivan DA. Prevalence of dry eye disease among US men: Estimates from the physicians' health studies. *Arch Ophthalmol* 2009;127:763-8.
9. Ram J, Gupta A, Brar G, Kaushik S, Gupta A. Outcomes of phacoemulsification in patients with dry eye. *J Cataract Refract Surg* 2002;28:1386-9.
10. Sutu C, Fukuoka H, Afshari NA. Mechanisms and management of dry eye in cataract surgery patients. *Curr Opin Ophthalmol* 2016;27:24-30.
11. Cho YK, Kim MS. Dry eye after cataract surgery and associated intraoperative risk factors. *Korean J Ophthalmol* 2009;23:65-73.
12. Li XM, Hu L, Hu J, Wang W. Investigation of dry eye disease and analysis of the pathogenic factors in patients after cataract surgery. *Cornea* 2007;26:S16-20.
13. Kohlhaas M. Corneal sensation after cataract and refractive surgery. *J Cataract Refract Surg* 1998;24:1399-409.
14. Liu Z, Luo L, Zhang Z, Cheng B, Zheng D, Chen W, *et al*. Tear film changes after phacoemulsification. *Zhonghua Yan Ke Za Zhi* 2002;38:274-7.
15. Al-Aqaba MA, Fares U, Suleman H, Lowe J, Dua HS. Architecture and distribution of human corneal nerves. *Br J Ophthalmol* 2010;94:784-9.
16. Müller LJ, Vrensen GF, Pels L, Cardozo BN, Willekens B. Architecture of human corneal nerves. *Invest Ophthalmol Vis Sci* 1997;38:985-94.
17. Khanal S, Tomlinson A, Esakowitz L, Bhatt P, Jones D, Nabili S, *et al*. Changes in corneal sensitivity and tear physiology after phacoemulsification. *Ophthalmic Physiol Opt* 2008;28:127-34.
18. Sitompul R, Sancoyo GS, Hutauruk JA, Gondhowiardjo TD. Sensitivity change in cornea and tear layer due to incision difference on cataract surgery with either manual small-incision cataract surgery or phacoemulsification. *Cornea* 2008;27 Suppl 1:S13-8.
19. Belmonte C, Acosta MC, Gallar J. Neural basis of sensation in intact and injured corneas. *Exp Eye Res* 2004;78:513-25.
20. Roberts CW, Elie ER. Dry eye symptoms following cataract surgery. *Insight* 2007;32:14-21.
21. Liu ZG, Li W. Dry eye relevant to ocular surgery. *Zhonghua Yan Ke Za Zhi* 2009;45:483-5.
22. Wilson WS, Duncan AJ, Jay JL. Effect of benzalkonium chloride on the stability of the precorneal tear film in rabbit and man. *Br J Ophthalmol* 1975;59:667-9.
23. Ishibashi T, Yokoi N, Kinoshita S. Comparison of the short-term effects on the human corneal surface of topical timolol maleate with and without benzalkonium chloride. *J Glaucoma* 2003;12:486-90.
24. Hardten DR. Dry eye disease in patients after cataract surgery. *Cornea* 2008;27:855.

How to cite this article: Shamsheer RP. Clinical Evaluation of Patients Undergoing Phacoemulsification for Dry Eye. *Int J Sci Stud* 2019;7(5):32-36.

Source of Support: Nil, **Conflict of Interest:** None declared.

Comparision of Atracurium Versus Cisatracurium Regarding Onset Time, Intubating Conditions and Haemodynamic Parameters During General Anaesthesia

Vishnu Vardhan Athaluri¹, M Santhi Sree², Tejesh Kumar Mallepogu³

¹Professor, Department of Anaesthesia, Rangaraya Medical College, Kakinada, Andhra Pradesh, India, ²Associate Professor, Department of Anaesthesia, Siddhartha Medical College, Vijayawada, Andhra Pradesh, India, ³Senior Resident, Department of Anaesthesia, Rangaraya Medical College, Kakinada, Andhra Pradesh, India

Abstract

Introduction: Cisatracurium unlike atracurium is devoid of histamine-induced cardiovascular effects and this would be the greatest advantage in replacing atracurium for the facilitation of endotracheal intubation.

Aim: The aim of the study was to compare the effectiveness of atracurium 0.5 (2 ED₉₅) mg/kg IV versus two different doses of cisatracurium, i.e., 0.1 (2 ED₉₅) and 0.15 (3 ED₉₅) mg/kg IV for intubation with regard to onset time for intubation, intubating conditions, duration of blockade, and hemodynamic parameters.

Materials and Methods: In this study, 150 patients of the American Society of Anesthesiologists Grades 1 and 2 undergoing elective surgeries under general anesthesia were taken up and divided into three groups of 50 each by computer-generated randomization. Group A received Inj. atracurium besylate 0.5 mg/kg IV, Group B received Inj. cisatracurium besylate 0.1 mg/kg IV, and Group C received Inj. cisatracurium besylate 0.15 mg/kg IV.

Results: The three groups were compared regarding the onset of blockade, duration of blockade, condition of intubation, hemodynamic effects, and results analyzed.

Conclusion: Cisatracurium 0.15 mg/kg provides excellent intubating conditions with rapid onset of action, with longer duration of action and no significant hemodynamic changes when compared with cisatracurium 0.1 mg/kg and atracurium 0.5 mg/kg and hence cisatracurium 0.15 mg/kg can be used as an ideal non-depolarizing muscle relaxant for intubation.

Key words: Atracurium, Cisatracurium, General anesthesia, Intubation

INTRODUCTION

Endotracheal intubation is an integral part of the administration of general anesthesia during the surgical procedure. Succinylcholine, introduced by Thesleff and associates in 1952, a depolarizing muscle relaxant with

rapid onset of action and short duration is still the relaxant of choice to facilitate tracheal intubation. However, in addition to fasciculations, succinylcholine has many side effects such as bradycardia, dysrhythmias, increased release of potassium, post-operative myalgia, increased intra ocular pressure, intracranial tension, intragastric pressure, prolonged recovery in patients with pseudocholinesterase deficiency, masseter spasm, and triggering malignant hyperthermia.^[1-6] Since these side effects are due to the depolarizing mechanism of action of succinylcholine, search has been focused onto find an ideal non-depolarizing muscle relaxant (NDMR) with rapid onset time and offering excellent intubating conditions.

Access this article online



www.ijss-sn.com

Month of Submission : 06-2019
Month of Peer Review : 07-2019
Month of Acceptance : 08-2019
Month of Publishing : 08-2019

Corresponding Author: Dr. M Santhi Sree, Dr. no.: 13-2-2, D1Apt, Sai Krishna Towers, Latchiraju Street, Suryaraopeta, Kakinada - 533 002, Andhra Pradesh, India.

Classification of non-depolarizing muscle relaxants:

	Long-acting (>50 min)	Intermediate-acting (20–50 min)	Short-acting (10–20 min)
Steroidal compounds	Pancuronium	Vecuronium	
		Rocuronium	
Benzylisoquinolinium compounds	Tubocurarine	Atracurium	Mivacurium
		Cisatracurium	

Cisatracurium is one of the 10 isomers of atracurium. The neuromuscular blocking potency of cisatracurium is approximately three-fold that of atracurium besylate. Cisatracurium has ED₉₅ of 50 µg/kg and atracurium has ED₉₅ of 0.2 mg/kg. The principal advantage of cisatracurium is lack of histamine release, which provides better cardiovascular stability in comparison to atracurium and other histamine-releasing neuromuscular blocking agents. Hence, these two drugs are compared in this study.

Aim of the Study

The aim of the study was to compare the effectiveness of atracurium 0.5 (2 ED₉₅) mg/kg IV versus two different doses of cisatracurium, i.e., 0.1 (2 ED₉₅) and 0.15 (3 ED₉₅) mg/kg IV for intubation following induction with etomidate (0.3 mg/kg), with regard to

- Onset time for intubation
- Intubating conditions
- Duration of blockade
- Hemodynamic parameters.

MATERIALS AND METHODS

Adult patients of both sexes in the age group of 18–60 years belonging to the American Society of

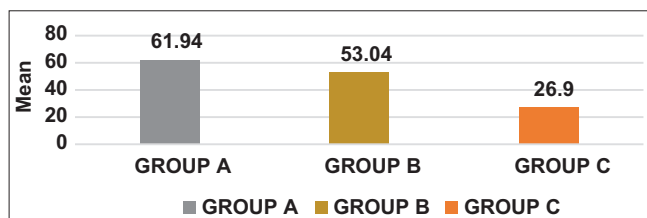


Figure 1: Distribution of study participants based on train-of-four % AT 60 s

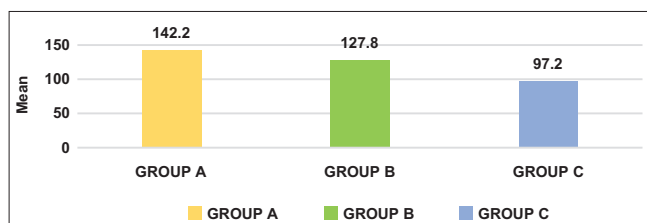


Figure 2: Comparison of time to maximum blockade between three groups

Anesthesiologists (ASA) I/II posted for various surgeries requiring general anesthesia at Rangaraya Medical College, Government General Hospital Kakinada were taken up for the study. The study was a prospective randomized double-blind study.

The study was performed after obtaining the Institutional Ethical Committee approval. Pre-study assessment was done, procedure explained and informed consent obtained, and patients requiring general anesthesia were randomly allocated into three groups based on computer-generated randomization.

Groups:

1. Group A: Fifty patients receiving Inj. atracurium besylate 0.5 mg/kg IV
2. Group B: Fifty patients receiving Inj. cisatracurium besylate 0.1 mg/kg IV
3. Group C: Fifty patients receiving Inj. cisatracurium besylate 0.15 mg/kg IV.

Patient Selection

Inclusion criteria

A total of 150 patients of ASA Grades I and II of age between 18 and 60 years of both genders posted for elective surgery requiring general anesthesia with endotracheal intubation without any comorbid illness are included in this study.

Exclusion criteria

The following criteria were excluded from the study:

- ASA Grade – III and Grade – IV
- Mallampati Grade – III and mallampati Grade – IV
- Anticipated difficult airway
- Comorbid systemic conditions, i.e., cardiovascular system, hepatic, and renal impairment along with neuromuscular disorders
- Patients who are on aminoglycosides, MgSO₄
- Known history of allergy to any of the study drugs
- Pregnant women.

Monitoring

Heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), SPO₂, five lead electrocardiogram (ECG), and train-of-four (TOF)-Watch SX 100 were recorded with space labs multipara monitor in the operating room.

Methodology

Preanesthetic evaluation and counseling for surgery were done the day before surgery and reviewed on the day of surgery. A detailed medical history was taken and systemic examination carried out and relevant investigations advised.

Table 1: Distribution of study groups based on demographic data

	Group A	Group B	Group C	P-value
Age (mean±standard deviation)	36.16±9.90	35.86±9.76	34.9±9.59	0.79
Sex (M: F)	25:25	23:27	26:24	0.83
Weight (kg)	59.84±7.1353	58.18±7.0093	59.94±7.04	0.37

Demographic data are not significant as $P>0.05$

An informed written consent was taken from all the patients and was informed about known effects, and side effects of study drug and consent are taken for the study.

The night before surgery tab. Diazepam 5 mg was given. On the day of surgery in operation theater,

1. IV line secured with 18G canula
2. All the ASA monitors such as ECG, non-invasive blood pressure, SpO₂, end-tidal carbon dioxide (EtCO₂), and temperature were connected
3. All baseline parameters noted such as HR, SBP, DBP, MAP, and SpO₂ were noted.

Premedication

All patients are given Inj. glycopyrrolate. 2 mg IV, Inj. ondansetron. 1 mg/kg IV, Inj. ranitidine 50 mg 1 h before surgery, Inj. fentanyl 1 µg/kg, and Inj. phenergan 0.5 mg/kg IM 45 min before surgery.

Preoxygenation

It is done with 100% O₂ for 3 min.

- TOF-Watch SX 100 nerve stimulator attached. TOF Watch SX turned on. Once the current and twitch height were standardized, instrument switched to TOF mode where supra maximal TOF stimuli are applied to ulnar nerve every 15 s. Calibration and baseline responses obtained before administering the neuromuscular blocking drug (NMBD). Randomization was done on computer-generated lottery method.

All patients received priming dose (1/10th of the bolus dose) of the study drug according to the allocated group,

- Group A: Received priming dose of atracurium (i.e., 0.05 mg/kg)
- Group B: Received priming dose of cisatracurium (i.e., 0.01 mg/kg)
- Group C: Received priming dose of cisatracurium (i.e., 0.015 mg/kg).

Just before induction to shorten the onset time.

Induction

Induction of general anesthesia for all patients was done with Inj. Etomidate 0.3 mg/kg with loss of eyelash reflex/loss of verbal response considered to be the

Table 2: Distribution of study participants based on train-of-four % AT 0 s

Groups	Mean±standard deviation	P-value
A	104.73±5.365	0.577
B	103.4±3.225	
C	105.27±5.958	

$P=0.577$ not significant

Table 3: Distribution of study participants based on train-of-four % AT 30 s

Groups	Mean±standard deviation	P-value
A	71.94±4.98	0.001
B	73.96±5.29	
C	68.92±6.64	

$P<0.05$ significant

Table 4: Distribution of study participants based on train-of-four % AT 60 s

Groups	Mean±standard deviation	P-value
A	61.94±4.6397	0.001
B	53.04±4.4307	
C	26.9±7.2005	

$P=0$ is significant

Table 5: Distribution of study participants based on train-of-four % AT 90 s

Groups	Mean±standard deviation	P-value
A	35.00±7.60	0.001
B	26.86±7.22	
C	8.54±7.68	

$P=0$ is significant

Table 6: Distribution of study participants based on train-of-four % AT 120 s

Groups	Mean±standard deviation	P-value
A	24.82±6.26	0.001
B	9.56±8.10	
C	1.32±1.99	

$P=0$ is significant

endpoint of induction. This was followed by an intubating dose of study drug, i.e., NDMR, over 5 s

- Group A received remaining bolus of an intubating dose of atracurium (0.45 mg/kg)
- Group B received remaining bolus of an intubating dose of cisatracurium (0.09 mg/kg)

- Group C received remaining bolus of an intubating dose of cisatracurium (0.135 mg/kg).

TOF-Watch SX showed TOF ratio as percentage and results recorded at 30 s interval.

Time to Maximum Blockade

- Time interval between administration of the dose of relaxant and disappearance of all four twitches in TOF monitor
- Intubation was done when the TOF ratio was 0%
- Assessment of intubation was done by scoring system given by Cooper *et al.*

Cooper <i>et al.</i> , scores				
Criteria	0	1	2	3
Jaw relaxation	Complete	Moderate	Minimal	None
Vocal cord status	Open	Slight moving	Closing	Closed
Diaphragmatic status	None	Slight moving	Coughing	Bucking

Intubating conditions and time required for intubation were graded by a senior anesthesiologist blinded to group allocation. Intubation confirmed by EtCO₂ and connected to a ventilator for intermittent positive pressure ventilation until completion of surgery.

Maintenance

Maintenance of anaesthesia done with N₂O 60% and Sevoflurane.

Onset time and intubating conditions for atracurium and cisatracurium assessed in allocated groups, respectively. The number of attempts of intubation was assessed and compared in between three groups. Hemodynamic parameters such as HR, SBP, DBP, and MAP were recorded before induction, immediately after induction, during laryngoscopy and intubation and immediately

after 1, 2, 3, 5, 10, and 15 min after tracheal intubation. After procedure patient was reversed with neostigmine (0.05 mg/kg) and glycopyrrolate (0.01 mg/kg). Any adverse events during intubation were recorded in all the three groups.

Statistical Analysis

The data are presented as mean and standard deviation. All categorical data analyzed using Fischer exact test and Chi-square test as required and continuous variables using Student's *t*-test. Value of *P* < 0.05 was considered significant. GraphPad prism version 7 (California corp.inc) was used for statistical analysis.

RESULTS

Demographic data analysed and found not significant as *p* value>0.05 [Table 1].

Hence, Group C provides good to excellent intubating conditions than the other two groups [Table 2-8].

Hence, Group C has a rapid onset of action than the other two groups [Table 9].

Hence, intubation time was found to be significantly faster in Group C than two other groups [Table 10 and Figure 1].

Hence, the duration of the blockade was found to be significant in Group C, which has a long duration of action than two other groups [Table 11 and Figure 2].

- Data expressed as mean±standard deviation in both groups
- P* > 0.05 statistically not significant.

The baseline hemodynamic parameters between the three groups are not significant statistically as *P* > 0.05 [Table 12].

Baseline hemodynamic parameters (HR, SBP, DBP, and MAP) are recorded and compared between three groups. There is no significant difference between them [Table 13]. Our study found no differences in hemodynamic parameters (SBP, DBP, and MAP) between three groups.

Table 7: Distribution of study participants based on train-of-four % AT 150 s

Groups	Mean±standard deviation	<i>P</i> -value
A	8.30±7.93	0.001
B	0.84±2.09	
C	0.00±0.00	

P=0 is significant

Table 8: Comparison of intubating conditions between three groups

	Intubating conditions (Cooper <i>et al.</i> , score)				Mean±standard deviation	<i>P</i> -value
	Excellent (0)	Good (1)	Poor (2)	Not possible (3)		
Group A (n=50)	19	21	10	0	0.82±0.7475	0.00001
Group B (n=50)	20	21	9	0	0.78±0.7365	
Group C (n=50)	36	12	2	0	0.24±0.4314	

P=0.00001 which is <0.05 significant

DISCUSSION

In 1942, Griffith and Johnson described d-tubocurarine (dTc) as a safe drug to provide skeletal muscle relaxation during surgery.^[7] In 1954, Beecher and Todd reported a six-fold increase in mortality in patients receiving dTc compared with patients who had not received muscle relaxant.^[8]

In 1952, Thesleff,^[9] foldes and associates,^[10] introduced succinylcholine, changed anesthetic practice drastically because the drug's rapid onset of effect and ultrashort duration of action allowed for both rapid endotracheal intubation and rapid recovery of neuromuscular strength.

In 1967, Baird and Reid first reported on the clinical administration of the first synthetic aminosteroid, pancuronium.^[11] The development of the intermediate-acting NMBDs built on the compounds metabolism and resulted in the introduction of vecuronium,^[12] an aminosteroid, and atracurium,^[13] a benzyloquinolinium,

into clinical practice in the 1980s. Vecuronium was the first muscle relaxant to have an intermediate duration of action and minimal cardiovascular actions. Mivacurium, the first short-acting non-depolarizing NMBD, was introduced into clinical practice in the 1990s,^[13] as was rocuronium,^[14] an intermediate-acting non-depolarizing blocker with a very rapid onset of neuromuscular blockade. These include pipecuronium, doxacurium, cisatracurium, and rapacuronium. Although all do not remain in use, each represented an advance or improvement in at least one aspect over its predecessors.

Endotracheal intubation is an integral part of the administration of general anesthesia during the surgical procedure.

Succinylcholine, a depolarizing muscle relaxant with rapid onset of action and short duration, is still the relaxant of choice to facilitate tracheal intubation. However, in addition to fasciculations, succinylcholine has many side effects such as bradycardia, dysrhythmias, increased release of potassium, post-operative myalgia, increased intraocular pressure, intracranial tension, intragastric pressure, prolonged recovery in patients with pseudocholinesterase deficiency, masseter spasm, and triggering malignant hyperthermia.^[1-6]

Since these side effects are due to the depolarizing mechanism of action of succinylcholine, search has been focused on to find an ideal NDMR with rapid onset time and offering excellent intubating conditions.

Cisatracurium is one of the 10 isomers of atracurium. The neuromuscular blocking potency of cisatracurium is approximately three-fold that of atracurium besylate. Cisatracurium has ED₉₅ of 50 µg/kg and atracurium has ED₉₅ of 0.2 mg/kg. The principal advantage of cisatracurium is lack of histamine release which provides better cardiovascular stability in comparison to atracurium and other histamine-releasing neuromuscular blocking agents. Hence, these two drugs are compared in this study. In this study, non-depolarizing, intermediate-acting, benzyloquinolinium compounds atracurium and cisatracurium were chosen, and their neuromuscular function was monitored using TOF-Watch SX 100.

Table 9: Comparison of time to maximum blockade between three groups

Group	Mean±standard deviation (s)	P-value
A	142.2±14.504	0.001
B	127.8±14.2914	
C	97.2±14.9202	

P=0.0 which is <0.05 significant

Table 10: Comparison of intubation time between three groups

Group	Mean±standard deviation (s)	P-value
A	144±9.4761	0.001
B	145.2±11.292	
C	135.2±11.102	

P=0 which is significant

Table 11: Comparison of duration of blockade between three groups

Group	Mean±standard deviation (min)	P-value
A	43.34±3.4736	0.001
B	43.06±4.3632	
C	52.06±3.8778	

P=0 which is <0.05 significant

Table 12: Comparison of baseline hemodynamic parameters

Parameters	A n=50 (mean±SD)	B n=50 (mean±SD)	C n=50 (mean±SD)	P-value
Heart rate	76.26±6.8148	76.02±97.5119	78.16±8.1375	0.2984
Systolic blood pressure	121.22±10.1966	122.8±9.8229	123.94±9.1147	0.37514
Diastolic blood pressure	75.16±7.9651	77.78±7.4458	76.88±7.8132	0.23161
Mean arterial pressure	90.42±8.0232	92.76±7.7921	92.62±7.7746	0.25168

SD: Standard deviation

Table 13: Comparison of heart rate between the three groups

Time	Groups	HR (mean±standard deviation)	P-value
Base line	A	76.26±6.8148	0.29
	B	76.02±7.5119	
	C	78.16±8.1375	
During laryngoscopy	A	97.94±6.4441	0.17
	B	97.18±6.986	
	C	99.7±7.2906	
After intubation 1 min	A	95.94±6.5072	0.30
	B	96.18±7.403	
	C	97.94±7.101	
2 min	A	90.88±5.9544	0.84
	B	90.22±6.7349	
	C	90.8±6.1246	
3 min	A	78.88±6.8053	0.15
	B	78.92±7.6394	
	C	81.4±7.7985	
5 min	A	79.72±6.8662	0.68
	B	80.08±7.5643	
	C	80.98±7.746	
10 min	A	79.82±7.2272	0.92
	B	79.8±7.7728	
	C	80.2±7.9076	
15 min	A	77.26±6.8148	0.23
	B	76.22±6.2639	
	C	78.62±8.0328	

$P > 0.05$ in all three groups. Hence, heart rate changes are not significant

Cisatracurium, the 1R *cis*-1' R *cis* isomer of atracurium, comprises approximately 15% of atracurium by weight but more than 50% in terms of neuromuscular blocking activity like atracurium, cisatracurium is metabolized by Hofmann elimination. It is approximately 4 times as potent as atracurium, and in contrast to atracurium, it does not cause histamine release, thus indicating that histamine release may be stereospecific. The principal advantage of cisatracurium is that there has been no evidence of histamine release at doses up to 8 times the ED_{95} ⁴⁹, whereas atracurium causes histamine release in humans at doses greater than $2.5 \times ED_{95}$. The onset time or time to maximum blockade for $2 \times ED_{95}$, $4 \times ED_{95}$, $8 \times ED_{95}$ are 5.2 min, 2.7 min, and 1.9 min, respectively, and as dose increases clinical duration also increases from 45 min, 68 min, and 91 min, respectively. The intubating dose cisatracurium is 0.15–0.2 mg/kg provides excellent intubating conditions. Doses of 0.1 mg/kg and 0.15 mg/kg of cisatracurium are used in this study.

Laryngeal adductors are more resistant to the action of cisatracurium than adductor pollicis, but onset and recovery are faster at the larynx. Adductor pollicis is most commonly used to monitor neuromuscular blockade, ulnar nerve was used to monitor in this study.

Atracurium is a bisquaternary ammonium benzyloquinoline compound of intermediate duration of action. Atracurium has histamine-releasing properties. Laryngeal adductors and orbicularis oculi have faster onset than adductor pollicis.

An intubating dose of $2 \times ED_{95}$ is 0.5 mg/kg onset of action is 3.2 min and clinical duration of action is 46 min. $2 \times ED_{95}$, i.e., 0.5 mg/kg is used this study.

To reduce the onset time priming technique has been used, when priming, a small, subparalyzing dose of the non-depolarizer ($\approx 20\%$ of the ED_{95} or $\approx 10\%$ of the intubating dose) is administered 2–4 min before the intubating dose of the compound. This procedure accelerates the onset of blockade for most non-depolarizing NMBDs only by 30–60 s, thereby indicating that intubation can be performed within 90 s of the second dose. Hence, in this study, two equipotent doses of cisatracurium and atracurium, i.e., $2 \times ED_{95}$ (0.1 mg/kg, 0.5 mg/kg, respectively) and $3 \times ED_{95}$ doses of cisatracurium are compared for onset time, intubating conditions, and hemodynamic parameters.

Duggappa *et al.* have studied that the onset time of atracurium on priming with 0.05 mg/kg, i.e., $1/10^{\text{th}}$ of the intubating dose 0.5 mg/kg was 147 s.

Deepika *et al.* have studied that the onset time of cisatracurium on priming with 0.01 mg/kg and 0.015 mg/kg, i.e., $1/10^{\text{th}}$ of the intubating dose 0.1 mg/kg and 0.15 mg/kg was found to be 126 s and 103 s, respectively.

El-Kasaby *et al.* have studied that the duration of action of 0.1 mg/kg of cisatracurium and 0.5 mg/kg of atracurium was 44 min and 43 min, respectively.

Bluestein *et al.* have studied that the duration of action of 0.1 mg/kg, 0.15 mg/kg of cisatracurium, and 0.5 mg/kg of atracurium was found to be 44 min, 55 min, and 43 min, respectively.

Teymourian *et al.* have compared modified and high dose of cisatracurium for rapid sequence intubation and found that 0.3 versus 0.4 mg/kg cisatracurium had the same effect in providing appropriate laryngoscopy condition for rapid sequence induction (RSI) after 90 s. It is safer to use 0.3 mg/kg instead of 0.4 mg/kg cisatracurium to achieve acceptable condition for RSI.

In this prospective randomized double-blind study, 150 patients satisfying selection criteria underwent general anesthesia with cisatracurium 0.1 mg/kg, 0.15 mg/kg, and atracurium 0.5 mg/kg. The onset of action, which was the disappearance of all four twitches and TOF ratio 0%, the duration of action and hemodynamic variables were assessed.

The mean onset of action or the time to maximum blockade was significantly faster in Group C (cisatracurium 0.15 mg/kg) than Group B (cisatracurium 0.1 mg/kg) than Group A (atracurium 0.5 mg/kg), the onset of action was 97 s for Group C, 128 s for Group B, and 142 s for Group A, as shown by Deepika *et al.* and Duggappa *et al.*

The mean duration of action was significantly longer in Group C (cisatracurium 0.15 mg/kg) than Group B (cisatracurium 0.1 mg/kg) and Group A (atracurium 0.5 mg/kg), the duration of action was 52 min in Group C, 43 min in Group B, and 43 min in Group A which were consistent with the El-Kasaby *et al.* and Bluestein *et al.*

The hemodynamic variables such as pulse rate, SBP, and DBP were not significantly altered in all the three groups. There were no significant changes in the hemodynamic variables during pre-operative, at the time of injecting the drug, during laryngoscopy and 1, 2, 3, 5, 10, and 15 min after laryngoscopy in all the three groups (A, B, and C) as shown in Jammam *et al.* and Amini *et al.*

No adverse reaction or complication occurred in any of the three groups.

CONCLUSION

Cisatracurium 0.15 mg/kg provides excellent intubating conditions with rapid onset of action, with a longer duration of action and no significant hemodynamic changes when compared with cisatracurium 0.1 mg/kg and atracurium 0.5 mg/kg and hence cisatracurium 0.15 mg/kg can be used as an ideal non-depolarizing muscle relaxant for intubation.

REFERENCES

1. Schoenstadt DA, Whitcher CE. Observations on the mechanism of succinylcholine-induced cardiac arrhythmias. *Anesthesiology* 1963;24:358-62.
2. Schwartz DE, Kelly B, Caldwell JE, Carlisle AS, Cohen NH. Succinylcholine-induced hyperkalemic arrest in a patient with severe metabolic acidosis and exsanguinating hemorrhage. *Anesth Analg* 1992;75:291-3.
3. Pandey K, Badola RP, Kumar S. Time course of intraocular hypertension produced by suxamethonium. *Br J Anaesth* 1972;44:191-6.
4. Salem MR, Wong AY, Lin YH. The effect of suxamethonium on the intragastric pressure in infants and children. *Br J Anaesth* 1972;44:166-70.
5. Booi LH. Is succinylcholine appropriate or obsolete in the intensive care unit? *Crit Care* 2001;5:245-6.
6. Bauer SJ, Orio K, Adams BD. Succinylcholine induced masseter spasm during rapid sequence intubation may require a surgical airway: Case report. *Emerg Med J* 2005;22:456-8.
7. Griffith H, Johnson GE. The use of curare in general anesthesia. *Anesthesiology* 1942;3:418.
8. Beecher HK, Todd DP. A study of the deaths associated with anesthesia and surgery: Based on a study of 599, 548 anesthetics in ten institutions 1948-1952, inclusive. *Ann Surg* 1954;140:2-35.
9. Thesleff S. Farmakologiska och kliniska forsok med L.T. I. (O, O-succinylcholine jodid). *Nord Med* 1951;46:1045.
10. Foldes FF, Mcnall PG, Borrego-Hinojosa JM. Succinylcholine: A new approach to muscular relaxation in anesthesiology. *N Engl J Med* 1952;247:596-600.
11. Baird WL, Reid AM. The neuromuscular blocking properties of a new steroid compound, pancuronium bromide. A pilot study in man. *Br J Anaesth* 1967;39:775-80.
12. Savage DS, Sleight T, Carlyle I. The emergence of ORG NC 45, 1-[2 beta, 3 alpha, 5 alpha, 16 beta, 17 beta)-3, 17-bis(acetyloxy)-2-(1-piperidinyl)-androstane-16-yl]-1-methylpiperidinium bromide, from the pancuronium series. *Br J Anaesth* 1980;52 Suppl 1:3S-9.
13. Savarese JJ, Ali HH, Basta SJ, Embree PB, Scott RP, Sunder N, *et al.* The clinical neuromuscular pharmacology of mivacurium chloride (BW B1090U). A short-acting nondepolarizing ester neuromuscular blocking drug. *Anesthesiology* 1988;68:723-32.
14. Wierda JM, De Wit AP, Kuizenga K, Agoston S. Clinical observations on the neuromuscular blocking action of ORG 9426, a new steroidal non-depolarizing agent. *Br J Anaesth* 1990;64:521.

How to cite this article: Athaluri VV, Sree MS, Mallepogu TK. Comparison of Atracurium Versus Cisatracurium Regarding Onset Time, Intubating Conditions and Haemodynamic Parameters During General Anaesthesia. *Int J Sci Stud* 2019;7(5):37-43.

Source of Support: Nil, **Conflict of Interest:** None declared.

Clinical and Radiological Study of Fistula in Ano in Tertiary Care Centre and Management

R Vidyasagar

Assistant Professor, Department of General Surgery, Mahatma Gandhi Memorial Hospital, Kakatiya Medical College, Warangal, Telangana, India

Abstract

Introduction: Fistula-in-ano form a good majority of treatable benign lesions of the rectum and anal canal. About 90% or so of these cases are end results of crypto glandular infections.

Materials and Methods: Patient placed in the lateral position and the external opening of the fistula is identified and cannulated, and saline is injected. The patient is then placed in a supine position in magnetic resonance (MR) gantry.

Results: Clinical examination less accurate to detect internal opening while MR fistulogram could detect most of the internal openings which were confirmed in surgical findings.

Key words: Crohn's disease, Fistula-in-ano, Magnetic resonance imaging

INTRODUCTION

“More is missed by not looking, then by not knowing “by Thomas M Crae.” Fistula-in-ano forms a good majority of treatable benign lesions of the rectum and anal canal. About 90% or so of these cases are end results of crypto glandular infections. As such, the vast majority of these infections are an acute and significant minority is contributed by chronic, low-grade infections, hence pointing to varying etiologies. The common pathogenesis, however, is the bursting open of an acute or inadequately treated anorectal abscess into the pen-anal skin. Most of these fistulas are easy to diagnose with a good source of light, a proctoscope, and a meticulous digital rectal examination. Despite the easy to diagnosis, establishing a cure is problematic on two accounts. First, many patients tend to let their ailment nag them rather than being subject to examination, mostly due to the site of affection of the disease. The more important second factor is that a significant percentage of these diseases persist or recur

when the right modality of surgery is not adopted or when the post-operative care is inadequate. Hence, these conditions affect the young and middle-aged persons causing loss of valuable productive hours.

The importance of imaging and treatment of a fistula-in-ano are attributed to the complex pelvic floor anatomy and the fistula's notorious reputation of recurrence despite utmost care taken during and after its surgery.

Surgery can be extremely demanding, especially if the fistula is complex. The objectives are to eradicate the tract and drain associated sepsis while simultaneously preserving continence. To achieve this surgeon needs the answer to the following questions:

1. What is the relationship between the fistula and anal sphincter? Will surgery risk incontinence and will sphincter-saving procedures be necessary, and
2. Are there secondary extensions from the primary tract which might cause relapse, and if so where are they?

Merely diagnosing a fistula by imaging is unlikely to help the surgeon, in all probability he has already seen it during an anal inspection. Instead, imaging needs to accurately determine the exact anatomy and roots of the fistula, which is originally the most important management objective. This will define the surgical approach and ensure that treatment is complete.

Access this article online



www.ijss-sn.com

Month of Submission : 06-2019
Month of Peer Review : 07-2019
Month of Acceptance : 08-2019
Month of Publishing : 08-2019

Corresponding Author: Dr. R Vidyasagar, H.no: 35-6-771, Gopalpur, TV Tower Colony, hanmkonda, Warangal 506009, Telangana, India.
Phone: 9573483633. E-mail: drvsrayapuri@gmail.com

Over the years, many imaging modalities have been tried, to achieve those objectives. These are conventional fistulography, anal endosonography (AES), computed tomography, and most recently, magnetic resonance fistulography (MRFG).

Contrast fistulography is the most traditional radiological technique used to define fistula anatomy. It involves catheterization of the external opening and injection of water-soluble contrast media which represent the fistulous tract.

AES, developed at St. Mark's Hospital Northwick Park, Harrow, UK, was the first technique to directly visualize the anal sphincter complex in detail. Modern 10 MHz rectal endoprobes are used to identify and study the sphincteric complex.

Computed tomography has also been utilized to evaluate fistula-in-ano. (However, its ability to image in axial planes only and poor soft tissue differentiation limits its ability to classify fistulae with sufficient accuracy).

The continuing need for a better imaging modality for fistula-in-ano led to the use of magnetic resonance imaging (MRI) as a diagnostic and pre-operative evaluation modality.

MRI is a recently devised modality to study fistula-in-ano. Imaging is done in axial, coronal and sagittal planes using T1, T2, short T1 for fat suppression and TRIM sequences. Various coils, namely, spine array, body array, and special endorectal coils may be used.

The following study involves detailed evaluation of fistula-in-ano, its complications and pelvic floor anatomy using magnetic resonance (MR) fistulography, and comparing it with clinical and surgical results.

Aims and Objectives of the Study

The objectives are as follows:

1. To study the different modes of clinical presentations of the fistula- in-ano.
2. To evaluate the role of MRI and its use as a pre-operative evaluation modality for perianal fistulae. This has been done by analyzing its ability to delineate.
 - a) The primary tract.
 - b) Secondary tracts and its ramifications.
 - c) Abscess/Source of persistent infection.
 - d) Relation of the tract to the sphincter complex.
 - e) Relation of the tract to levator ani.

PATIENTS AND METHODS

A prospective study of 30 patients with suspected fistula in ANO, primary or recurrent presenting to the Mahatma

Gandhi Memorial Hospital, Warangal, between June 2016 and September 2018 admitted in the Department of General Surgery. All 30 patients will be examined clinically and later subjected to MRFG.

MRFG will be performed using GE 1.5 Tesla using HDX using PA coils.

Method

Patient placed in the lateral position and the external opening of the fistula is identified and cannulated, and saline is injected. The patient is then placed in a supine position in magnetic resonance (MR) gantry.

MR Technique Used

A scout sagittal section is obtained through the anal canal region which will be used for planning of coronal, sagittal, and axial views.

1.	STIR	Coronal
2.	T1	Coronal
3.	T2	Sagittal
4.	T1	Axial
5.	T2	Axial
6.	T2 fat sat	Axial

STIR: Short T1 for fat suppression

These sections will be taken extending from perianal region to above the level of the levator ani muscle.

Inclusion Criteria

All the patients included in the study presented to the surgery department for any of the following indications.

- Age group from 30 to 80 years.
- Pre-operative evaluation for all clinically proven fistula-in-ano.
- Single/Multiple discharging sinuses in the perianal region.
- Recurrent perianal abscess for detection of undetected tracks.

Exclusion Criteria

The following criteria were excluded from the study:

- Patients with MR incompatible devices or implant
- Patients on the life support system.
- Patients with profound septicemia with an inability to lie down in supine position.
- Patient with claustrophobia.

RESULTS

Distribution of Cases by Age and Sex

There are 30 cases undergone for MRFG for suspicion of fistula-in-ano Table 1.

Table 1: Age distribution in patient with fistula-in-ano

Age group (Years)	No. of cases	Percentage
31–40	4	13.33
41–50	10	33.00
51–60	11	36.66
61–70	4	13.33
71–80	1	3.33
Total	30	100

Table 2: Sex incidence of 30 patients with fistula-in-ano

Sex	No. of cases	Percentage
Male	26	86.6
Female	4	13.4

Table 3: Incidence of primary and recurrent fistulas in 30 patients

Types	No. of cases	Table N%
Primary	12	39.96
Recurrent	18	60.0

Table 4: Primary cases with risk factors

Associated diseases	No. of cases	Table N%
DM	3	25
Nil	4	33.33
TB	4	33.33
TB, DM	1	8.33

DM: Diabetes mellitus, TB: Tuberculosis

There were 4 females in the age group 50–75 years Table 2. Out of 26 males, 13 (50%) were in the age group of 41–60 years. The number of male patients is significantly higher when compared to females.

In our study, majority of the cases (60%) reviewed by MRFG had recurrent fistulas Table 3.

It was observed that at least 67% of the patients with primary fistulas had some associated risk factor Table 4. This shows the importance of the presence of risk factors in the occurrence of fistula-in-ano.

It was observed that at least 39% of the patients with recurrent fistulas had some associated risk factor Table 5. This shows the importance of the presence of risk factors in recurrence.

Most of the patients (83%) were found to have complicated fistula, i.e., Grade-II and above Table 6.

Only 30% of the patients with no risk factors were found to have higher grade fistulas, i.e. \geq Grade II, whereas the

Table 5: Recurrence rate with high-risk factors

Associated diseases	No. of cases	Table N%
DM	4	22.22
Nil	11	61.11
TB	2	11.11
TB, DM	1	5.55

DM: Diabetes mellitus, TB: Tuberculosis

Table 6: Distribution of cases according to various MRI grades of fistula-in-ano

Grade	No. of cases	Percentage
1	5	16.66
2	9	30.00
3	4	13.33
4	6	20.00
5	6	20.00

MRI: Magnetic resonance imaging

high-risk population had more cases, 46.6% with higher grade fistula Table 7. Patients with risk factors (tuberculosis [TB]/diabetes mellitus [DM]/Both) were found to have more incidence of higher grade fistulas as compared to fistulas at low risk.

Almost half (50%) of the patients evaluated by MRFG were found to have abscess collections in various sphincteric planes Table 8. It was observed that in 17% of the patients, abscess collections occurred in multiple planes, the detection of which has significant implications on the outcome of the surgery.

Distribution of abscess collection with regard to type of presentation does not appear to be significantly different Table 9.

It was observed that the majority (70%) of the patients who underwent MRFG were found to have secondary tracts which have utmost importance in surgical planning Table 10.

It was observed that the occurrence of secondary tracts was significantly higher in recurrent cases, which were almost 77.77%. Hence, it is important to look for secondary tracts in recurrent cases Table 11.

About 83% of the cases found to have supralelevator (SLA) collection had recurrent fistulas, and 17% of cases found to have SLA collection had primary fistula. It is important to look for SLA collection in the recurrent fistula Table 12.

It was observed that 83% of the cases with SLA collections had an associated high-risk factor, whereas only 17% of the cases had no risk factor Table 13.

Table 7: Evaluation of different grades of fistula in risk group as compared to the non-risk group

Associated diseases	No. of cases in each MR grade				
	1	2	3	4	5
DM	1	2	1	2	1
Nil	4	6	2	2	1
TB	0	1	1	2	2
TB, DM	0	0	0	0	2

DM: Diabetes mellitus, TB: Tuberculosis, MR: Magnetic resonance

Table 8: Breakup of cases with abscess collection in relation to the various sphincteric planes (IS/ES/SL) as seen on MRFG

Collection plane	No. of cases	Percentage
ES	3	10.0
ES+SL	2	6.7
IS	5	16.7
IS+ES	1	3.3
IS+ES+SL	1	3.3
IS+SL	1	3.3
Nil	15	50.0
SL	2	6.7

MRFG: Magnetic resonance fistulography

Table 9: Distribution of abscess collection by type of presentation (Primary/Recurrent)

Types	ES		ES+SL		IS		IS+ES		IS+ES+SL		IS+SL		SL	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Primary	1	3	1	3	3	10	0	0	0	0	0	0	0	0
Recurrent	2	7	1	3	2	7	1	3	1	3	1	3	2	7

Table 10: Distribution of secondary tracts

Types	Present	
	No. of cases	Percentage
Primary	7	58.33
Recurrent	14	77.72

Table 11: Distribution of secondary tracts in various grades of fistula

MR grade	Secondary tract	
	Primary	Recurrent
1	0	0
2	3	6
3	1	0
4	2	4
5	1	4

Among the 30 patients diagnosed to have primary tracts by MRFG the diagnosis for the internal opening was found to match with the surgical report in 24 patients, which gives the 86% for detection of internal opening by MRFG Table 14.

Table 12: Percentage of primary and recurrent fistulas with supralelevator collection

Type	No. of cases	Percentage
Primary	1	17
Recurrent	5	83

Table 13: SLA collections in relation to high-risk factors

SLA abscess	No. of cases	Percentage
TB	2	33.33
DM	1	16.66
Both	2	33.33
None	1	16.66

SLA: Supralelevator, DM: Diabetes mellitus, TB: Tuberculosis

Table 14: Comparison between findings of MRI and surgery

Internal opening	Detected by MRFG	Confirmed by surgery
Primary	11	11
Recurrent	17	13
Total	28	24

MRFG: Magnetic resonance fistulography, MRI: Magnetic resonance imaging

Table 15: Male female ratio

My study	9:1
Suraj <i>et al.</i>	7:1
Spencer <i>et al.</i>	7:1

DISCUSSION

MRFG was performed on 30 patients for the confirmation and grading of fistula-in-ano. Out of the 30 patients, 26 (86.6%) were male patients and 4 (13.4%) were female patients male:female – 9:1.

Male preponderance may be related to an increased number of anal glands, which also tend to be more cystic and ramified when compared with women Table 15.^[1,2]

These patients were in the age groups ranging from 31 to 80 years.

Out of the 26 males, 13 (50%) were in the age group of 41–60 years.

Broadly, the patients fell into two groups, i.e., primary and recurrent. Patients in the primary group were those who had a fistula-in-ano for the first time and had never been operated for the same. Patients in the recurrent group were those whose fistulae had been operated on at least once previously.

In our study, the majority of the patients, (60%), had recurrent fistulas. This was probably due to our center is a tertiary center referred from the periphery.

Two risk groups were identified in our study of 30 patients. These were TB and DM. In our study group, six patients were found to have TB and seven patients had DM. Two of these patients had both TB and DM. In all 39% of recurrent fistulas had some associated risk factor.

It was consecutively observed that of the 18 (60%) patients with recurrent fistula, 2 (11%) had TB, 5 (22%) had DM, 1 (5.5%) had DM and TB. Totally, 39% of the recurrent cases were found to have some associated risk factor which signified the influence of these risk factors on the morbidity of fistula-in-ano and especially its recurrence.

It was noted that in almost all grades of fistula the accuracy of MRFG grading tallied more closely with surgical grading in comparison to the correlation of clinical grading with surgical grading.

In the studies conducted by Beets-Tan *et al.*^[3] (12 of 56) and others, Crohn's disease was found to be the major risk factor. The reason being that the studies were conducted in western countries. Crohn's disease, which is relatively uncommon in the Indian subcontinent, was not found to be a risk factor in any of the patients.

After per rectal examination of the 30 patients, they were subjected to MRFG and each patient was evaluated by scrutinizing the coronal, axial, and sagittal sections.

According to the presence and position of the primary tracts, secondary tracts, presence and absence collections, and their locations, each fistula was graded according to the St. James University Hospital classification.^[4] The distribution of cases according to various MRI grades is depicted in.

Almost half (50%) of the patients evaluated by MRFG were found to have abscess collections in various sphincteric planes. It was observed that in 17% of the patients, abscess collections occurred in multiple planes, the detection of which has significant implications on the outcome of the surgery.

It was observed that the majority of the cases, i.e., 83%, had a complicated fistula Table 16. Grades-II and above were designated as complicated because of the presence of secondary tracts or abscess collections and/or involvement of the planes other than the intersphincteric plane. In the study conducted by Beets-Tan *et al.*,^[3] the percentage of complex fistulas was 57% and in the study by Spencer *et al.*^[5] 40% of patients had complex fistulas.

It was felt that the higher percentage of complex fistulas in our study was due to our institute being a tertiary care center, more number of complex and recurrent cases tend to be referred.

Only 30% of the patients with no associated risk factor were found to have higher grade fistulas, (i.e., Grade II and above), whereas 60% of the high-risk population had higher grade fistulas. Hence, patients with risk factors (TB/DM/Both) were found to have increased incidence of higher grade fistulas as compared to fistulas in low-risk population.

The detection and prevalence of the surgically relevant criteria have been separately dealt with Table 17. These include internal opening of the fistula, primary tract, secondary, and abscess collections, SLA extensions, and additional findings.

The correct location of the internal opening of the fistula, as diagnosed on MRFG and confirmed by surgery was evaluated. Although the exact opening was not seen in all the cases, it was inferred according to the course and plane of the primary tract.

An internal opening was considered as correctly identified when it was at the correct level in the anal canal and was within the correct quadrant.

Among the 30 patients diagnosed to have primary tracts by MRFG, the diagnosis for internal opening was found to match with the surgical report in 24 patients, which gave the sensitivity of 86% for detection of internal opening by MRFG, compared to 96% sensitivity obtained in the study by Beets-Tan *et al.*^[3]

As regard the detection of primary tracts, we obtained sensitivity and specificity of 100%, in comparison to a sensitivity of 100% and specificity 86% in the study of Beet-Tan *et al.*^[3]

Table 16: Complicated fistulas

My study	83%
Beet-Tan <i>et al.</i>	57%
Spencer <i>et al.</i>	40%

Table 17: Comparison of various studies

Studies	Sensitivity for internal opening (%)	Sensitivity for primary tracts (%)
My study	86	100
Beet-Tan <i>et al.</i>	100	86
Suraj <i>et al.</i>	96	100

As the detection of secondary tracts has significant implications on the prognosis and outcome of surgery for fistulae-in-ano, their detection by MRFG is crucial.

If not identified and properly eradicated, these extensions and tracts may lead to recurrences. Results of the study by Lunniss *et al.*^[6,7] suggested that MR imaging could depict more extensions than could surgical exploration. In the study by Beets-Tan *et al.*^[3] they concluded that pre-operative MR imaging was 100% accurate in the detection of secondary extensions.

Secondary tracts are ramifications from the primary tract. Because the presence of horseshoe tracts greatly alters the surgical approach and its outcome, they have been separately mentioned.

About 70% of the patients in our study were found to have secondary tracts. Comparatively in a study of 56 patients by Beets-Tan *et al.*,^[2] 39% of the cases had secondary tracts.

It was observed that the occurrence of secondary tracts was significantly higher in recurrent cases, which were almost 50% Table 18. Hence, it is important to look for secondary tracts in recurrent cases.

It was also observed that the majority (78%) of the cases with secondary tracts were those who had recurrent fistulas. It was felt that secondary tracts were more common in recurrent cases.

Out of the 30 patients with primary tracts, the grading was found to be surgically correct in 28 patients, which gives an agreement of grading in 93%. The two remaining patients were found to have fistulas of lower grades on surgery. Hence, it was observed there was a tendency for over grading (7%) by MRFG.

Abscess collections were found in 50% of the cases evaluated. The presence of collections was divided according to their location in relation to the various sphincteric planes. These planes were intersphincteric, extrasphincteric, and the supralelevator planes. It was observed that in 17% of the patients, the abscess collections occurred in multiple planes (i.e. in combination). The detection of these collections, especially those present in multiple planes, has significant implication on the outcome of the surgery for complete eradication of the disease process.

The other most important additional finding for which MRFG was evaluated was for the detection of SLA collections or extensions. Those cases in which there is SLA collection or tract fall into the Grade-V. This has very high surgical significance, as it alters the surgical approach, and also it has serious implications on the outcome of the surgery.

Table 18: Secondary tracts

My study	70%
Beet-Tan <i>et al.</i>	39%

In our study, 6 cases were found to have SLA component by MRFG. About 83%^[5] of these had an associated risk factor (TB/DM/Both) which was quite significant.

Patients with risk factors (TB/DM/Both) were found to have more incidence of higher grade fistulas as compared to fistulas in low-risk population.

On clinical exam, the presence of SLA collection was suspected in only one patient. MRFG gave a diagnosis of SLA extension in an additional five patients.

On surgery, 6 of the six patients detected by MRFG (sensitivity of 100%) were found to have a SLA component of fistula/abscess collections. In comparison, 100% sensitivity for the detection of SLA collections was observed in the study by Beets-Tan *et al.*^[3] Importantly, no case with SLA extension was missed by MRFG. MRFG was thus found to be more sensitive than clinical grading for detection of SLA extensions.

Finally, the correlation between MRFG grading and surgical grading was done. The surgical findings (grading) were considered a gold standard. The MRFG findings and grades were discussed with the radiologist before the surgery. The MRFG findings were then confirmed on surgery.

Out of the 30 patients with suspected fistula-in-ano, MRFG grading was found to be surgically correct in 28 patients, which gave a concordance of 93% similar to the study by Morris *et al.*^[4]

In 7% of the cases with non-concordance, 1 case was diagnosed to be of Grade II was found to be only Grade I. The other case was diagnosed as Grade IV which were subsequently found to be Grade III on surgery. Hence, it was observed that there was a slight tendency for over grading by MRFG. The overdiagnosis may be due to epithelialized tracts.

Similarly, out of the 30 patients with suspected fistulas, grading by pre-operative clinical assessment was found to be surgically correct in 8 patients only, which is significantly lower than MRFG correlation. Complete concordance between clinical and surgical grading was found in 26% of the patients only. It was also observed that there was a tendency for under grading by the pre-operative clinical assessment method.

In almost all the grades of fistulae, the accuracy of MRFG grading was observed totally more closely with surgical grading in comparison to clinical grading.

In addition to the 6 cases with SLA components, 4 other cases were detected to have additional findings on MRFG, which significantly altered the surgical approach and final prognosis. Three of these patients were found to have scrotal abscesses and 1 patient who was a diabetic had an abscess in the thigh. In all these cases, there was no clinical suspicion of any additional finding. Therefore, in at least 30% of the cases, additional information was provided by MRFG.

MRFG was performed in 30 patients for pre-operative evaluation of fistula-in-ano. Male to female ratio was 9:1. The patients belonged to age groups ranges from 31 to 60.

A majority (60%) of the 30 patients were patients with recurrent fistula-in-ano.

TB and DM were the two major risk factors and were found to be important contributory factors for recurrence of the lesion. About 83% of the patients had a complicated fistula (i.e., Grade II).

MRFG was extremely useful in identifying the internal opening of the fistula (86% sensitivity), presence of secondary tracts 100% sensitivity, detecting abscess collection in multiple planes, and in visualizing SLA extensions of the lesion.

However, in our study, MRFG was seen to overestimate the grading for fistula in 2 patients as confirmed on surgery.

MRFG grading was found to have a 93% concordance with surgical (pre-operative) grading compared to 26% concordance of pre-operative clinical assessment method to surgery.

MRFG significantly altered the surgical approach due to its ability to demonstrate clinically undetectable abscesses and secondary tracts.

CONCLUSION

Clinical examination is less accurate to detect internal opening while MR fistulogram could detect most of

the internal openings which were confirmed in surgical findings.

High spatial resolution MR imaging with HDX PA coils is accurate for the detection of perianal fistulas. It shows the surgical anatomy and maps out the perianal fistulas accurately and provides additional information on secondary extensions in patients with complex fistulas.

The largest additional value from preoperative MRFG was obtained in patients with complex fistulas that were associated with TB and DM and in patients with recurrences. Our study showed that the surgical approach and procedure were drastically affected by MR findings of additional tracts and abscess.

Long term follow-up is required to evaluate the impact of MRFG in patients with recurrent fistulas. However, our study clearly showed that pre-operative MRFG led to more aggressive surgery for the removal of complex tracts which may have a significantly long-term effect.

Finally, we conclude that MRFG is a rapid, well-tolerated accurate technique with excellent surgical correlation but less concordance with clinical assessment and is, therefore, an ideal pre-operative imaging modality for fistula-in-ano.

REFERENCES

1. Beets-Tan RG, Beets GL, van der Hoop AG, Kessels AG, Vliegen RF, Baeten CG, *et al.* Preoperative MR imaging of anal fistulas: Does it really help the surgeon? *Radiology* 2001;218:75-84.
2. Lilius HG. Fistula-in-ano, an investigation of human foetal anal ducts and intramuscular glands and a clinical study of 150 patients. *Acta Chir Scand Suppl* 1968;383:7-88.
3. Hallingans S. Imaging fistula in ano. *Clin Radiol* 1998;53:85-95.
4. Morris J, Spencer JA, Ambrose NS. MR imaging classification of perianal fistulas and its implications for patient management. *Radiographics* 2000;20:623-35.
5. Spencer JA, Chapple K, Wilson D, Ward J, Windsor AC, Ambrose NS, *et al.* Outcome after surgery for perianal fistula: Predictive value of MR imaging. *AJR Am J Roentgenol* 1998;171:403-6.
6. Lunniss PJ, Amstong P, Barker PG, Reznick RH, Philips PK. MR Imaging of anal fistula. *Lancet* 1992;340:394-6.
7. Lunniss PJ, Barker PG, Sultan AH, Armstrong P, Reznick RH, Bartram CI, *et al.* Magnetic resonance imaging of fistula-in-ano. *Dis Colon Rectum* 1994;37:708-18.

How to cite this article: Vidyasagar R. Clinical and Radiological Study of Fistula in Ano in Tertiary Care Centre and Management. *Int J Sci Stud* 2019;7(5):44-50.

Source of Support: Nil, **Conflict of Interest:** None declared.

An Interventional Study to Enumerate the Causes of Lactation Failure, its Prevention and Management

P Murugalatha¹, M Krithiga²

¹Associate Professor, Department of Pediatrics, Theni Government Medical College and Hospital, Theni, Tamil Nadu, India,

²Assistant Professor, Department of Pediatrics, Theni Government Medical College and Hospital, Theni, Tamil Nadu, India

Abstract

Background: Three quarters of the world's population living in developing countries migrated from rural to an urban area. Since the health professionals are concentrated in the urban areas, the existing health services cater to only 20% of the rural population. Hence, there is an increased risk of bottle feeding in both urban and rural areas. There is a sharp decline in the practice of breastfeeding and an increase in the number of infants being artificially fed. In India, there is a decrease in the incidence of exclusive breastfeeding.

Aim: The aim of the study was to study an intensive educational program for mothers in the antenatal period, immediate postpartum period and during follow-up for 4–5 months in a tertiary care institute, and to achieve an exclusive breastfeeding rate of 80% among the mothers and study the impact of the intervention program.

Methodology: A prospective randomized study was done allocating the mothers into two groups – study and control group.

Conclusion: Exclusive breastfeeding has shown a definite decline globally. The practice of breastfeeding is down but definitely not out. Hence, it becomes our duty as health-care providers to teach mothers about the importance of breastfeeding. In the present study, even though a majority of mothers had adequate knowledge about breastfeeding, many of them did not practice what they knew. Hence, we should try to analyze the factors which hinder their breastfeeding practice.

Key words: Breastfeeding, Bottle feeding, Health professionals, Knowledge, Lactation failure

INTRODUCTION

The breast milk is unique and scientifically adapted for the growth and development of each mammalian species. The ultimate objective remains the same – safeguarding growth and development until the offspring is able to acquire its own food and survive without mother.

Western countries where the incidence of breastfeeding is low, having realized the importance of breast milk are now actively campaigning for exclusive breastfeeding for the first 6 months.^[1,2] However, in our country, despite breastfeeding being a traditional practice, it has lost its

importance, and more and more people are changing to bottle feeds.

“Bottle” is the biggest killer of babies in developing countries. Bottle-fed babies have 2–7 times increased risk of mortality compared to breastfed babies.

Need for the Study

Three quarters of the world's population live in developing countries. Because of the migration from rural to an urban area, 80% of our population live in urban areas, and 20% of our people are rural residents. Since the health professionals are concentrated in the urban areas, the existing health services cater to only 20% of the rural population. Hence, there is an increased risk of bottle feeding in both urban and rural areas. There is a sharp decline in the practice of breastfeeding and an increase in the number of infants being artificially fed. In India, there is a decrease in the incidence of exclusive breastfeeding. The practice of giving pre-lacteal feeds is almost universal in rural, urban slums, and urban rich.

Access this article online



www.ijss-sn.com

Month of Submission : 06-2019
Month of Peer Review : 07-2019
Month of Acceptance : 08-2019
Month of Publishing : 08-2019

Corresponding Author: Dr. M Krithiga, Plot No.: 419, K.K. Nagar, Madurai - 625020, Tamil Nadu, India.

Some factors contributing to the increasing incidence of artificial feeding in India are:

- 1) Changing lifestyles and increased number of working mothers
- 2) Availability of easy alternatives to breast milk
- 3) Aggressive publicity and deceptively appealing advertisement regarding formula feed in mass media.

Working women, those belonging to the lower socioeconomic class are forced to return to work early following childbirth forcing them to use formula feeds for their infants.

Why does the mother not breastfeed her baby? What makes her to take bottle feeds after successful initiation of breastfeeds? Hence, our study was planned to answer the above questions.

Aim of the Study

The aim of the study was to study an intensive educational program for mothers in the antenatal period, immediate postpartum period and during follow-up for 4–5 months in a tertiary care institute, and to achieve an exclusive breastfeeding rate of 80% among the mothers and study the impact of the intervention program.

MATERIALS AND METHODS

Place of Study

The antenatal outpatient department, postnatal and post-operative wards in the department of obstetrics and gynecology, at a tertiary care institute.

Follow-up of cases to be done in the well-baby clinic and pediatrics outpatient department; house visits were made to nearby areas using the vehicle and staff available in the postpartum program.

Duration of Study

This study was 1 year from June 2018 to May 2019.

Study Design

A prospective randomized study was done allocating the mothers into two groups – study and control groups.

1. Study group: Mothers attending the antenatal outpatient department on Mondays and Tuesdays were enrolled under study group. These mothers were given extensive advice about the importance of breastfeeding, its advantages, the technique of breastfeeding by showing posters, placards.
2. Control group: Mothers coming on Thursdays and Fridays to the above outpatient department were enrolled in the control group. These mothers formed the nonintervention group and were merely registered in the control group.

Three different precoded, prestructured, and pro forms were prepared, one to be used in the antenatal period, one in the postnatal period, and one for follow-up visits.

After preliminary nutrition and health status, presence or absence of major systemic illness, their knowledge, and attitude toward breastfeeding were recorded for each group.

As outlined before, the study group received the intervention. Mothers were then followed up in the postnatal wards, and post-operative wards following delivery and advice continued for the study group.

The counseling and follow-up were done by two social workers specifically trained for this work and by the research fellow.

Exclusion Criteria

Babies admitted in the preterm ward and sick neonatal ward of our hospital were not included in our study.

Data Analysis

Data analysis was performed using the epidemiological information package developed by world health organization. Comparison of data was done by univariate analysis. *P* value was determined using the ANOVA method.

RESULTS

Total number of cases: 500.

Number of cases in the study group: 304.

Number of cases in the control group: 196.

DISCUSSION

In the present study, the percentage of exclusive breastfeeding in the study group was 69% and that of the control group was 21% [Figure 1]. Previous studies have shown the incidence of exclusive breastfeeding in an urban population to be 36.6%. The national family health survey^[3] has shown that the incidence of exclusive breastfeeding in Tamil Nadu to be 55.8% and in India to be

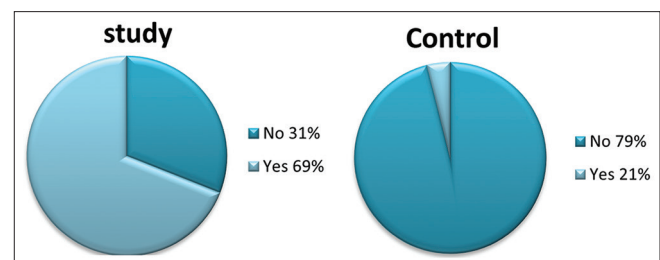


Figure 1: Percentage of exclusive breastfeeding

51%. In our study, the incidence of exclusive breastfeeding in the control group where no intervention is given to the mothers is 21%, this is much less than all Indian figures since the study was done in a predominantly urban area^[4,5] where the incidence of breastfeeding is less than rural areas. This shows how simple intervention like advice to mothers about the importance of breastfeeding, the technique of breastfeeding, time of initiation of breastfeeds after delivery has gone a long way in improving the exclusive breastfeeding rate.

The maternal weight [Table 1] has no role in determining the exclusive breastfeeding rate. This has been in many previous studies of preterm and low birth weight (LBW) babies.^[6] The socioeconomic status was assessed using the Kuppasamy's scale. Mothers with a total monthly family income of <Rs. 1500, had better exclusive breastfeeding rates when compared to mothers with a total monthly family income of more than Rs. 1500, the results were also statistically significant ($P < 0.05$) [Table 1].

About 48.3% of mothers in our study were primiparous women [Table 1]. However, there was no statistically significant difference ($P > 0.1$) in exclusive breastfeeding practice between the primiparous and multiparous women.

The percentage of booked cases was 98.7% and 94.1% in both study and control group [Table 2]. This percentage is higher when compared to our hospital statistics since our hospital does not consider antenatal checkups done outside the hospital as being booked cases. In Tamil Nadu, about 93% of mothers in rural areas and 97% of mothers in urban areas received antenatal care. In the whole of India, only 62% of the mothers received antenatal care.

The mean age of mothers enrolled in the study group is 23.59 years and in control group is 24 years. About 24% of the mothers were still younger than 20 years at the time of pregnancy. There was no statistically significant difference in the rate of exclusive breastfeeding among the different age groups.

Breast examination should be done routinely during the antenatal checkup to look for retracted nipples, inverted nipples since there are potentially correctable conditions if treatment is started early. If not corrected, they may cause a delay in the initiation of breastfeeding. Unfortunately, only about 6.7% of mothers said that their breasts were examined in the antenatal period in the present study. Examination of the breast was not done in 94% of the case, in spite of the study being conducted in a referral hospital [Table 2].

The number of times the health worker makes contact with the mother in the antenatal period to give advice

about breastfeeding is also important in the present study. It has been shown that mothers who had received advice about breastfeeding more than 3 times had a better exclusive breastfeeding rate than those received a lesser number of times of advice [Table 2]. This was also found to be statistically significant ($P < 0.01$).^[7] The results were the same for advice given by doctors, nurses, or social workers.^[8]

Table 1: Sociodemographic data

Particulars	Study %	Control %
Mothers age (years)		
<20	19.1	23.9
21–25	59.6	41.3
26–30	17.4	30.5
31–35	2.8	4.3
>35	1.1	0
Mean age (years)	23.5	24.0
Mothers weight (kg)		
<35	0	0
36–40	7.9	13
41–45	26.5	17.4
46–50	27.7	23.9
51–55	17.6	21.7
56–60	10.9	8.7
>60	9.6	15.2
Mean weight (kg)	49.7	50.93
Height of mothers (cm)		
<140	7.3	2.2
141–145	10.2	8.7
146–150	28.8	15.2
151–155	26.4	34.8
>155	27.3	39.1
Mean height (cm)	151.0	153.0
Residence		
Urban	56.9	48.8
Rural	43.1	51.2
Educational status of mother (standard)		
Illiterate	14.1	18.9
1–5	28.8	21.6
6–8	24.3	27.0
9–10	19.8	21.6
11–12	9.6	8.2
Graduate	3.4	2.7
Occupation		
Housewife	825	80.0
Unskilled	15.2	508
Semiskilled	0.6	14.3
Skilled	1.7	0
Family status		
Nuclear	54.5	66.7
Joint	45.5	33.3
Socioeconomic status		
<500	0.6	-
500–1000	36.6	35.6
1001–1500	29.8	28.8
>1500	33.1	35.6
		(P value=0.04)
Parity		
Primi	48.3	43.5
Gravida2	32.4	34.8
Gravida3	13.6	15.2
Multigravida	5.7	6.5

Table 2: Antenatal data

Particulars	Study %	Control %
Booked	98.7	94.1
Unbooked	1.3	5.9
Place of booking		
GRH	70.6	50.2
PHC	7.4	5.3
Subcenter	11.7	33.2
Private hospital	10.4	14.4
Number of visits		
<3	17.2	3.2
3–5	49	54.4
6–8	32.5	31.9
>8	1.3	0.4
FST given		
Yes	99.2	96.0
No	0.8	4.0
Tetanus toxoid given		
Yes	100	98.9
No	0	1.1
Number of doses of tetanus toxoid		
1	5.5	9.7
2	94.5	90.3
Number of times breastfeeding advice given		
≤3	55	-
4–5	32.2	-
>6	12.8	-
By whom?		
GRH staff	95.5	-
Others	4.5	-
Breast examination done		
Yes	6.7	3.7
No	93.3	96.3
Nature of delivery		
Normal	88.8	86.0
Cesarean	11.2	14.0
Sex of the baby		
Male	52.9	47.2
Female	47.1	52.8
Mean weight of the baby (gm)	2833.5	2733.11
Gestational age		
Preterm	1.4	2
Term	98.0	97
Post-term	0.6	1
Nature of the feeds given to the baby		
Breast milk	87.2	81.9
Others	12.8	18.1
Time after which feeds given to the baby (minutes)		
<30	37.2	10.7
31–60	1.8	22.6
61–120	14.6	11.9
121–180	6.7	7.8
>181	0	39.6
Colostrum		
Given	100	98.9
Not given	0	1.1
Discharge particulars		
Length of the baby (cm)	46.59	46.26
Weight of the baby (gm)	2768	2784

GRH: Government hospital, PHC: Primary health centre,
FST: Ferrous sulfate tablets

This shows that the basic requirement for breastfeeding is to motivate the mothers, instill confidence in her ability to breastfeed and clear her doubts about lactation. This

Table 3: Knowledge about breastfeeding

Knowledge about breastfeeding	Yes %	No %
A. Benefits of breastfeeding to the newborn with respect to		
1. Nutritional aspects	80.5	19.5
2. Protective value	79.9	20.1
3. Psychological aspects	79.3	20.7
B. Benefits of breastfeeding to the mother	79.9	20.1
C. Benefits of colostrum	76.8	20.1
D. No prelacteal feeds	77.4	22.6
E. Exclusive breastfeeding for a minimum period of 4 months	78.7	21.3
F. Breast milk can be fed soon after cesarean section	78	22
G. Proper breastfeeding technique	77.4	22.6
H. Demand feeding, rooming in practices	76.8	23.2
I. Mothers diet during pregnancy and lactation	82.3	17.7
J. Artificial feeds are an economic burden to the family	80.5	19.5

Table 4: Time of transfer

Time of transfer of the baby toward (minutes)	Study %	Control %
<30	1.8	3.8
31–60	7.3	12.0
61–120	31.6	24.6
121–180	17.6	18.1
>180	41.7	41.5
<30	1.8	4.4
31–60	8.6	13.1
61–120	32.9	24.0
121–180	15.8	17.5
>180	40.9	41.0

shows how a simple intervention can go a long way in reducing morbidity and mortality due to the use of formula feeds. As previously mentioned, the economic benefits are also enormous. Breast milk was given initially in 87% of babies in the study group in contrast to 82% of babies in the control group [Table 2]. This difference was not statistically significant.

Colostrum was not discarded by mothers in this study in contrast to previous studies.^[9] Almost 100% of the mothers gave colostrum to their babies [Table 2]; this is a very welcoming trend. This could be due to the hospital-based nature of the study.

There is a sharp increase in the introduction of artificial feeds between 2 and 3 months of age. Hence, effective intervention in this period (60–90 days) of postnatal life in the form of lactation counseling will benefit in the long run.

There is a greater incidence of exclusive breastfeeding in male babies than female babies. However, in the present study, no such statistically significant difference was noted [Table 2].

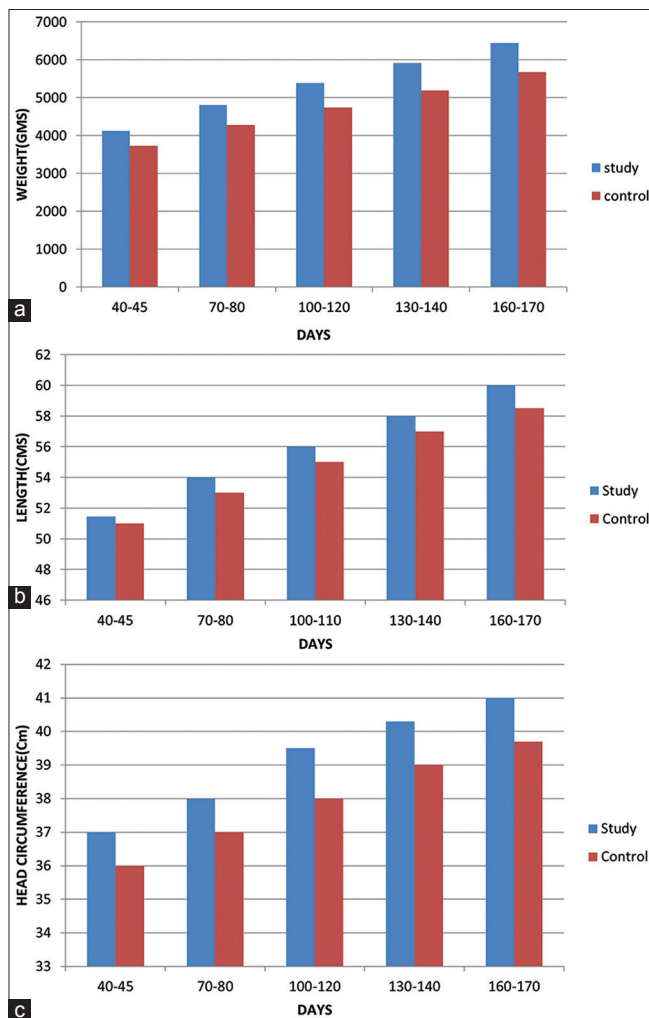
Table 5: Postnatal data - Anthropometry

Particulars	Visit 1		Visit 2		Visit 3		Visit 4		Visit 5	
	S	C	S	C	S	C	S	C	S	C
Age (days)	45	45	75	75	105	105	134	134	165	165
Weight (gm)	4127	3732	4803	4275	5387	4734	5917	5192	6448	5669
Length (cm)	51.46	51	54	53	56	55	58	57	60	58.5
Head circumference (cm)	37.0	36	38	37	39.5	38	40.3	39	41	39.7
					$P<0.01$		$P<0.01$		$P<0.01$	

S: Study, C: Control

Table 6: Number of breastfeeds per day

Group	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5
Study	13	11	10	8	7
Control	11	10	8	7	6
			$P<0.01$	$P<0.01$	$P<0.01$

**Figure 2: Anthropometry (a) weight of the baby, (b) length of the baby, (c) head circumference of the baby**

The gestational maturity of the baby, birth weight, and nature of delivery had no influence on the outcome of exclusive breastfeeding [Table 2].

Iron and folic acid tablets were received by 99% of mothers [Table 2]. Overall, in India, 51% of mothers received iron and folic acid tablets.^[5]

Two doses of tetanus toxoid (TT) were given to 94.5% of women in our present study [Table 2]. In Tamil Nadu, mothers received two or more TT injections for 90% of the birth.^[9] In India, mothers received two doses of TT in only 54% of births.

Before giving advice to mothers, their existing knowledge about breastfeeding was assessed. Following this, advice was given to them and their doubts cleared. The following percentage of mothers had existing knowledge about breastfeeding [Table 3]. About 81% of the mothers knew about the nutritional value of breast milk. About 79% of the mothers had knowledge about the protection offered to infants and psychological benefits of breastfeeding. About 80% of the mothers knew about the benefits of breastfeeding to them and about the lactational amenorrhea in preventing pregnancy. About 77% of the mothers knew about the importance of colostrum and that it should not be discarded after birth. About 79% of the mothers had the knowledge that only breast milk and not any other feeds including prelacteal feeds should be given to the baby after birth. A similar percentage of women said exclusive breastfeeding should be continued for at least 6 months of age. About 77% of the mothers said that they knew about the technique of breastfeeding and feeding on demand. About 81% of the mothers felt that the artificial feeds given to the babies resulted in a severe economic burden to the family. About 83% of the mothers said that they had to increase their nutritional requirements during lactation.

Another interesting aspect of this study is to note the time taken to shift the mother and baby from the labor ward and operation theater to the postnatal and post-operative wards, respectively [Table 4]. Only 2% of the mothers and babies were shifted to the postnatal ward from labor ward within 30 min of delivery. Babies were not given to mothers to breastfeed in the labor ward within 30 min of delivery as suggested by the “baby-friendly hospital initiative.” Sometimes babies were given to the relatives waiting outside, and prelacteal feeds were given by them.

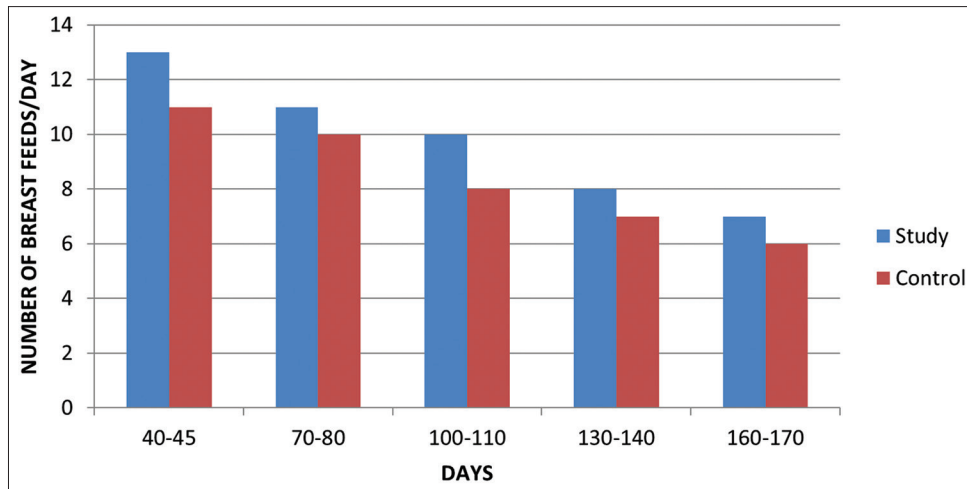


Figure 3: Number of breastfeeds per day

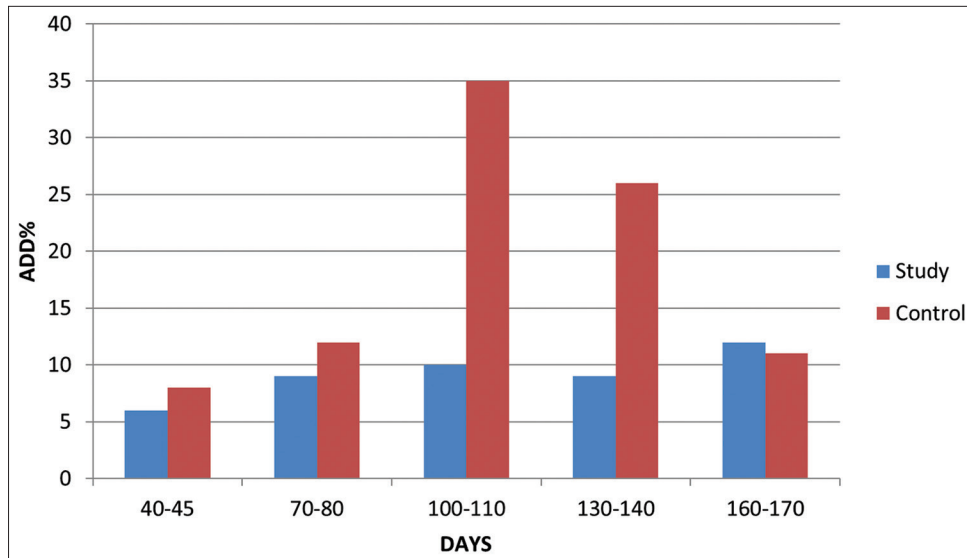


Figure 4: Illness in the child-acute diarrheal disease

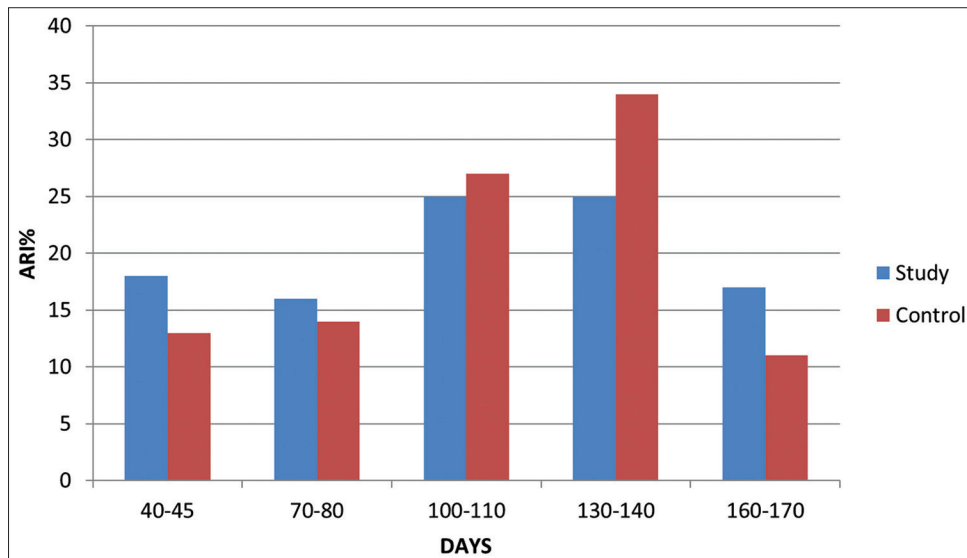


Figure 5: Illness in the child – acute respiratory infection

This resulted in a delay in the initiation of breastfeeding. With regard to cesarean section, only a few of the mothers and babies were transferred to post-operative ward within 30 min of delivery. Majority of them were shifted between 1 and 2 h after delivery. This is comparable to the national family health survey data which say only 22% of babies in Tamil Nadu are put to the breast within 1 h of birth. This indicates the need to educate mothers, her relatives, healthcare workers concerning the importance of immediate commencement of breastfeeding after delivery.

The anthropometric measurements show a statistically significant difference ($P < 0.01$) in the height, weight, and head circumference of the babies in the study and control groups [Table 5]. There was better growth of the babies who were exclusively breastfed than in those babies for whom supplementary feeds were started early [Figure 2a-c]; this also applies to preterm babies and LBW babies.^[5] Various studies have clearly shown this difference. The number of breastfeeds given per day in both groups varied from 7 to 12 in the first 4 months of life [Table 6], but in the study group there was a statistically significant ($P < 0.01$) difference in the number of breastfeeds per day during the 3rd–4th visits in contrast to the control group where the introduction of supplementary foods was common during these visits [Figure 3], reinforcement of the advice to these mothers during their postnatal follow-up motivated them to continue exclusive breastfeeding. With decreasing breastfeeds per day in the control group, the mothers thought that their milk production was declining and turned toward bottle feeds to supplement breast milk. This leads to cut down of their prolactin reflex, resulting in lactation failure. It has been shown that nearly 30% of infants are given water or other supplements by 1 month of life.

The mean duration of exclusive breastfeeding in the study group is 104 days and that in the control group is 88 days. This difference is statistically significant ($P < 0.01$) [Table 7].

In our present study, nearly 85% of mothers continued to give breast milk in addition to weaning foods even after 4 months of age of the baby [Table 7], this is comparable to the all India figure of 95%. In the present study, only 7% in the study group and 15% in the control group stopped breastfeeds completely before 4 months of age [Table 7]. This shows that with good advice to the mother, the introduction of supplementary foods can be avoided and exclusive breastfeeding practiced.

In the present study, the incidence of acute diarrheal disease and acute respiratory infection is more in the control group [Table 8] where the incidence of exclusive breastfeeding rate is less, similar to other study.^[10] The incidence of acute

diarrheal disease and acute respiratory infection showed a statistically significant reduction in the 3rd–4th visits in the study group as compared to control group ($P < 0.05$) [Figures 4 and 5], this shows that with continued advice about breastfeeding to the mother, exclusive breastfeeding can be achieved resulting in healthier babies.

Thus, overall, nearly 80% of mothers had knowledge about breastfeeding. The importance of exclusive breastfeeding was reinforced, and their doubts cleared during their antenatal visits.

The nutritional deficiency was found in 4% of the mothers. Anemia (who criteria of hemoglobin <10 gm/dl) and angular stomatitis were the most common deficiencies noted.

The mean weight of the mothers was 50 kg. There was no statistically significant difference in exclusive breastfeeding practice in a different distribution of weights. Similarly, the height of the mother and the age of the father had no influence over the exclusive breastfeeding practice.

About 51.2% of the mothers in rural areas and 48.8% of the mothers in urban were enrolled in our study. There was no difference in the exclusive breastfeeding rate among the two groups. This was against the results available in previous studies. These studies showed that rural mothers had a better exclusive breastfeeding rate than urban mothers.

Literacy and occupation of the mothers in the present study made no difference in exclusive breastfeeding practiced by them.

Table 7: Details about breastfeeding

Particulars	Study	Control
Number of days exclusively breastfed (mean days)	104	88
Number of days after which breastfeeding was stopped (days)	%	%
<30	2.3	3.2
31–60	0.3	0.8
61–90	1.6	1.6
91–120	2.9	2.4
>120	7.4	7.1

Table 8: Illness in the child

Particulars	Visit 1		Visit 2		Visit 3		Visit 4		Visit 5	
	S	C	S	C	S	C	S	C	S	C
ADD%	6	8	9	12	10	35	9	26	12	11
ARI%	18	13	16	14	25	27	25	34	17	11
					$P < 0.05$		$P < 0.05$			

S: Study, C: Control, ADD: Acute diarrheal disease, ARI: Acute respiratory infection

Around 54% of the mothers came from nuclear families and 46% of the mothers from joint family. There was no difference in breastfeeding practice between the two groups. Some mothers took galactagogues but there was no statistical difference in the exclusive breastfeeding rate. Relactation was not initiated in this study, unlike another study.^[7]

CONCLUSION

Exclusive breastfeeding has shown a definite decline globally since the second half of the last century. The practice of breastfeeding is down but definitely not out. Hence, it becomes our duty as health-care providers to teach mothers about the importance of breastfeeding.

In the present study, even though a majority of mothers had adequate knowledge about breastfeeding, many of them did not practice what they knew. Hence, we should try to analyze the factors which hinder their breastfeeding practice. The factors which contributed to lactation failure in the study are:

1. Lack of motivation on the part of the mother to breastfeed her baby. Lack of support from other members of the family particularly from mother in law aggravated this problem
2. There is a traditional belief that breastfeeds should not be given at times of illness to the babies. Hence, the mothers stopped breastfeeding during acute diarrhoeal disease and acute respiratory infection in their babies
3. Lack of adequate maternal leave forced the mothers to return work early
4. Retracted and inverted nipples which were not looked after in the antenatal period caused difficulty in breastfeeding

5. Family problems lead to emotional turmoil in the mother resulting in decreased prolactin reflex which further diminished milk production.

Hence, the above study, although limited to an urban hospital, more or less reflects the breastfeeding habits in our society. It also shows areas of lacunae and indifference on the part of healthcare workers in educating and guiding mothers about breastfeeding. They are actually in a strategic position to help these mothers since contact is established with them even in the antenatal period.

REFERENCES

1. Sinha B, Chowdhury R, Sankar MJ, Martinez J, Taneja S, Mazumder S, *et al.* Interventions to improve breastfeeding outcomes: A systematic review and meta-analysis. *Acta Paediatr* 2015;104:114-34.
2. Kliegman RM, Stanton BF, St Geme JW, Schor NF. *Nelson Textbook of Paediatrics*. 20th ed., Vol. 1. Philadelphia, PA: Elsevier; 2016. p. 286.
3. Ministry of Health and Family Welfare. *National Family Health Survey-4. India: Ministry of Health and Family Welfare; 2015-2016*. p. 3.
4. Srivastava NM, Aswathi S. Breast feeding practices for newborn among urban poor in Lucknow-Northern India. A prospective follow up study. *Clin Epidemiol Glob Health* 2014;2:66-74.
5. Ochola SA, Labadarios D, Nduati RW. Impact of counselling on exclusive breast-feeding practices in a poor urban setting in Kenya: A randomized controlled trial. *Public Health Nutr* 2013;16:1732-40.
6. Singh D, Devi N, Raman TsR. Exclusive breast feeding in low birth weight babies. *Med J Armed Forces India* 2009;65:208-12.
7. Tomar RS. Initiation of relactation army based study of 381 cases. *Int J Contemp Pediatrics* 2016;3:635-8.
8. Haider R, Ashworth A, Kabir I, Huttly SR. Effect of community-based peer counsellors on exclusive breastfeeding practices in Dhaka, Bangladesh: A randomised controlled trial [see comments]. *Lancet* 2000;356:1643-7.
9. Abie BM, Goshu YA. Early initiation of breastfeeding and colostrum feeding among mothers of children aged less than 24 months in Debre Tabor, Northwest Ethiopia: A cross-sectional study. *BMC Res Notes* 2019;12:65.
10. Raheem RA, Binns CW, Chih HJ. Protective effects of breastfeeding against acute respiratory tract infections and diarrhoea: Findings of a cohort study. *J Paediatr Child Health* 2017;53:271-6.

How to cite this article: Murugalatha P, Krithiga M. An Interventional Study to Enumerate the Causes of Lactation Failure, its Prevention and Management. *Int J Sci Stud* 2019;7(5):51-58.

Source of Support: Nil, **Conflict of Interest:** None declared.

Clinical Study of Solitary Thyroid Nodule

R Vidyasagar

Assistant Professor, Department of General Surgery, Mahatma Gandhi Memorial Hospital, Kakatiya Medical College, Warangal, Telangana, India

Abstract

Introduction: Solitary thyroid nodule (STN) presents a challenge in their diagnosis, evaluations, and management. Often, these abnormal growths/lumps are large in size and develop at the edge of the thyroid gland so that they are felt or seen as a lump in front of the neck.

Materials and Methods: The study is carried out in upgraded Department of General Surgery, Kakatiya Medical College and Mahatma Gandhi Memorial Hospital, during the period of February 2017–October 2018.

Results: Among the 62 patients studied in this research, 52 were female and there were 10 males. Females accounted for 83.9% of the cases while males accounted for 16.1%. The male-to-female ratio was 5.2:1.

Conclusions: Incidence of STN is common in the age group of 18–30 years. Hemithyroidectomy was commonly performed on maximum cases.

Key words: Malignancy, Solitary thyroid nodule, Swelling

INTRODUCTION

Solitary thyroid nodule (STN) presents a challenge in their diagnosis, evaluations, and management. Often, these abnormal growths/lumps are large in size and develop at the edge of the thyroid gland so that they are felt or seen as a lump in front of the neck. The prevalence of these nodules in a given population depends on a number of factors such as age, sex, diet, iodine deficiency, and even therapeutic and environmental radiation exposure. Prevalence increases with age, with spontaneous nodule occurring at a rate of 0–0.8% per year, beginning early in life and extending into the eighth decade.^[1,2]

True STN occurs in 4–7% of the adult population. They are present in 5% of persons at an average of 60 years. They are more common in females (6.4%) as compared to males (1.5%) and this predisposition exists throughout all age groups. Many palpable thyroid nodules, thought to be

solitary, are actually part of a multinodular thyroid gland. In general, a nodule could be adenomas or neoplasms. Most thyroid nodules are benign hyperplastic lesions, but 5–20% of these nodules are true neoplasms in nature. STN first seen can be due to asymmetrical enlargement of one lobe as in chronic lymphocytic thyroiditis (i.e., Hashimoto's thyroiditis), simple goiter.

STNs can be classified into benign and malignant nodule. In general, most (90%) thyroid nodules are benign and can be classified as adenomas, colloid nodules, cysts, infectious nodules, lymphocytic or granulomatous nodules, hyperplastic nodules, thyroiditis, and congenital abnormalities.^[3]

Predisposing pathological features increase clinical importance of thyroid nodule(s). A significant feature is nodule size. A palpable thyroid nodule at physical examination, especially >2 cm of diameter, carries a considerable risk of annoying disorder.^[4] Another main feature is structural (solid and cystic) nature of the nodule. Especially, management of a larger solid nodule merits a distinct importance.^[4] A third feature is functional status of the nodule. The activity of a nodule may be established by chemical-hormonal analysis and nuclear imaging method. A hyperactive or hypoactive nodule significantly influences clinical outcome of a patient.^[5] A fourth important characteristic of the nodule is its solitary features. A solitary nodule carries greater

Access this article online



www.ijss-sn.com

Month of Submission : 06-2019
Month of Peer Review : 07-2019
Month of Acceptance : 08-2019
Month of Publishing : 08-2019

Corresponding Author: Dr. R Vidyasagar, H.no: 35-6-771, Gopalpur, TV Tower Colony, hanmkonda, Warangal 506009, Telangana, India.
Phone: 9573483633. E-mail: drvsrayapuri@gmail.com

clinical importance than multinodular formation.^[6] Based on clinical, chemical, and image characteristics, the thyroid nodule which possesses all these four pathological features ("large size," "solitary," "solid," and "hypo or hyperactive") is generally treated by surgical intervention.

The ultimate aim of the study of STN is to find out the incidence of malignancy. At present, many investigations including diagnostic imaging studies, serologic and cytogenetic tests, as well as histopathological techniques are available to evaluate STNs. Out of all these investigations, fine-needle aspiration cytology (FNAC) has become the important diagnosis tool of choice for the initial evaluation of STNs.^[3] It can be done by clinician himself. It does not require costly instrument setup. It can be easily repeated. There is patient tolerance as it is very less painful. Furthermore, there are neither reports of needle track deposit nor any significant complications.

Due to the above-said reason, the usefulness of FNAC was evaluated in center like ours in cases of STN. In addition to investigation with available history of patients and clinical examination, we have tried to put clinical diagnosis and we have correlated clinical findings with histopathological examination and patients were managed accordingly.

For the long time, the solitary nodule in thyroid gland due to its malignant potential and possibility of toxicity in the nodule, it has become more sensitive topic for the research worker. Majority of these are localized, hyperinvolvement, colloid containing tumefactions, but a small significant group of about 25–30% is comprised carcinoma, true adenoma, and toxic nodule. This important group needs very different management for hyperinvolvement nodules and has, in recent times, dominated the philosophy of therapeutic approach to the management of thyroid nodule, due to this I had considered to study the said topic for the present study.

MATERIALS AND METHODS

The present study is carried out in the upgraded Department of General Surgery, Kakatiya Medical College and Mahatma Gandhi Memorial Hospital, during the period of February 2017–October 2018.

Study Type

This was a prospective study

Study Population

The study population was 62 cases.

Inclusion Criteria

The following criteria were included in the study:

1. Age groups – 18–60 years

2. Single, visible, or palpable nodule in one lobe or at the junction of one lateral lobe and the isthmus
3. Single nodule with whatever pathology on FNAC
4. Single nodule with features of toxicity (toxic nodule) or hypothyroidism.

Exclusion Criteria

1. Visibility or palpability of the opposite lobe
2. Multinodularity
3. Those patients who refused to give an informed consent to be a part of the study.

Clinical presentation was studied in detail with respect to their history symptoms (presenting complaints) followed by clinical examination. History obtained and included details of swelling such as onset, duration, and rate of growth, whether patient had any obstructive symptoms due to swelling. Symptoms and signs of thyrotoxicosis and hypothyroidism were also looked for in detail. Local examination of gland included.

METHODOLOGY

Inspection

Gland was inspected from front. In short-necked individuals, Pizzillo's method was used. The inspection of thyroid gland was rendered easier by patient throwing her/his head backward and pressing his/her occiput against his/her clasped hands movement with protrusion of tongue and retrosternal extension if any noted.

Palpation

Palpation of each lobe was carried out by Lahey's method. In Lahey's method, examiner stands in front of patient. To palpate the left lobe properly, the thyroid gland is pushed to left from right side by the left hand of the examiner. This makes the lobe more prominent so that examiner can palpate thoroughly with his right hand. During palpation, patient is asked to swallow and size, surface, consistency, and mobility, to get below the swelling is noted. Kocher's test is done to rule out tracheomalacia. In Kocher's test, slight push on lateral lobe will produce stridor suggestive of positive Kocher's test.

Investigations

Besides routine investigations, specific investigations include:

Thyroid function test

Thyroid function test is done in every patient to assess functional status. Triiodothyronine (T₃), tetraiodothyroxine (T₄), and thyroid-stimulating hormone were done regularly and free hormones (FT₃) and (FT₄) obtained in selected cases.

Ultrasound examinations

Ultrasound examination of thyroid accurately measures

the size of the gland, the number of nodules within, and dimensions of the nodule. Most of the solitary nodule on clinical examination turns out to be multinodular goiter on ultrasound, which can be managed conservatively.

Conventional B-mode or gray scale ultrasound can classify nodules as solid, cystic, or mixed and cystic lesions with accuracy of more than 90%. A cystic lesion is usually characterized by sonolucent pattern with well-defined walls. Solid nodules have characteristic ultrasonic echo.

Cystic lesions can again be classified as purely cystic which are rarely malignant and complex cyst where there is solid component within the cyst. The presence of echogenic component in nodule increases chances of malignancy. Ultrasound also aids in FNAC of complex cystic lesion. High-resolution ultrasonography with real-time capability visualizes nodules as small as 5 mm. Purely cystic lesions >4 cm can be managed by aspiration.

However, it cannot differentiate between a benign and a malignant nodule.

FNAC

Material for needle aspiration cytology:

- a. 10 or 20 cc disposable syringe
- b. 22 or 23 gauge disposable needle (1.5 inches)
- c. Slides and coverslips
- d. Fixative in Koplik jar, 95% alcohol
- e. Methylated spirit
- f. Cotton swabs
- g. Stains papanicolaou stain
- h. Microscope.

Method for Needle Aspiration

The technique is described by Lowhagen Torsten *et al.*, in 1979. The skin over anterior part of the neck is cleaned with spirit. The puncture of thyroid nodule is performed with patient in supine position, neck moderately extended. No anesthesia is required. The aspiration is performed with proper aseptic precaution using 10–20 cc syringes and 23 gauge needle. The needle is introduced into the lesion with the handle in resting state. The plunger is retracted to create a vacuum in the syringe. The needle is moved back and forth in different directions under constant suction to detach the tissue fragments.

The plunger released to eliminate vacuum to reach pressure equilibrium in the system. Then, the needle is withdrawn from the lesion avoiding aspiration of material into the syringe. Thyroid aspirates often consist of gelatinous, semisolid material, or drops of blood or tissue fluids mixed with the cell or very tiny tissue bits. The needle containing sample is detached from the syringe, plunger is withdrawn to allow air into the syringe, needle reattached

to syringe, and content blown out on slide by pushing down the plunger. Thus, smears are prepared with the help of another slide by spreading gently to avoid trauma to cellular architecture.

Fixation is done by ethyl alcohol 95%. Staining is performed by papanicolaou and hematoxylin and eosin staining methods.

X-ray Neck and X-ray Chest

It was done to rule out tracheal shift. Soft tissue extension in the retrosternal was noted in lateral view. X-rays were also done to rule out any cervical spine pathology to prevent injury to cervical spine in hyperextended position during operation.

Indirect Laryngoscopy (IDL)

It is done as routine in all cases preoperatively and postoperatively to know the vocal cord status. Asymptomatic vocal cord palsy can be encountered in about 3% of patients, and hence, pre-operative IDL was carried out for medicolegal record. In all patients, postoperatively, IDL was done to rule out recurrent laryngeal nerve injury.

After this, provisional diagnosis was made and patients were subjected to surgery. Any intraoperative/post-operative complication, if any, was noted. Final diagnosis was settled with histopathology. Post-operative medication after discharge if needed was advised. Follow-up was kept in patients who reported after specific period outpatient department (OPD).

OBSERVATIONS AND RESULTS

Patient Demographics

Among the 62 patients studied in this research, 52 were female and there were 10 males Table 1. Females accounted for 83.9% of the cases while males accounted for 16.1%. The male-to-female ratio was 5.2:1.

Most of the cases were seen in the 18–30 years age group Table 2. About 50% of the cases were in this age group accounting for 31 cases. The 31–40 age group accounted for 25.8% of the cases. Only 8.1% of the cases were in the 51–60 age group.

Aims and Objectives

The aims of this study were as follows:

1. To study the incidence of STN according to age and sex
2. To study the role of FNAC in STN
3. To study the incidence of malignancy in STN
4. To study the management of STN
5. To study post-operative complication.

Clinical Features at Presentation

All 62 cases presented with swelling in the anterior part of the neck. There was pain associated with the swelling in eight cases. Five cases had dysphagia. Five of these 62 cases had dyspnea. Four cases had tremors and palpitations. Two of the cases had a history of weight loss while three cases had a history of sweating.

Distribution According to Site

A solitary nodule was seen in the right lobe in 40 of the 62 cases while it was present in the left lobe in 22 cases. The right lobe was involved in 64.5% of the cases while the left side in 35.5% of the cases Table 3.

Distribution According to Duration of Swelling

Majority of the cases presented within the first 6 months after noticing the swelling. This group accounted for 34 of the 62 cases (54.83%). Another 8 cases (12.90%) in this study had noticed their swelling between 6 months to a year earlier. Only 2 cases (3.22%) in this study had swelling for more than 5 years.

Correlation between Ultrasound and Histopathological Diagnosis

There were 57 cases that were diagnosed as a benign lesion on ultrasound examination Table 4. Of these 55 were confirmed to be benign on histopathology examination. Two of these cases were found to be malignant on histopathology study. Of the three cases diagnosed to be suspicious on ultrasound study; one case turned out to be malignant. Both the cases diagnosed to be malignant on ultrasound turned out to be malignant on histopathology.

Thyroid Function Tests

Of the 62 cases in this study, 54 cases (87.1%) had a normal thyroid function as assessed by thyroid function tests Table 5. Four cases (6.45%) had subclinical hyperthyroidism while two cases (3.22%) had subclinical hypothyroidism. There was one case of hypothyroidism and one case of hyperthyroidism.

Sensitivity of FNAC

Among the 62 cases, in 55 cases (88.7%), the FNAC report tallied with the histopathology study Table 6. The sensitivity of FNAC was 88.7%. In 11.3% of the cases, the FNAC study and the histopathology study did not tally.

Histopathological Correlation with FNAC Study

Of the 62 cases, the FNAC study showed a benign morphology in 55 cases (88.7 %) Table 7. Among these benign studies, on histopathological examination, 35 cases had colloid goiter, 11 had follicular adenoma, 6 had chronic lymphocytic thyroiditis, 1 was a hemorrhagic cyst, 1 case had papillary carcinoma, and 1 case had follicular

Table 1: Distribution according to sex

Sex	Number of cases	Percentage
Female	52	83.9
Male	10	16.1

Table 2: Distribution according to age

Age	Number of cases	Percentage
18–30	31	50
31–40	16	25.8
41–50	10	16.1
51–60	5	8.1

Table 3: Distribution according to site

Lobe involvement	Number of cases	Percentage
Right	40	64.5
Left	22	35.5

Table 4: Investigations

USG	Number of cases	Histopathological diagnosis	
		Benign	Malignant
Benign	57	55	2
Suspicious	3	2	1
Malignant	2	0	2
Total	62	57	5

Table 5: Thyroid function tests

Cases	Number of cases	Percentage
Euthyroid	54	87.1
Subclinical hypothyroidism	2	3.22
Clinical hypothyroidism	1	1.61
Subclinical hyperthyroidism	1	1.61
Clinical hyperthyroidism	4	6.45

Table 6: Sensitivity of FNAC

FNAC	Number of cases	Percentage
Correlated with HPE	55	88.70
Did not correlate with HPE	7	11.30

carcinoma. Of these 55 cases, 53 cases were found to be benign on histopathology. Two cases were malignant on FNAC study which was confirmed by histopathology.

Among the five cases, where FNAC study was inconclusive and an opinion was not possible, four cases were benign and one case had follicular carcinoma. One case had colloid goiter, one case had follicular adenoma, one case had hemorrhagic cysts, and one case had chronic lymphocytic thyroiditis.

Table 7: Correlation of fine-needle cytology with histopathological diagnosis

Histopathological Diagnosis	Fine-needle aspiration cytology			Total (%)
	Benign	Malignant	ONP	
Colloid goiter	35	0	1	36 (58.06)
Follicular adenoma	11	0	1	12 (19.35)
Chronic lymphocytic thyroiditis	6	0	1	7 (11.3)
Hemorrhagic cyst	1	0	1	2 (3.22)
Papillary carcinoma	1	1	0	2 (3.22)
Follicular carcinoma	1	0	1	2 (3.22)
Medullary carcinoma	0	1	0	1 (1.61)
Total	55 (88.7%)	2 (3.22%)	5 (8.06%)	62 (100)

ONP: Opinion not possible

Histopathological Analysis Study

Among the 62 cases, 36 cases were diagnosed as colloid goiter accounting for 58.1% of the cases Table 8.

Follicular adenoma was the second most common cause for thyroid swelling in this study. There were a total of 12 cases (19.4%).

There were 7 cases (11.3%) of chronic lymphocytic thyroiditis.

Hemorrhagic cysts were seen on histopathological examination in 2 cases (3.2%).

Incidence of Malignancy

There were five malignant lesions detected in this study Table 9. Follicular carcinoma was diagnosed in 2 cases (3.2%). Papillary carcinoma was seen in 2 cases (3.2%). There was 1 case (1.6%) of medullary carcinoma of the thyroid.

Among the 62 cases, 5 cases (8.06%) had malignant lesions. Fifty-five cases had benign lesions.

Management of STNs

Hemithyroidectomy of the side of the nodule was the preferred course of management in this study Table 10. There were a total of 57 hemithyroidectomies done (91.93%). In 5 cases (8.06%), total thyroidectomy was done. In two cases, completion thyroidectomies were done after histopathology.

Complications

The major complication was recurrent laryngeal nerve palsy which was seen in 2 cases (3.2%) Table 11.

The most common complications seen post-surgery in this study were wound infection (four cases) and hypocalcemia (three cases). One case had both.

Hypothyroidism was seen in 1 case (1.6%) and wound hematoma was seen in one case.

Table 8: Histopathological diagnosis

Diagnosis	Number of cases	Percentage
Colloid goiter	36	58.1
Follicular adenoma	12	19.4
Chronic lymphocytic thyroiditis	7	11.3
Hemorrhagic cyst	2	3.2
Follicular carcinoma	2	3.2
Papillary carcinoma	2	3.2
Medullary carcinoma	1	1.6
Total	62	100

Table 9: Incidence of malignancy

Lesion	Number of cases	Percentage
Benign	57	91.94
Malignant	5	8.06

Table 10: Management

Management	Number of cases	Percentage
Hemi thyroidectomy	57	91.93
Total thyroidectomy	5	8.06
Completion thyroidectomy	2	3.22

Table 11: Complications

Complications	Number of cases	Percentage
Recurrent laryngeal	2	3.2
Nerve palsy	0	0
Respiratory distress	0	0
Wound hematoma	1	1.6
Thyroid storm	0	0
Wound infection	4	6.4
Hypothyroidism	1	1.6
Hypocalcemia	3	4.83
	0	0

DISCUSSION

The present study is a hospital-based prospective study done in the Department of General Surgery at Kakatiya Medical College and Mahatma Gandhi Memorial Hospital, from the period of February 2017 to October

2018. Sixty-two cases of STN were selected from surgery OPD.

Sex Incidence

Thyroid enlargement is commonly seen in females; in the present study, female-to-male ratio was 5.2:1 suggestive of female predominance and contributing almost 83.9% of the total study population.

Age Incidence

The age group for the highest incidence of thyroid swelling was in the 41–60 years age group with 371 cases (45.2%), followed by 352 cases (42.9%) in the 21–40 years age group, 66 cases (8.1%) in the >60 years age group, and 31 cases (3.8%) in the group of <21 years.

In the present study, maximum number of 31 cases, i.e., 50% were seen in 18–30 years age group, while the only five cases, i.e., 8.1% were seen in 51–60 years age group.

Clinical Presentation

The majority of both benign (91%) and malignant (84.6%) solitary nodule presented with lump in neck. Pain in swelling was not a prominent feature in the benign or malignant group. Change of voice noted in 17 cases, of which benign condition was 11 and malignant account in six cases.

Side of Involvement

STNs involved the right side of the thyroid more commonly than the left. In the present study, STN was more common in the right lobe of thyroid (64.5%) followed by the left lobe (35.5%).

Duration

In the present study, maximum 24 cases, i.e., 54.83% presented within 1–6 months after appearance of swelling while eight cases, i.e., 12.90% presented after 1–2 years, one case was seen in 4–5 years after the appearance of swelling, and only two cases were seen after 5 years.

Size of Swelling

In the present study, the size of swelling varied from 1–6 cm. This is supported by Ananthakrishnan *et al.*, Kovacevic *et al.*, and Cappelli. However, histological type and local aggressiveness were largely independent of nodule size.

Consistency

In the present study, of 62 operated cases, the most common consistency encountered was firm in 59 cases, cystic in two cases (one case was papillary carcinoma and one hemorrhagic cyst) and one hard in consistency which was follicular carcinoma.

Thyroid Function Test

In the present study, thyroid function test was used to evaluate the functional status of thyroid. All patients underwent thyroid function test and it was found that maximum 54 cases, i.e., 87.1% were euthyroid, while four cases, i.e., 6.45% were hyperthyroid and only one case was hypothyroid.

Ultrasonography

In the present study, of 57 cases diagnosed as benign lesion on USG, 55 were confirmed to be benign on histopathology and three cases were suspicious on USG, of which one case was malignant on histopathology, all the two cases of malignant tumor were confirmed on histopathology.

FNAC

In the present study on FNAC, 55 cases were benign, of which 53 cases (35 colloid goiter, 11 follicular adenoma, 6 chronic lymphocytic thyroiditis, and 1 hemorrhagic cyst) were confirmed to be benign on histopathology and rest of two cases (one case each of papillary carcinoma and follicular carcinoma) were malignant of histopathology.

Two cases were malignant on FNAC, of which one case is papillary carcinoma and one is medullary carcinoma which were confirmed malignant on histopathology.

Opinion was not possible in five cases on FNAC, of which one was confirmed colloid goiter, one case was of hemorrhagic cyst, one was chronic lymphocytic thyroiditis, one was follicular adenoma, and one was follicular carcinoma on histopathology.

FNAC is very precious diagnostic tool which is also easy minimally invasive, inexpensive, and simple which can be done in OPD basis. Using FNAC diagnosis of colloid goiter, thyroiditis, papillary carcinoma, medullary carcinoma, and anaplastic carcinoma are possible. Follicular carcinoma cannot be differentiated from benign follicular neoplasm by FNAC as differentiation depends on histological and not on cytological criteria, i.e., capsular and vascular invasion.

Distribution of Various Solitary Thyroid Swellings

In the present study, of 62 operated cases presented for histopathological examination, colloid goiter was most common histopathological diagnosis contributing 36 cases, i.e., 58.1% followed by follicular adenoma 12 cases, i.e., 19.4% and chronic lymphocytic thyroiditis 7 cases, i.e., 11.3%.

Operative Procedure

In the present study, 62 operated cases of STN, hemithyroidectomy was the most common operation performed in 56 (90.32%) of cases followed by total thyroidectomy.

Post-operative Complications

In the present study, wound infection was the most common complication in four cases, i.e., 6.4% while recurrent laryngeal nerve palsy was seen in two cases, i.e., 3.2%, and hypocalcemia and hypothyroidism in 3, i.e., 4.83% and 1, i.e., 1.6% of cases, respectively. In the present study, temporary laryngeal nerve palsy occurred in two patients, i.e., 3.2%, but all of them recovered over the due period. All two cases had undergone total thyroidectomy. No permanent recurrent laryngeal nerve palsy was seen.

CONCLUSIONS

The present study was carried out in upgraded Department of General Surgery, in Kakatiya Medical College and Mahatma Gandhi Memorial Hospital, from February 2017 to October 2018. The study was conducted on selected 62 cases of STN coming to OPD of the department of general surgery.

Incidence of STN was common in females than males. Incidence of STN is common in the age group of 18–30 years. FNAC is an important diagnostic tool which is also easy minimally invasive inexpensive and less painful procedure. It is single most sensitive and specific investigation on STN for etiological diagnosis. Incidence of malignancy of STN was 8.06% as compared to benign incidence. Hemithyroidectomy was commonly performed on maximum cases. Wound infection was common post-operative complication seen.

Fifty-two cases, i.e., 83.9% were female while 10 cases, i.e., 16.1% were male, and female-to-male ratio was 5.6:1; 31 cases, i.e., 50% were seen in the age group of 18–30 years, while only five cases, i.e., 8.1% were seen in the age group of 51–60 years. The right lobe of thyroid is more commonly involved than the left lobe. The most common presenting feature was swelling in the neck seen in 62 cases while sweating was seen in three cases and weight loss seen in two cases. Maximum 34 cases, i.e., 54.83% presented within 0–6 months after the appearance of swelling. While eight cases, i.e., 12.9% presented after 1–2 years and only one case, i.e., 1.6% was seen in 4–5 years after the appearance of swelling. Two cases were seen after 5 years. Of 57 cases diagnosed as benign lesion of USG, 55 were confirmed to be benign and two malignant on histopathology and three

cases which were suspicious on USG, of which one case was malignant and two were benign on histopathology, all the two cases of malignant tumor on USG were confirmed on histopathology. Euthyroid state was seen in 54 cases, i.e., 87.71% while four cases, i.e., 6.45% were clinical hyperthyroid and only one case, i.e., 1.61% was clinical hypothyroid. On FNAC, 55 cases were benign, of which 53 cases (35 colloid goiter, 11 follicular adenoma, 6 chronic lymphocytic thyroiditis, and 1 hemorrhagic cyst) were confirmed to be benign on histopathology and rest of two cases (one case each of papillary and follicular carcinoma, respectively) were malignant on histopathology. Two cases were malignant on FNAC, of which two cases (one each of papillary and medullary carcinoma, respectively) were confirmed malignant on histopathology, while two cases (one each case of follicular adenoma and chronic lymphocytic thyroiditis, respectively) were benign on histopathology. Opinion was not possible in five cases on FNAC, of which one was confirmed colloid goiter, one was chronic lymphocytic thyroiditis, and one case was of hemorrhagic cyst, one was follicular adenoma and one was follicular carcinoma on histopathology. Sensitivity of FNAC of 62 cases, 55 cases, i.e., 88.70% was tallied with histopathology while the rest of seven cases, i.e., 11.30% were not tallied with histopathology. Fifty-five, i.e., 91.94% were benign while five cases, i.e., 8.06% were malignant. Maximum 57 cases (91.9%) had undergone hemithyroidectomy while in 5 cases (8.06%), total thyroidectomy was performed. Two cases underwent completion thyroidectomy. The most common complication was wound infection in four cases, i.e., 6.4% while recurrent laryngeal nerve palsy was seen in two cases, i.e., 3.2%, and hypocalcemia and hypothyroidism in 3, i.e., 4.83% and 1, i.e., 1.6% of cases, respectively.

REFERENCES

1. Larsen PR, Ingbar SH. The thyroid gland. In: Williams Textbook of Endocrinology. 8th ed. Philadelphia, PA: WB Saunders Co.; 1992. p. 357-487.
2. Fraker DL. Radiation exposure and other factors that predispose to human thyroid neoplasia. *Surg Clin North Am* 1995;75:365-75.
3. Sadler GP, Clark OH. Principles of Surgery: Schwartz. 10th ed. New York: McGraw Hill Professional; 2014. p. 1537-640.
4. Iwata M, Kasagi K, Hatabu H, Misaki T, Iida Y, Fujita T, *et al.* Causes of appearance of scintigraphic hot areas on thyroid scintigraphy analyzed with clinical features and comparative ultrasonographic findings. *Ann Nucl Med* 2002;16:279-87.
5. Lawrence W Jr., Kaplan BJ. Diagnosis and management of patients with thyroid nodules. *J Surg Oncol* 2002;80:157-70.
6. Abdullah M. Thyroid cancer: The Kuala Lumpur experience. *ANZ J Surg* 2002;72:660-4.

How to cite this article: Vidyasagar R. Clinical Study of Solitary Thyroid Nodule. *Int J Sci Stud* 2019;7(5):59-65.

Source of Support: Nil, **Conflict of Interest:** None declared.

A Comparable Study on Efficacy of Granisetron and Promethazine in Controlling Hyperemesis Gravidarum

Akriti Prasad¹, Mamta Singh²

¹Senior Resident, Department of Obstetrics and Gynaecology, Nalanda Medical College and Hospital, Patna, Bihar, India,

²Professor, Department of Obstetrics and Gynaecology, Nalanda Medical College and Hospital, Patna, Bihar, India

Abstract

Purpose: Hyperemesis gravidarum is one of the leading causes of hospitalization during pregnancy. This randomized study was aimed to compare and evaluate the efficacy of granisetron and promethazine in controlling nausea and vomiting in pregnancy.

Materials and Methods: This study was done in the Department of Obstetrics and Gynaecology, Nalanda Medical College and Hospital, Patna, Bihar, over a period of 6 months from February 2019 to July 2019. The included patients were administered granisetron and promethazine randomly and evaluated for nausea and vomiting by senior gynecologist blinded to designated drugs.

Results: This study showed that granisetron was more effective than promethazine in controlling nausea and vomiting in pregnant patients. Greater patient satisfaction and less adverse drug reaction were observed in women receiving granisetron.

Conclusion: Hyperemesis gravidarum is a health-related problem with social, economic, and psychological dimensions. All efforts, especially simple outpatient strategies, can reduce the severity of this condition and will help pregnant women to continue her pregnancy with satisfaction.

Key words: Granisetron, Hyperemesis gravidarum, Promethazine

INTRODUCTION

Pregnancy frequently causes nausea and vomiting; the cause appears to be rapidly increasing levels of estrogen or the beta-subunit of human chorionic gonadotropin (β -hCG). Vomiting usually develops at about 5-week gestation, peaks at about 9 weeks, and disappears by about 16 or 18 weeks. It usually occurs in the morning, although it can occur at any time of day. Women with morning sickness continue to gain weight and do not become dehydrated.

Hyperemesis gravidarum is probably an extreme form of normal nausea and vomiting during pregnancy. It can be distinguished because it can cause the following.

- Weight loss (>5% of weight)
- Dehydration
- Ketosis
- Electrolyte imbalance.

Hyperemesis gravidarum may cause mild transient hyperthyroidism. Hyperemesis gravidarum that persists the past 16–18 weeks is uncommon but may seriously damage the liver causing severe centrilobular necrosis or widespread fatty degeneration and may cause Wernicke's encephalopathy or esophageal varices rupture.

Clinician's suspects hyperemesis gravidarum based on symptoms such as onset, duration, and frequency of vomiting; exacerbating and relieving factors; and type and amount of emesis. Serial weight measurements can support the diagnosis. If hyperemesis gravidarum is suspected, urine ketones, thyroid-stimulating hormone, serum electrolytes, blood urea nitrogen, creatinine, aspartate aminotransferase, alanine aminotransferase, magnesium, phosphorus, and, sometimes, body weight are measured. Obstetrics ultrasonography should be

Access this article online



www.ijss-sn.com

Month of Submission : 06-2019
Month of Peer Review : 07-2019
Month of Acceptance : 08-2019
Month of Publishing : 08-2019

Corresponding Author: Dr. Mamta Singh, Department of Obstetrics and Gynaecology, Nalanda Medical College and Hospital, Patna, Bihar, India.

done to rule out hydatidiform mole and multifetal pregnancy.

The management includes dietary changes, intravenous fluid infusion, electrolyte imbalance correction, vitamin supplementation, antiemetic therapy, and psychological support. Dehydrated and ketotic patient should be hospitalized for the management of hyperemesis gravidarum. A number of dopamine antagonist (phenothiazines such as prochlorperazine and promethazine), 5HT₃ receptor antagonists (ondansetron and granisetron), and steroids have been used for the treatment of nausea and vomiting.^[1,2] Treatment of hyperemesis gravidarum is initiated with intravenous fluid and antiemetics. Granisetron (selective 5HT₃ receptor antagonist) has not been regularly used for hyperemesis gravidarum.^[3] In contrast, promethazine (an H₁ receptor blocking agent) is being used for prevention and control of post-operative nausea and vomiting and hyperemesis gravidarum.^[4,5] This double-blinded, randomized controlled clinical trial was planned to assess the efficacy of oral granisetron and oral promethazine for the management of hyperemesis gravidarum and to determine whether granisetron may be a superior antiemetic over promethazine.

MATERIALS AND METHODS

This randomized controlled, double-blinded clinical trial was conducted at the Department of Obstetrics and Gynaecology, Nalanda Medical College and Hospital, Patna, Bihar, from February 2019 to July 2019. Twenty patients between 18 and 35 years with hyperemesis gravidarum attending gynecology outpatient department (GOPD) and labor room were enrolled in this trial.

Inclusion Criteria

The following criteria were included in the study:

1. Clinical symptoms such as nausea and vomiting
2. Ketonuria by urine dipstick (more than +1 ketonuria)
3. Gestational age 20 weeks or less.

Exclusion Criteria

The following criteria were excluded from the study:

1. Molar pregnancy and multifetal pregnancy
2. Hepatic and thyroid dysfunction

3. Pre-existing medical conditions such as urinary tract infection, gastrointestinal infection, and diabetic ketoacidosis
4. Hypersensitivity reaction to drugs being studied.

On arrival in labor room and GOPD, the patients were randomized into two treatment groups of 10 patients each. On admission, the patients with hyperemesis gravidarum receive intravenous fluid, ranitidine, and pyridoxine. Based on the history of vomiting, patients were quantified with Pregnancy-Unique Quantification of Emesis scoring system [Table 1]. Patients with score of 13 or higher were included in the study.

The patients and the nurse were blinded to the randomization and treatment type. The drugs were labeled as (a) promethazine, 25 mg/ml or (b) granisetron, 1 mg/ml. The drugs were given through intravenous line over 2 min. The adverse effect of drugs was assessed in patients after 30 min of intravenous administration.

From the 2nd day onward, both drugs were administered orally until 2 weeks after discharge. Tab promethazine 25 mg was administered 4 times a day or every 6 h. Tab granisetron 1 mg was administered every 12 hourly with two placebo tablets to maintain blindness of study. The patients were assessed for nausea and vomiting by gynecologist blinded to designated drugs.

Nausea is an unpleasant feeling associated with awareness of the urge to vomit, whereas vomiting was defined as forceful expulsion of gastric content from mouth.^[6] Severity of nausea and vomiting was assessed at the time of admission, after 48 h, 1 week, and 2 weeks after discharge. Nausea was scored using a 5-point linear verbal rating scale from 0 to 5, with "0" representing no nausea and "5" representing nausea as bad as it can possibly be.

At 1 week and 2 weeks following discharge, the patients were contacted to assess the adverse drug reaction and satisfaction with the antiemetic drug using a 0 (very dissatisfied) to 10 (very satisfied) scale. The adverse effects were fever, headache, constipation, dyspepsia, allergic reaction, seizure, anorexia, dry mouth, difficulty in urination, hypertension, and arrhythmia.

Table 1: PUQE scoring system

In the past 12 h, for how long you feel nauseated or sick to your stomach?	Not at all (1)	1 h or less (2)	2–3 h (3)	4 h (4)	>6 h (5)
In the past 12 h, have you vomited or thrown up?	≥7 times (5)	5–6 times (4)	3–4 times (3)	1–2 times (2)	Nil (1)
In the past 12 h, how many times have you had retching or dry heave without bringing anything up?	≥7 times (5)	5–6 times (4)	3–4 times (3)	1–2 times (2)	Nil (1)

PUQE score: Mild ≤6; moderate: 7–12; severe: 13–15. PUQE: Pregnancy-Unique Quantification of Emesis

Table 2: Vomiting episodes and nausea scores after treatment (first outcome)

Variables	Granisetron (n=10)			Promethazine (n=10)		
	Base	After 48 h	P-value	Base	After 48 h	P-value
Nausea scores (0–5)	4.5	0.2	0.001	4.7	2.3	0.002
Vomiting episodes/day (n)	6.3	0.8	0.001	5.4	1.2	0.002

Descriptive statistics were used to characterize the population using the Statistical Package for the Social Sciences. Wilcoxon signed-rank test was used to compare vomiting episode frequencies on admission day and 48 h later within each group. Mann scores on admission day and 48 h later between groups. $P < 0.05$ was considered statistically significant.

RESULTS

In this study, it was found that granisetron group was superior to promethazine group at 48 h after treatment. The number of vomiting was significantly lower in granisetron group than promethazine group. The nausea scores were significantly lower in the granisetron group than promethazine group. The patients on granisetron were more satisfied than those in promethazine group [Table 2].

There was no serious adverse reaction noted in any of the patients. Less rehospitalization at the end of the 1st week was noted in granisetron group. Three patients in promethazine group showed drug reactions including somnolence, anorexia, and dry mouth [Table 3].

DISCUSSION

This study showed that granisetron was more effective than promethazine in decreasing symptoms of nausea and vomiting in pregnant patients. Greater patient satisfaction, less adverse drug reaction, and rehospitalization in granisetron group suggest that it can be introduced as more safer and effective drug as compared to promethazine. Hyperemesis gravidarum is the most severe form of nausea and vomiting in pregnancy and is characterized by intractable nausea and vomiting that leads to dehydration, electrolyte, and metabolic disturbances, and nutritional deficiency that may require hospitalization.^[7,8] Hyperemesis gravidarum has also been defined as severe vomiting with onset at <16 weeks of estimated gestational age that causes 5% weight loss and considerable ketonuria.^[9,10] The cause of hyperemesis gravidarum is not well understood but appears to have both physiological and psychological components. Estrogen, progesterone, adrenal, and pituitary hormones have been proposed as cause, but currently, there is no conclusive evidence implicating any of them. The main

Table 3: Adverse drug reactions and patient satisfaction after treatment (second outcome)

Variables	Granisetron (n=10)	Promethazine (n=10)
Patient satisfaction level (score 0–5) mean	4.9	4.4
Adverse drug reaction (n=number)	0	3
Hospital stay (day) mean±standard deviation	2.4±1.2	2.8±1.4
Rehospitalization (n=number)	0	1

treatment of hyperemesis gravidarum is supportive care. Various lifestyle and diet changes can help patients to tolerate oral intake. Patients should try to avoid unpleasant odors; eat bland, dry, carbohydrate diet; eat small, frequent meals; and separate solid and liquid foods by at least 2 h. Immediate correction of fluids and electrolyte deficits and base disorders must be accomplished.^[11] The patients should initially have nothing by mouth until deficits are corrected. One study found that treatment with intravenous fluid led to cessation of vomiting and increase tolerance to oral intake within 24 h in hyperemesis gravidarum patients.^[12]

Promethazine is an H1 receptor blocking agent used for prevention and control of post-operative nausea and vomiting and motion sickness.^[13] Although Promethazine is classified as drug Group C in pregnant patients but, is widely used for controlling nausea and vomiting in pregnancy. Granisetron is a selective 5-HT₃ receptor antagonist and is classified as drug Group B in pregnant patients and approved by the Food and Drug Administration for the treatment of post-operative nausea and vomiting in adults.^[14] In comparison with ondansetron, granisetron is more potent antagonist with longer duration of action.^[15] Not much data had been published so far to support the superiority of granisetron over promethazine.

Ashraf *et al.* had done double-blinded clinical trial on 32 antenatal patients in Iran. Her study showed that the episodes of nausea and vomiting in granisetron group were much less than in promethazine group. Furthermore, patients were more satisfied and had less adverse drug reaction in granisetron group as compared to promethazine group.^[16] This was similar to this study which also supports the superiority of granisetron over promethazine.

Guikontes *et al.* found no benefit of ondansetron compared to promethazine.^[17] Regarding the management of hyperemesis gravidarum, promethazine has been compared with ondansetron, but not much controlled clinical trial has been reported for granisetron.

CONCLUSION

Hyperemesis gravidarum is a health-related problem with economic, social, and psychological dimensions. Efforts should be made to reduce its severity and help pregnant women to continue her pregnancy with more satisfaction. According to this study, granisetron has more benefits over promethazine. Granisetron is more effective in controlling nausea and vomiting as compared to promethazine. Less drug adverse reaction and rehospitalization suggest aforementioned benefits of granisetron over promethazine.

REFERENCES

1. Badell ML, Ramin SM, Smith JA. Treatment options for nausea and vomiting during pregnancy. *Pharmacotherapy* 2006;26:1273-87.
2. Bottomley C, Bourne T. Management strategies for hyperemesis. *Best Pract Res Clin Obstet Gynaecol* 2009;23:549-64.
3. Tan PC, Khine PP, Vallikkannu N, Omar SZ. Promethazine compared with metoclopramide for hyperemesis gravidarum: A randomized controlled trial. *Obstet Gynecol* 2010;115:975-81.
4. Hsu ES. A review of granisetron, 5 hydroxytryptamine receptor antagonists, other antiemetics. *Am J Ther* 2010;17:476-86.
5. Barrett TW, Dipersio DM, Jenkins CA, Jack M, McCain NS, Storow AB, *et al.* A randomized, placebo-controlled trial of ondansetron, metoclopramide, and promethazine in adults. *Am J Emerg Med* 2011;29:247-55.
6. Ferreira E, Gillet M, Lelièvre J, Bussi eres JF. Ondansetron use during pregnancy: A case series. *J Popul Ther Clin Pharmacol* 2012;19:e1-e10.
7. Broussard CN, Richter JE. Nausea and vomiting of pregnancy. *Gastroenterol Clin North Am* 1998;27:123-51.
8. Abell TL, Riely CA. Hyperemesis gravidarum. *Gastroenterol Clin North Am* 1992;21:835-49.
9. Safari HR, Alsulyman OM, Gherman RB, Goodwin TM. Experience with oral methylprednisolone in the treatment of refractory hyperemesis gravidarum. *Am J Obstet Gynecol* 1998;178:1054-8.
10. Hershman JM. Human chorionic gonadotropin and the thyroid: Hyperemesis gravidarum and trophoblastic tumors. *Thyroid* 1999;9:653-7.
11. Borgeat A, Fathi M, Valiton A. Hyperemesis gravidarum: Is serotonin implicated? *Am J Obstet Gynecol* 1997;176:476-7.
12. Godsey RK, Newman RB. Hyperemesis gravidarum. A comparison of single and multiple admissions. *J Reprod Med* 1991;36:287-90.
13. van Stuijvenberg ME, Schabert I, Labadarios D, Nel JT. The nutritional status and treatment of patients with hyperemesis gravidarum. *Am J Obstet Gynecol* 1995;172:1585-91.
14. Board T, Board R. The role of 5-HT₃ receptor antagonists in preventing postoperative nausea and vomiting. *AORN J* 2006;83:209-16, 219-20.
15. Bhatnagar S, Gupta D, Mishra S, Srikanti M, Singh M, Arora R, *et al.* Preemptive antiemesis in patients undergoing modified radical mastectomy: Oral granisetron versus oral ondansetron in a double-blind, randomized, controlled study. *J Clin Anesth* 2007;19:512-6.
16. Aleyasin A, Saffarieh E, Torkamandi H, Hanafi S, Sadeghi F, Mahdavi A, *et al.* Comparison of efficacy of granisetron and promethazine in control of hyperemesis gravidarum. *J Obstet Gynaecol India* 2016;66:409-14.
17. Guikontes E, Spantideas A, Diakakis J. Ondansetron and hyperemesis gravidarum. *Lancet* 1992;340:1223.

How to cite this article: Prasad A, Singh M. A Comparable Study on Efficacy of Granisetron and Promethazine in Controlling Hyperemesis Gravidarum. *Int J Sci Stud* 2019;7(5):66-69.

Source of Support: Nil, **Conflict of Interest:** None declared.

Evaluation of Acceptability, Safety, and Efficacy of Intrauterine Device Insertion during the Postpartum Period: A Prospective Analysis

Shilpa Jain¹, Priyanka Priyadarshini², Hiralal Konar³

¹Assistant Professor, Department of Obstetrics and Gynaecology, IQ City Medical College and Narayana Multispecialty Hospital, Durgapur, West Bengal, India, ²Senior Resident, Department of Obstetrics and Gynaecology, Calcutta National Medical College and Hospital, Kolkata, West Bengal, India, ³Professor and Head, Department of Obstetrics and Gynaecology, Agartala Government Medical College, Agartala, Tripura, India

Abstract

Background: Intrauterine contraceptive devices (IUCD) are a rapidly reversible method of contraception. It is necessary to assess the acceptability and uptake of IUCD in parturients elaborating its safety and success.

Aims and Objectives: The aim of the study was to evaluate the acceptability, safety, and follow-up of postpartum insertion of IUCD both in vaginal and cesarean section deliveries among parturients with the ultimate goal is to avoid unplanned pregnancies and to expand the usage of IUCD.

Materials and Methods: The study was a prospective one conducted during the period of January 2014–January 2015. All the antenatal patients at their visits after 30 weeks of gestation were taken in the study and parturients accepted for postpartum IUCD (PPIUCD) insertion constitute the study population.

Results: A total of 202 patients were included in the study population. Majority of cases accepted for PPIUCD had at least a primary level of education, were primiparous, and had their last childbirth >2 years ago consisting of 90.10%, 46.53%, and 44.55%, respectively. About 27.72% of the parturients were aware of the PPIUCD and 58.91% of parturients accepted PPIUCD due to its long-term effect. PPIUCD insertion done for the study was three types such as: Within 10 min, immediate (within 24 h), and trans-cesarean consisting of 23.76%, 15.35%, and 60.89%, respectively. About 96.04%, 79.70%, and 60.90% cases were attaining for follow-up at 6 weeks, 3 months, and 6 months, respectively. At 6 week follow-up, pelvic inflammatory disease, irregular cycles, and pain were the chief concerns consisting of 34.16%, 23.27%, and 16.83%, respectively, whereas bleeding per vagina, lost string, and expulsion were less seen. PPIUCD expulsion was seen in 14.85% of the parturients.

Conclusions: Awareness of the PPIUCD among women was poor despite high acceptance and needs strategies to increase awareness. The PPIUCD was demonstrably safe, having no reported incidence of perforation with low rates of expulsion, pelvic infection, and few lost strings.

Key words: Acceptance, Intrauterine contraceptive devices, Postpartum insertion, Safety

INTRODUCTION

Intrauterine contraceptive devices (IUCD) to prevent pregnancy are among the oldest methods of contraception. Increasing numbers of women in the developing world

are having their babies in hospitals. Many of these women welcome the opportunity to delay their next pregnancy. The postpartum insertion of an IUCD offers several advantages in such instances. Having just given birth, the woman is not pregnant, and she may be very motivated to consider long-acting methods. IUCDs work primarily by preventing fertilization and do not act as abortifacients. When the uterus is exposed to an IUCD, a sterile inflammatory reaction occurs, which is toxic to sperms and impairs fertilization.

The modern IUCD is a highly effective, safe, long-acting, coitus independent, and rapidly reversible method of contraception with few side effects of contraception. Many

Access this article online



www.ijss-sn.com

Month of Submission : 06-2019
Month of Peer Review : 07-2019
Month of Acceptance : 08-2019
Month of Publishing : 08-2019

Corresponding Author: Dr. Priyanka Priyadarshini, Calcutta National Medical College and Hospital, Kolkata - 700 014, West Bengal, India.

women also find IUCD to be very convenient because it requires little action once it is in place. The Cu T 380A has a remarkably low failure rate of $<1/100$ women in the 1st year of use. IUCD insertion in the immediate postpartum period offers an effective and safe method for spacing and limiting births.^[1] Delivery is the best opportunity for the IUCD insertion in developing countries when the healthy women come in contact with the health-care providers and maybe the best scope to curtail the fertility rate.^[2] Immediate postplacental insertion should be done only after adequate prenatal counseling and giving her informed consent.

Appropriate times for IUCD insertion in the postpartum periods include the postplacental IUCD insertion, the immediate postpartum IUCD (PPIUCD) insertion, and the trans-cesarean IUCD insertion. The postplacental IUCD insertion is done within 10 min after the expulsion of the placenta, following vaginal delivery. The immediate PPIUCD insertion is done after the postplacental period, but within 48 h of delivery and the trans-cesarean IUCD insertion is done when the insertion takes place following cesarean delivery before the uterus incision is sutured.

Immediate PPIUCD insertion has a higher retention rate if the IUCD is inserted postplacentally, but the IUCD can be inserted safely at any time during the first 48 h after delivery. IUCDs can also be inserted after the 6th week postpartum and after an abortion.

IUCDs inserted postplacentally have a much lower expulsion risk than those inserted later in the postpartum period. The risk of expulsion can be reduced significantly by properly inserting the IUCD. There is no increased risk of pelvic infection, the low risk of uterine perforation, and no effect on breast milk quantity or quality with PPIUCD insertion.

Therefore, the present study was conducted to assess the acceptability and uptake of post placental, immediate, and trans-cesarean insertion of IUCD (copper T 380 A) in parturients and to elaborate in its safety and success by the end of postpartum.

MATERIALS AND METHODS

The study was a prospective interventional analytical one conducted in the Department of Obstetrics and Gynecology of Calcutta National Medical College and Hospital, a tertiary care teaching hospital during the study period of January 2014–January 2015. Institutional Ethics Committee approval was taken for the study under the Helsinki Declaration of 1975 that was revised in 2000. All the antenatal patients at their visits after 30 weeks

of gestation were taken in the study. The patients with 18–40 years old, desire to have Cu-T after counseling, no systemic or pelvic infection, hemoglobin >8 g/dl, and no major systemic illness (diabetes mellitus and heart disease in pregnancy) were included in the study. The patients having stillbirth, sepsis (temp. $>38^{\circ}\text{C}$ during or after labor), rupture of membranes for >24 h before delivery, and postpartum hemorrhage were excluded from the study.

Parameters to be studied were a history of the patient, insertion timings, follow-up, and complications. History of the patient includes age, parity, gravida, education, knowledge, and previous use of any contraceptive, any complicating factor. Insertion timings were during the postpartum period, i.e., within 24 h of placental expulsion. Follow-up was done at 6 weeks, 3 months, and 6 months after IUCD insertion. Pain, bleeding per vagina, perforation, infection, pregnancy, and missing thread were the complications encountered.

Study Tools

Instruments which were used in the study included a structured questionnaire, a checklist, and a PPIUCD follow-up card. A structured open-ended questionnaire was used to extract important information from the parturient and the following variables were collected: Social-demographic characteristics of the women studied, obstetric and gynecological characteristics, previous contraceptive methods used, source of information and awareness of the PPIUCD, reasons for acceptance or decline to PPIUD insertion, and their future pregnancy desires. The checklist was used to counter check the eligibility of the parturient, to ensure that all the instruments required were set before insertion and to check any immediate complications. A PPIUCD follow-up card was given to all the parturients after insertion of the IUCD. This included instructions about recognizing expulsion, for example, through the string length or even vivid expulsion, postpartum warning signs, i.e., bright red bleeding of which the woman needs to change her pad more than 6 times a day, unusual abdominal or pelvic pain (not after-birth pain), and unusual vaginal discharge or pain, or fever. The PPIUCD card also contained information on the date of insertion and follow-up visit, type of IUCD inserted, date of expiry of the IUCD, and the telephone number of the principal investigator (PI).

Data Collection and Sampling Technique

General health education was done for all parturients who had normal vaginal and cesarean section deliveries during their antepartum visits and hospitalization period. During these sessions, postpartum contraception with IUCD was offered together with other options that include Nexplanon, depot medroxyprogesterone acetate, and

minipills suitable for breastfeeding mothers. The merits of each method, their common side effects, and possible complications were explained to all the women. Each eligible woman was then counseled individually, following which PPIUCD was introduced. This approach was used to enable the woman to make a voluntary, informed, and well-considered choice. The ultimate choice was respected. In all cases, reasons for acceptance and refusals were recorded. Counseling for postpartum family planning was offered every morning and afternoon before the parturient was discharged from the hospital. Counseling was done by the research assistant and the PI.

Data were collected conveniently among the eligible parturients. Eligibility was sought by checking their files for the labor events and by asking the woman if she was planning to stay around the area for a month. Those women who were eligible for PPIUCD were identified and approached in the postnatal ward. A written informed consent was given to the parturients on their participation in the study. Questionnaires were filled by the PI and the research assistants. After contraceptive counseling and filling of the questionnaire, those who accepted the PPIUCD insertion had the IUCD inserted immediately. In case of non-acceptance, other methods of postpartum family planning were advised. The IUCD was inserted in a side room adjacent to the postnatal ward.

Women in whom the PPIUCD was inserted were assessed before discharge and followed at 6 weeks after IUCD insertion. On discharge a PPIUCD follow-up card was given which contained information of the date of insertion and follow-up visit, type of IUCD inserted, date of expiry of the IUCD and the telephone number of the PI. These women were advised to phone or come back any time if she had any concern or experiences any warning sign or if the IUCD is expelled. The PI crosschecked the checklist and questionnaire after every shift to ensure proper filling of information.

At 6 weeks interval, those women whom the PPIUCD was inserted were reassessed by the PI at the examination room in the antenatal/postnatal clinic. The follow-up checklist was filled by checking their oral temperature, and an abdominal examination for suprapubic tenderness and involution of the uterus was done. A speculum examination was then performed to check if the strings were visible and any discharge noted. The visible IUCD strings were trimmed at approximately 3 cm. A digital vaginal examination was then done to assess for cervical motion tenderness. Those women who had a pelvic infection were treated with antibiotics (Injection Ceftriaxone 250 mg stat followed by oral Erythromycin 500 mg 12 hourly and Metronidazole 400 mg 8 hourly for 2 weeks). Women

who reported expulsion of the IUCD or those whom their strings were not visible had a pelvic ultrasound to confirm expulsion.

Insertion Techniques

All necessary instruments (Copper T 380A, 2 ring forceps, Sim's speculum, headlamp, Povidone-iodine, Savlon, kidney dish, and cotton swabs) were arranged on top of an auxiliary table covered with a sterile drape. IUCD insertion was performed by the PI under proper aseptic techniques throughout the procedure. The IUCD was inserted through the dilated cervix to the level of the uterine fundus, as confirmed by palpation with a hand placed on the abdomen overlying the fundus. The ring forceps were oriented, so the arms of the IUCD lies parallel to the anterior and posterior walls of the uterus and then the forceps were opened to release the IUCD. The cervical os was then gently inspected with the Sims Speculum for the strings. If the strings were visible then the IUCD was reinserted. Before discharge, the patient was assessed for comfortability by the research assistants.

Data Analysis

Statistical analysis was performed using SPSS version 17.0. The Chi-square test was used to measure the strength of associations between variables, $P < 0.05$ was considered to be statistically significant.

RESULTS

Among the total 587 parturients counseled for PPIUCD, 385 cases declined for the PPIUCD and the majority of the women declined due to their preferences for other forms of contraception (30.3%) and need to discuss with their partners and other family members (28%). Only 202 cases (34.4%) accepted for PPIUCD insertion and constitute the study population.

Table 1 showed the socio-demographic factors of the parturients studied. The majority were in the age range 20–29 (48.51%). Most of the study population had at least a primary level of education (90.10%). The majority were of Muslim religion (56.93%). Median parity was two (Range: 1–7). Grand multipara made up a small percentage (3.47%) of the study sample while the majority (46.53%) were primiparous. Majority of the women accepted for IUCD had their last childbirth <2 years ago consisting of 44.55% of cases.

While the majority never had used any method of contraception (46.04%), natural methods (20.30%) and oral contraceptives pills (16.34%) were commonly used methods of contraception. Nearly a quarter of the parturients (27.72%) were aware of the PPIUCD,

Table 1: Socio-demographic factors

Parameters	Number (n=202) with percentage (%)
Age in years	
≤19	61 (30.20)
20–29	98 (48.51)
30–39	38 (18.81)
≥ 40	5 (2.48)
Education status	
No formal education	20 (9.90)
Primary	66 (32.67)
Secondary	93 (46.04)
Higher education	23 (11.39)
Religion	
Hindu	64 (31.68)
Muslim	115 (56.93)
Christian	23 (11.39)
Occupation status	
Housewife	153 (75.74)
Business lady	5 (2.48)
Employed	44 (21.78)
Parity	
1	94 (46.53)
2	66 (32.67)
3	35 (17.33)
4	4 (1.98)
≥5	3 (1.49)
Last childbirth (years)	
0–2	90 (44.55)
February 3	62 (30.69)
March 4	27 (13.37)
≥5	23 (11.39)
Future pregnancy desire: Year	
1–2	19 (9.41)
3–5	138 (68.32)
>5	13 (6.43)
Not sure	17 (8.42)
No intension	15 (7.42)

i.e., having source of information. Among these, the majority (48.21%) had the antenatal clinic as their source of information followed by family planning clinic (17.86%), relative/friend (17.86%), and media (16.07%) as other sources of information. Majority of the PPIUCD was inserted after placental expulsion during cesarean deliveries (60.89%) [Table 2]. More than half (58.91%) of those women who accepted PPIUCD were due to the reason of its long-term effect [Table 3].

The type of follow-up of the parturients was clinic and telephone contact. About 96.04%, 79.70%, and 60.90% of the parturients attended follow-up at the schedule of 6th week, 3rd month, and 6th month, respectively. After 6 weeks, the majority of the parturients came to the clinic for follow-up (70.79%) while 25.24% parturients followed up over the telephone. Infection, irregular cycles, and pain were the common complaints among the parturients during the three follow-up schedules. About 35.57%, 24.23%, and 17.33% of the parturients attaining first follow-up at 6th week had complaints of infection, irregular cycles,

Table 2: Previous contraceptive method used, source of information and type of PPIUCD insertion

Sources	Number (202) percentage (%)
Previous contraceptive method used	
Never used	93 (46.04)
Natural	41 (20.30)
OCPs	33 (16.34)
Male condom	24 (11.88)
Internal IUCD	2 (0.99)
Depot medroxyprogesterone acetate	8 (3.96)
Spermicidal agents	1 (0.49)
Source of information	
Unaware	146 (72.28)
Aware	56 (27.72)
Type of PPIUCD insertion	
Within 10 min	48 (23.76)
Immediate (within 24 h)	31 (15.35)
Trans cesarean	123 (60.89)

IUCD: Intrauterine contraceptive devices, PPIUCD: Postpartum IUCD

Table 3: Reasons for acceptance

Sources	Number (n) percentage (%)
Reasons	
Long-term effect	119 (58.91)
Safe	32 (15.84)
Fewer clinic visit	24 (11.88)
Non-hormonal	21 (10.40)
No remembrance once inserted	15 (7.43)
Reversible	7 (3.47)
No interference with breastfeeding	3 (1.49)

and pain, respectively, whereas the percentage for the same complaints will be 34.16%, 23.27%, and 16.83%, respectively, when compared to the total study population. About 12.42%, 31.68%, and 22.36% of the parturients attaining second follow-up at 3rd month had complaints of infection, irregular cycles, and pain, respectively. About 21.14%, 37.40%, and 12.20% of the parturients attaining third follow-up at 6th month had complaints of infection, irregular cycles, and pain, respectively. Missing thread was seen in 8.76% of the parturients and expulsion, and refusal to continue IUCD insertion was seen in 7.22% of the parturients attaining 6th week of follow-up [Table 4]. In overall, PPIUCD expulsion was seen in 10.89% of the parturients and refusal to continue IUCD was seen in 7.43% of the parturients attaining study population.

DISCUSSION

This study was carried out to determine the acceptability, safety, and complications at 6 weeks follow-up in PPIUCD placement together with assessing the success that is the continuation rate at the end of puerperium in a cohort of

Table 4: Follow-up schedules

Complaint	Number (n) with percentage (%)		
	6 weeks	3 months	6 months
No complaint	48 (24.74)	31 (19.25)	15 (12.20)
Pain	34 (17.53)	36 (22.36)	15 (12.20)
Bleeding per vagina	12 (6.19)	15 (9.32)	9 (7.32)
Infection	69 (35.57)	20 (12.42)	26 (21.14)
Irregular cycles	47 (24.23)	51 (31.68)	46 (37.40)
Missing thread	17 (8.76)	12 (7.45)	10 (8.13)
Expulsion and refusal to continue	14 (7.22)	11 (6.83)	12 (9.76)

mothers who underwent vaginal delivery or cesarean delivery and required a long term, reversible method of contraception.

Data from India show that 61% of births occur at intervals shorter than the recommended interval of 36 months, i.e., 27% of births occur within 24 months after a previous birth, and 34% of births occur between 24 and 35 months. Lack of awareness is one of the common reasons for non-use of contraception. Less number of women is using any method of family planning during the 1st year postpartum consisting of only 26%.^[1,3]

Majority of the women (90.10%) in our study population had at least a primary level of education. Acceptance of PPIUCD was higher among women with primary and secondary education (32.67% and 46.04%) than those with no formal education (9.90%). This finding confirms the importance of education in deciding future pregnancy. This was similar to a study done in Egypt by Safwat *et al.*, where women with no formal education had an acceptance of 9.4%, while those with formal education were 19.4%.^[4]

Education has a positive effect on contraceptive use, as shown in a study done in Zimbabwe. It was only apparent among women who completed secondary education (12 years or more). Women who completed secondary school were about twice as likely to use modern contraceptive methods as women who did complete primary education. In this study, it is as high as four-fold.^[5]

A study by Halder *et al.* showed that mothers with >2 living children have lower acceptance of IUCD (1%) among cesarean group in comparison to vaginal group (13%) possibly due to their preference to permanent sterilization and acceptance of the PPIUCD was higher among parity 1 and parity 2,^[1] whereas study done by Safwat *et al.* in Egypt showed 16% of primipara mothers accepted the use of PPIUCD compared to one-third of grand multiparous possibly due to the higher educational status of the urban population compared to rural in India.^[4]

Acceptance of IUCD was the most common among primigravida clients (46.53%). In case of multiparous, it

was 3.47%; thus, this finding is contrary to that of the study by Grimes *et al.* where they found higher acceptance in multiparous clients (65.1%).^[6] Furthermore, the majority (72.28%) of the study population was not aware of the PPIUCD. Among women who had the PPIUCD inserted, 48.21% have ever heard about the PPIUCD from the antenatal clinic. This could be because PPIUCD is a relatively new method of contraception in this community.

The duration since last childbirth was significantly associated with acceptance of PPIUCD. About 44.55% of the PPIUCD acceptors had their last childbirth <2 years. Women on the first delivery and with short pregnancy interval felt the necessity of a long acting and reliable method of contraception. In a report released by WHO in 2006, better family planning and birth-spacing services resulted in improved maternal and neonatal outcome. About 32% of all maternal deaths and over 1 million deaths of children under 5 could be prevented in countries with high birth rates. This finding in the study indicates toward positive maternal health in the future.^[7] Future pregnancy desire remains almost the same in both groups of accepters and non-accepters. This finding suggests that the program managers must give priority toward effective antenatal counseling on PPIUCD, as the minimal effort would bring about a huge change.

Total acceptance rates remain low consisting of 34.41%. This was similar to the study done by Safwat *et al.* in Egypt (28%).^[4] Findings on the reason for acceptance are surprising. A majority of the acceptors rely on their physician. They value the advice of the doctor. Many are attracted for its long acting and reversibility properties.

A significant number of women declined PPIUCD because of partner's noninvolvement during counseling and decision making. When the partner is involved in contraceptive counseling and decision-making, the acceptance and continuation rates were higher. Unfortunately, in our setup, women who visit the antenatal clinic are usually not accompanied by their partners, and the care providers do not allow them during the process even if they are present. Thus, couple counseling is lost during this period. Therefore, it is most important to include proper counseling of the couple together to choose a contraceptive method which will, in turn, increase the compliance.

During follow-up, the present study showed that pelvic inflammatory disease (PID) and irregular cycles were the chief complaints and supported by the data which showed infections are common in developing countries increasing the risk of pelvic infection.^[8,9] However, Shukla *et al.* found no case with PID.^[10] Prophylactic antibiotics may be required in our setting where the incidence of

post-delivery sepsis is high as compared to developed countries. Fifteen women (7.43%) among those inserted with PPIUCD had lost strings during the first follow-up at 6 weeks. It should be noted that there were no serious complications in this study.

Expulsion rates vary according to clinician's skill in PPIUCD insertion.^[2] Therefore, it requires additional training to the clinicians and the provision of a special kit for PPIUCD insertion to the health centers where deliveries are conducted.^[11] In a systematic review by Kapp and Curtis, expulsion rates were lower in post-placental insertions during cesarean section in comparison to postplacental vaginal insertions without any added complications.^[12] Expulsion rate in a prospective study by Halder *et al.* was 4% in the vaginal group and 2% in intra-cesarean group which were much lower in comparison to few studies such as Celen *et al.* found the 1-year cumulative expulsion rate of 12.3% in early postplacental insertion of IUCD and another study found 17.6% expulsion rate in intra-cesarean IUCD.^[1,13,14] Expulsion rate of immediate PPIUCD in a study done in China by Chi *et al.* 1994, was 25–37%, while postplacental was 9.5–12.5%. Expulsion of PPIUCD usually occurs in the first few months after insertion.^[15]

A study by Shukla *et al.* showed that only 11.3% came for follow-up at 6 months whereas 78% came for follow-up at 6 weeks affecting the true data on the rate of expulsion at 6-month checkup.^[10] In our study, 60.90% came for follow-up at 6 months, whereas 96.04% came for follow-up at 6 weeks. These findings indicate a poor integration of vertical programs at all levels.

Limitations

The sample size of this study is small which may not reflect the true picture. Lost to follow-up observed in the study made it difficult to draw a clear conclusion as what happened to those who did not complete their follow-up schedule. The study is a single institution one and it will better for a multicentric study for more representative and powerful.

CONCLUSIONS

In the present study, awareness among women for the PPIUCD was very poor despite high acceptance. The PPIUCD was demonstrably safe, having no reported incidence of perforation with low rates of expulsion,

pelvic infection, and few lost strings. We can conclude that Inserting CuT 380 A in the postpartum period is safe and effective, has a high retention rate.

The government needs to develop strategies to increase public awareness of the PPIUCD through different media sources. It is also important to arrange for training on PPIUCD to increase knowledge and skills among health-care providers. This will also further promote PPIUCD use and aid in the reduction of the expulsion rates. Data on the safety of PPIUCD insertion is less from our country. There is a need for more studies in different settings before declaring the PPIUCD insertion as completely safe.

REFERENCES

1. Halder A, Sowmya MS, Gayen A, Bhattacharya P, Mukherjee S, Datta S, *et al.* A prospective study to evaluate vaginal insertion and intra-cesarean insertion of post-partum intrauterine contraceptive device. *J Obstet Gynaecol India* 2016;66:35-41.
2. Suri V. Post placental insertion of intrauterine contraceptive device. *Indian J Med Res* 2012;136:370-1.
3. Post-partum IUCD Reference Manual. Family Planning Division Ministry of Health and Family Welfare. Vol. 1. India: IUCD; 2010. p. 2.
4. Mohamed SA, Kamel MA, Shaaban OM, Salem HT. Acceptability for the use of postpartum intrauterine contraceptive devices: Assiut experience. *Med Princ Pract* 2003;12:170-5.
5. Thomas D, Maluccio J. Fertility, contraceptive choice, and public policy in Zimbabwe. *World Bank Econ Rev* 1996;10:189-222.
6. Grimes D, Schulz K, van Vliet H, Stanwood N. Immediate post-partum insertion of intrauterine devices: A Cochrane review. *Hum Reprod* 2002;17:549-54.
7. Aamir F, Mahesh A, Karim SA. To evaluate the compliance of postpartum intrauterine contra-ceptive device (PPIUCD) in Jinnah medical college hospital. *Ann ASH KMDC* 2018;23:79.
8. Marai W. Lower genital tract infections among pregnant women: A review. *East Afr Med J* 2001;78:581-5.
9. Kurewa NE, Mapingure MP, Munjoma MW, Chirenje MZ, Rusakaniko S, Stray-Pedersen B, *et al.* The burden and risk factors of sexually transmitted infections and reproductive tract infections among pregnant women in zimbabwe. *BMC Infect Dis* 2010;10:127.
10. Shukla M, Qureshi S, Chandrawati. Post-placental intrauterine device insertion a five year experience at a tertiary care centre in North India. *Indian J Med Res* 2012;136:432-5.
11. Muthal-Rathore A. Immediate postpartum insertion for intrauterine devices: RHL commentary. The WHO Reproductive Health Library. Geneva: World Health Organization; 2010.
12. Kapp N, Curtis KM. Intrauterine device insertion during the postpartum period: A systematic review. *Contraception* 2009;80:327-36.
13. Celen S, Möröy P, Sucak A, Aktulay A, Danişman N. Clinical outcomes of early postplacental insertion of intrauterine contraceptive devices. *Contraception* 2004;69:279-82.
14. Çelen Ş, Sucak A, Yıldız Y, Danişman N. Immediate postplacental insertion of an intrauterine contraceptive device during cesarean section. *Contraception* 2011;84:240-3.
15. Chi IC, Bardin CW, Mishell DR. Postpartum IUD Insertion: Timing, Route, Lactation and Uterine Perforation. *Proceedings from the Fourth International Conference on IUDs*; 1994. p. 219-27.

How to cite this article: Jain S, Priyadarshini P, Konar H. Evaluation of Acceptability, Safety, and Efficacy of Intrauterine Device Insertion during the Postpartum Period: A Prospective Analysis. *Int J Sci Stud* 2019;7(5):70-75.

Source of Support: Nil, **Conflict of Interest:** None declared.

Etiological and Clinical Study of Atrial Fibrillation

C Mamatha Reddy¹, Bingi Srinivas²

¹Assistant Professor, Department of Cardiology, Kakatiya Medical College, Mahatma Gandhi Memorial Hospital, Warangal, Telangana, India,

²Assistant professor, Department of Medicine, Kakatiya Medical College, Mahatma Gandhi Memorial Hospital, Warangal, Telangana, India

Abstract

Introduction: Atrial fibrillation (AF) is the common arrhythmia seen in clinical practice. It is characterized by worm-like writhing movements of atrial muscle resulting in loss of atrial transport function.

Materials and Methods: A total of 50 cases of AF, admitted in Medical and Cardiology wards of Mahatma Gandhi Memorial General Hospital, Warangal, from 2006 to 2008 formed the study material.

Results: A clinical study of 50 patients (aged from 20 to 80) with electrocardiographically documented AF.

Conclusion: Atrial fibrillation due to rheumatic aetiology is more common in younger age group, while that due to other causes like hypertension, ischemic heart disease common in older age. Chronic AF due to pulmonary disease is most commonly observed in males.

Key words: Atrial fibrillation, RHD, IHD

INTRODUCTION

Atrial fibrillation (AF) is the common arrhythmia seen in clinical practice. It is characterized by worm-like writhing movements of atrial muscle resulting in loss of atrial transport function.^[1-5] It is responsible for increased mortality from all cardiovascular causes and shortens average life span. The uncontrolled high ventricular rate in patients with AF over a period may result in progressive cardiomegaly increased functional mitral regurgitation and decreased left ventricular function leading to congestive cardiac failure and risk of sudden deaths.^[6-10] Irrespective of underlying cause, it increases the risk of thromboembolic phenomenon.

Its incidence varies with age ranging from 0.5% in young adults to 1.5% in the age group of 40–70 years and 10% in people of more than 70 years of age. The high incidence of this problem and its significant contribution to both cardiovascular and cerebrovascular morbidity and mortality aroused interest in us to study the problem.^[11-16]

This study is aimed at assessing the incidence, clinical features, etiology, Atrial size, and mitral valvular area in AF.

Aim of the Study

AF is the most common rhythm disturbance in the heart due to different etiology and it causes both morbidity and mortality.

The aim of the present study is as follows:

1. To know the prevalence of AF
2. To know the various clinical presentations in AF
3. To detect various etiological factors of AF
4. To know the relation between AF and left atrial size
5. To know relation between mitral valvular area dimensions and AF.

MATERIALS AND METHODS

A total of 50 cases of AF, admitted in Medical and Cardiology wards of Mahatma Gandhi Memorial General Hospital, Warangal, from 2006 to 2008 formed the study material.

A total of 50 cases were examined in detail as per pro forma with special reference to cardiovascular system. Other systems were also examined in detail, whenever it was found necessary. In each case, history of present and past illness was carefully inquired into so as to obtain a complete historical background of case.

Access this article online



www.ijss-sn.com

Month of Submission : 06-2019
Month of Peer Review : 07-2019
Month of Acceptance : 08-2019
Month of Publishing : 08-2019

Corresponding Author: Dr. Bingi Srinivas, Flat no 301, Balaji residency, OPP OLD RTA office, Nayeemnagar, Hanmakonda, Warangal 506009, Telangana, India

Investigations such as urine examination, complete blood picture, erythrocytes sedimentation rate, blood urea, serum creatinine, blood sugar, serum electrolytes, and chest X-ray (CXR) examination have been carried out. Special investigations such as electrocardiogram (ECG), echocardiogram, and transesophageal echocardiogram (TEE) were also done. Whenever necessary blood for culture and sensitivity, computed tomography-brain in case of stroke. The ECG was studied for rate and “f” wave pattern.

The echocardiogram was studied to assess the valvular lesions, mitral valve area (MVA) in mitral stenosis cases, and enlargement of chambers particularly the left atrium size. TEE to detect any thrombi or bacterial vegetation in the cardiac chambers or on valves.

For few patients, TEE not done due to patient III health, sometimes patient unwillingness.

RESULTS

A clinical study of 50 patients (aged from 20 to 80 years) with electrocardiographically documented AF Table 1.

The present study consists of 50 cases, of which there were 27 females and 23 males showing female predominance.

Their age ranging from 21 years to 80 years, AF was seen more in the patients of age group ranging from 31 to 40 years.

AF patients with rheumatic etiology commonly presented below 50 years, but hypertension (HTN), ischemic heart disease (IHD), and dilated cardiomyopathy (DCM) presented after 50 years.

In this study, the main complaints were dyspnea, palpitations, pedal edema, chest pain, hemoptysis, and weakness of limbs.

The duration of symptoms ranged from 15 days to 20 years Table 2. Shorter duration in cases of ischemic heart disease, hypertensive heart diseases, thyrotoxicosis, cardiomyopathies, and lone AF but longer duration in rheumatic heart disease.

Etiological Incidence

In this series of 50 cases, an attempt has been made to establish the etiology by history, clinical examination, ECG, CXR, and two-dimensional echocardiogram Table 3. Their incidence has been analyzed.

In this study, rheumatic heart disease (RHD) (52%) is the most common cause, followed by IHD (14%), HTN (10%), and DCM (10%).

Table 4 shows that female preponderance is seen in rheumatic and hypertensive heart disease etiology and male preponderance is seen in IHD and DCM.

Table 5 shows that AF commonly presented in 21–50 years of age group. Rheumatic etiology is most commonly seen below 50 years of age, and IHD and

Table 1: Age and sex distribution

Age group	Male	Female	Total	Percentage
0–10	-	-	-	-
11–20	-	-	-	-
21–30	6	6	12	24
31–40	4	11	15	30
41–50	4	3	7	14
51–60	5	4	9	18
61–70	4	1	5	10
71–80	-	2	2	4

Table 2: Clinical presentation in 50 cases of chronic AP

S. No.	Complaint	Number of patients	Percentages
1.	Dyspnea	44	88
2.	Palpitations	40	80
3.	Pedal edema	26	52
4.	Chest pain	19	38
5.	Hemoptysis	6	12
6.	Paralysis	7	14
7.	Syncope	1	2

Table 3: Etiology of 50 cases of AF

S. No.	Disease	Number of patients	Percentage
1.	RHD	26	52
2.	IHD	7	14
3.	HTN	5	10
4.	Thyrotoxicosis	1	2
5.	DCM	5	10
6.	Constrictive pericarditis	1	2
7.	Lone AF	1	2
8.	Marfan's syndrome	1	2
9.	Pulmonary disease	3	6

IHD: Ischemic heart disease, DCM: Dilated cardiomyopathy, HTN: Hypertension, AF: Atrial fibrillation, RHD: Rheumatic heart disease

Table 4: Distribution

Etiological incidence in 50 cases of AF in sex				
S. No.	Disease	Male	Female	Total
1.	RHD	9	17	26
2.	IHD	4	3	7
3.	HTN	2	3	5
4.	Thyrotoxicosis	-	1	1
5.	DCM	4	1	5
6.	Constrictive pericarditis	-	1	1
7.	Lone AF	1	-	1
8.	Marfan's syndrome	1	-	1
9.	Pulmonary disease	3	-	3

RHD: Rheumatic heart disease, HTN: Hypertension, IHD: Ischemic heart disease, DCM: Dilated cardiomyopathy, AF: Atrial fibrillation

Table 5: Age and sex incidence according to etiology

A. Female									
Age group	RHD	IHD	HTN	THY	Pulmonary diseases	HCM	C.P.	Lone AF	Marfan's
11–20	-	-	-	-	-	-	-	-	-
21–30	5	-	-	-	-	-	-	-	-
31–40	9	-	-	1	-	1	-	-	-
41–50	1	-	1	-	-	-	-	-	-
51–60	1	1	1	-	-	-	1	-	-
61–70	-	1	1	-	-	-	-	-	-
71–80	1	1	-	-	-	-	-	-	-
B. Male									
11–20	-	-	-	-	-	-	-	-	-
21–30	4	-	-	-	-	-	-	1	1
31–40	3	1	-	-	-	-	-	-	-
41–50	1	1	2	-	-	1	-	-	-
51–60	1	1	-	-	1	2	-	-	-
61–70	-	1	-	-	2	1	-	-	-
71–80	-	-	-	-	-	-	-	-	-

IHD: Ischemic heart disease, RHD: Rheumatic heart disease, HTN: Hypertension, AF: Atrial fibrillation, HCM: Hypertrophic cardiomyopathy

Table 6: Different valvular affection in rheumatic heart disease with AF (26 cases)

S. No.	Valve	Number of patients	Percentage
1.	MS	9	34.6
2.	MR	3	11
3.	MS+MR	7	26.9
4.	MS+MR+AR	2	7.6
5.	MS+AR	2	7.6
6.	MR+AR	1	3.8
7.	MS+MR+AS	1	3.8
8.	MR+AS+AR	1	3.8

MS: Mitral stenosis, MR: Mitral regurgitation, AR: Aortic regurgitation

hypertensive heart disease commonly seen above 50 years of age.

In all groups, female preponderance is noted, up to 50 years and male preponderance after 50 years.

Table 6 shows that M.S. is the most common lesion, of 26 cases, 21 cases have MS (80.7%) followed by MR (57.6%) next AR+MS/MR (23%).

Only MS cases are 9 (34.6%), only MR, 3 (11%) cases other common valvular lesion are MS+MR; MS+MR+AR.

DISCUSSION

The study population comprised “50” patients with electrocardiographic documented “AF” during the period of 2006–2008 in MGM Hospital, Warangal.

Age and Sex Distribution

In our present study, AF was seen more in the patient's age group below 50 years (maximum 31–40 years).

According to Paul Wood and Lip G Y H, Golding D majority of people fibrillated after the age of 50 years.

In anticoagulation and risk factors in AF (ATRIA) study, 45% were aged ≥ 75 years.

In Rotterdam study of prevalence, incidence, and lifetime risk of AF, the prevalence of AF increased with age.

This difference is due to etiological cause of A.F. In our study, rheumatic etiology is common, but in above-mentioned studies HTN and IHD was common etiology.

In ATRIA and Rotterdam study, AF was more common in men than in women (etiological difference).

According to Lok NS and Lan CP, the ratio of female to male is 1.8: 1. In our study, the sex ratio of female to male is 1.2:1; showing female preponderance.

The common cause of AF in women, 50 years are RHD and common causes for AF in males, 50 years are non-rheumatic. This is collaborated with other studies.

Clinical Presentation

In the present study, dyspnea (88%) and palpitations (80%) were the most common presentation and stroke was observed in 14% cases.

The symptoms are of longer duration in rheumatic etiology and shorter duration in other causes.

In ALFA study by S. Levy, M. Marek, and L. Gulze in France (clinical presentation and underlying conditions in AF), palpitations (79%) were common presentation.

In Lok Ns and Lau CP study, dyspnea (38.1%) and palpitations (42.3%) were the most common presentation.

In S.S. Das, S.N. Dutta palpitations (90%), effort intolerance (82%), angina (60%), heart failure (28%), and stroke (15%) were observed.

Etiological Incidence

There is a significant variation in the incidence of various causes between the first five studies and the last two studies Table 7.

The RHD is the most common cause of AF in our country whereas in west IHD and HTN are the most common cause.

Table 7: Etiological incidence of chronic A.F. by various authors

Author	Number of cases	RHD%	IHD %	HTN %	Others %
Kannel <i>et al.</i> (Framingham study 1982)	98	17	10	47	-
Hinton <i>et al.</i> 1977	333	30	51	10	10
Hansberg	642	14.8	13.4	47.5	24.3
Lok NS and Lau CP	291	17.5	-	28.9	-
Lib Gy and Golding DJ	111	-	28.8	36.9	-
Raman TK (Madras)	100	58	33	3	6
S. Sharma and S. Joshi (New Delhi)	70	60	24	4.2	11.8
Present study	50	52	14	10	24

IHD: Ischemic heart disease, RHD: Rheumatic heart disease, HTN: Hypertension,

According to ICMR research report, the national incidence of RHD is 6/1000 population. Hospital-based studies from all over India show RHD ranging from 26.6 to 60 (average 40).

Valvular Affection in RHD with AF

In our present study, AF in RHD occurred in 34.6% of patients with isolated MS and 11.5% of patients with isolated MR.

Combination lesions (26.9%) in MS + MR, 7.6% in MS + MR + AR, 7.6% in MS + MR, and 3.8% in MR + AR.

In Dicker E study, 29% of patients were with isolated MS and 16% of patients were with isolated MR. In our study, combination of the lesion is common.

MVA in RHD Associated with MS

In our present study, MVA ranges from 0.4 to 2.8 cm².

Most of the cases of AF associated with MVA is <1 mm² (severe).

Isolated MS have less MVA as comparatively associated with other valvular lesions.

Left Atrial Size

In our present study, LA size ranged from 3 cm to 7–8 cm. In most of the cases, the LA size between 4 and 5 cm (56%).

Large LA commonly associated with regurgitations (MR).

In the study of left atrial diameter in AF, echo study (Stroke Prevention in Atrial Fibrillation investigations) DiHrich HC, Pearce LA, and A Singer RW, the mean left atrial diameter was 47 ± 8 mm an average 6 mm larger than with sinus rhythm.

In Høglund C, Rosenhanrg (echo study) of the left atrial size >4–4.5 cm was associated with recurrent intermittent AF.

In the study of WL Henry, J. Morganroth, AS personal, and Clark (relationship between echocardiographically detected left

atrial size and AF). Left atrial dimension >40 mm common in AF, if LA >45 mm – cardioversion unlikely to be successful.

Clots in Cardiac Chambers

In our study of 50 cases, 7 cases have clots in the left Of 7 cases, 6 cases are of rheumatic etiology, in that three cases were of left atrium clot, two cases were of left atrial appendage (LAA) clots, and one case has vegetation over anterior mitral leaflets/posterior mitral leaflets.

Of seven cases, on case in IHD, have a large soft clot in the left ventricle.

Two cases presented with stroke and two cases with infective endocarditis.

In the study of Gleen Davidson and Philip Greenland (about predictors of left atrial thrombus in mitral valve disease in AF), MS patients with AF had a preponderance of the left atrial thrombus of 18%. MS with sinus rhythm had 2.4% ± 3.3% preponderance of the left atrial thrombus. In MR with AF, the preponderance of the left atrial thrombus is 0.7%.

In TEE study of the left atrial body, LAA clot in patients with mitral valve disease in AF by Srimannarayana J; Varma R.S; Sathesh S; and Anil Kumar; left atrial clots were found in 33% of patients with mitral valve disease with AF.

ECG Changes

- In this study, most of the cases shows (60%) tachycardia with ventricular rate >100/min. Ten cases showing ventricular rate >150/min
- RHD Cases showing high ventricular rate, comparative to other causes
- Most of the RHD cases showed RAD and RVH.

HTN cases were showing LVH.

Complications in 50 Cases of A.F.

- In our study, CCF (60%) is the most frequent complication followed by angina (32%)

- Other major complications are stroke (14%), hemoptysis (12%), and infective endocarditis (4%)
- In most of the stroke patients, the etiology was rheumatic
- In lip GU Golding DJ study, the common complications are CCF (30.6%) and stroke (18%).^[17-20]

CONCLUSION

AF due to rheumatic etiology is more common in younger age group, while that due to other causes such as HTN and IHD common in older age. Rheumatic heart disease is the most common cause, followed by ischemic heart disease, HTN, and DCM. Most of the chronic, AF is associated with large left atrial size, 4–5 cm (56%). Chronic AF due to pulmonary disease is most commonly observed in males. Congestive cardiac failure (60%), angina (32%), and embolic stroke (14%) are common complications. Incidence of congestive cardiac failure is high in patients of chronic AF with fast ventricular rate. Incidence of angina is high in patients of chronic AF with fast ventricular rate and old age.

REFERENCES

- Hinton RC, Kistler JP, Fallon JT, Friedlich AL, Fisher CM. Influence of etiology of atrial fibrillation on incidence of systemic embolism. *Am J Cardiol* 1977;40:509-13.
- Falk RH. Etiology and complications of atrial fibrillation: Insights from pathology studies. *Am J Cardiol* 1998;82:10N-17N.
- Acc/AHA/ESC Guidelines; 2006.
- Dulli DA, Stanko H, Levine RL. Atrial fibrillation is associated with severe acute ischemic stroke. *Neuroepidemiology* 2003;22:118-23.
- Anthony D, Toft MD. Thyroid hormone replacement one hormone or two. *N Engl J Med* 1999;345:512-6.
- Aronson RS. Mechanism of arrhythmias in ventricular hypertrophy. *J Cardiovasc Electrophysiol* 1991;2:249-61.
- Mackstaller LL, Alpert JS. Atrial fibrillation: A review of mechanism, etiology, and therapy. *Clin Cardiol* 1997;20:640-50.
- Wyse DG, Waldo AL, DiMarco JP, Domanski MJ, Rosenberg Y, Schron EB, et al. A comparison of rate control and rhythm control in patients with atrial fibrillation. *N Engl J Med* 2002;347:1825-33.
- Echocardiographic predictors of stroke in patients with atrial fibrillation: A prospective study of 1066 patients from 3 clinical trials. *Arch Intern Med* 1998;158:1316-20.
- Camm AJ, Obel OA. Epidemiology and mechanism of atrial fibrillation and atrial flutter. *Am J Cardiol* 1996;78:3-11.
- Bhatia A, Sra J. AF Epidemiology, mechanism, management. *Ind Heart J* 2000;52:120, 164.
- Blomsrom P. Amiodarone in AF. *Acta Med Scand* 1984;216:517.
- Bogun F, Anh D, Kalahasty G, Wissner E, Bou Serhal C, Bazzi R, et al. Misdiagnosis of atrial fibrillation and its clinical consequences. *Am J Med* 2004;117:636-42.
- Cameron A, Schwartz MJ, Kronmal RA, Kosinski AS. CAD in AF CASS registry. *Am J Card* 1988;61:714.
- Petersen P, Godtfredsen J. Atrial fibrillation a review of course and prognosis. *Acta Med Scand* 1984;216:5-9.
- Clari – Kenned- Qynim in AF- *Q J Med* 1922, 16-205.
- Alpert JS, Petersen P, Godtfredsen J. Atrial fibrillation: Natural history, complications, and management. *Annu Rev Med* 1988;39:41-52.
- Davidson E. Afacuse and time of onset. *Arch Intern Med* 1988;149:457-9.
- Simpson MA. *Davidsons Principles and Practice of Medicine*. 19th ed. Edinburgh: Churchill Livingstone; 2003.
- Diker E, Aydogdu S, Ozdemir M, Kural T, Polat K, Cehreli S, et al. Prevalence and predictors of atrial fibrillation in rheumatic valvular heart disease. *Am J Cardiol* 1996;77:96-8.

How to cite this article: Reddy CM, Srinivas B. Etiological and Clinical Study of Atrial Fibrillation. *Int J Sci Stud* 2019;7(5):76-80.

Source of Support: Nil, **Conflict of Interest:** None declared.

Clinical Study of Diagnostic Hysteroscopy in Abnormal Uterine Bleeding and its Histopathological Correlation

P Padmaja, P Deepa

Assistant Professor, Department of Obstetrics and Gynecology, Government Maternity Hospital, Kakatiya Medical College, Warangal, Telangana, India

Abstract

Background: Abnormal uterine bleeding (AUB) is the most common complaint in gynecology and an important source of morbidity. It may be evaluated by hysteroscopy or by dilatation and curettage.

Materials and Methods: Between January 2015 and August 2016, 50 patients with AUB who got admitted at MNR Medical College in the Department of Obstetrics and Gynaecology were subjected to panoramic hysteroscopy and subsequent dilatation and curettage. Data were collected and analyzed.

Results: AUB was more common in 30–39 years. The most common presenting complaint was menorrhagia. Negative hysteroscopic view was seen in 54% of cases. Abnormalities seen were endometrial hyperplasia, polyps, submucous myoma, and endometrial atrophy. Both hysteroscopy and curettage were accurate when an abnormality was diagnosed, giving a specificity of 96.15% and positive predictive value of 96.65%. However, the ability to diagnose a lesion (sensitivity) was more with hysteroscopy in comparison to curettage (91.66 vs. 79.16). Forty-one patients (82%) had the same tissue diagnosis in both hysteroscopy and curettage. Hysteroscopy revealed more information than curettage in 12% and curettage had more information in 6% of cases.

Conclusion: This study confirms the conclusion of many others that hysteroscopy is superior to dilatation and curettage in evaluating patients with AUB.

Key words: Abnormal uterine bleeding, Dilatation and curettage, Hysteroscopy

INTRODUCTION

Although uterine bleeding is a normal physiologic episodic occurrence for most women, its characteristics nevertheless vary considerably. The broad range of normal variation causes difficulty in identifying abnormal patterns. The problem is that uterine bleeding has a wide range of diagnostic possibilities, and confusion is generated when review and reports fail to outline the diagnostic evaluation of the patient who presents with abnormal uterine bleeding (AUB) patterns.

Goals of clinical management are primarily dependent on attaining a correct etiological diagnosis. The patient

history and physical and pelvic examinations attempt to determine the site of the bleeding and its source. Information gathered from this will suggest what direction the investigation would take. Traditionally, dilatation and curettage and ultrasonography were the most common investigations employed in the evaluation of the causes of AUB.^[1]

Ultrasonography, though it can determine and confirm the presence or absence of pelvic pathology; determine size, texture, and contour of the lesion; and establish the origin and anatomic relationship of lesion with other pelvic structures and the status of the ovary, fails to provide adequate information regarding the endometrium.

Dilatation and curettage is a blind procedure, mainly diagnostic, useful in AUB to study the hormonal pattern causing abnormal bleeding. The endometrial sample collected is sent to the pathologist to study the histological pattern.

Access this article online



www.ijss-sn.com

Month of Submission : 06-2019
Month of Peer Review : 07-2019
Month of Acceptance : 08-2019
Month of Publishing : 08-2019

Corresponding Author: Dr. P Padmaja, H. No 35-6-771, Gopalpur, TV Tower Colony, Hanmkonda, Warangal - 506 009, Telangana, India.

Hysteroscopy is the inspection of the uterine cavity by endoscopy. It allows the diagnosis of intrauterine pathologies such as endometrial hyperplasia and early diagnosis of endometrial carcinoma and uterine polyps. It also serves as a method for surgical intervention (operative hysteroscopy) for various gynecological conditions such as submucous myoma, intrauterine adhesions, septa, and corneal and interstitial tubal obstruction.

AUB has been used to cover all forms of abnormal bleeding for which an organic cause cannot be found. It is one of the most common complaints with which a patient presents to a gynecologist. Dilation and curettage (D and C) has long been the diagnostic test for AUB. However, endometrial polyps and submucous fibroids are frequently undetected by curettage alone.^[1-8]

The judicious use of hysteroscopy to manage this medical entity adds a new dimension in handling this often perplexing problem. This study has been taken up to analyze the place of hysteroscopy in the evaluation of AUB in terms of accuracy of hysteroscopic findings and the contribution of the procedure to clinical diagnosis. It also aims to correlate hysteroscopic findings with histopathological results.

Aims and Objectives of the Study

The aim of the study is to evaluate the role of hysteroscopy in the diagnosis of cases with AUB and its correlation with histopathological findings.

MATERIALS AND METHODS

Source of Data

The present study “a clinical study of diagnostic hysteroscopy in abnormal uterine bleeding and its histopathological correlation” is a prospective study, which has been carried out in the Department of Obstetrics and Gynecology, Kakatiya Medical College and C.K.M Hospital, Warangal.

The material for the present study was collected from patients who attended and were admitted in the Department of Obstetrics and Gynecology with AUB. Fifty consecutive cases of AUB were taken up for the study. All the patients in this study underwent hysteroscopy, followed by dilatation and curettage, and the curettings were sent for histopathology analysis.

The period of the study was from 2014 to 2016; the results of hysteroscopy and endometrial histopathology were studied and analyzed. The analyzed data were compared with other series in literature and discussed. A master chart dealing with all aspects has been designed and presented.

All patients were well informed about the study in all aspects, and informed written consent was obtained.

Method of Collection of Data

Inclusion criteria

1. Patients with age between 20 and 60 years with AUB
2. Both parous and nulliparous women
3. Patients who do not require any emergency management.

Exclusion criteria

1. Patients with severe anemia due to menorrhagia were excluded since they required immediate intensive care
2. Patients with profuse bleeding
3. Cases with large or multiple fibroids
4. Infection in the uterine tract
5. Cases of cervical carcinoma.

Cases were selected by diagnosis on history, general physical examination, abdomen and pelvic examination, and routine investigations. Pro forma specially made for the study was used.

Patients were advised to have a light dinner before 10 pm on the night prior to hysteroscopy. The patients were prepared as for any other surgical procedure.

RESULTS

In the present study, panoramic hysteroscopy was performed using a 4 mm hysteroscope with 30° for oblique lens (Kalelkar, India) in 50 patients who presented with AUB, followed by dilatation and curettage. The curetted endometrium was sent for histopathological analysis.

In the present study, the maximum age incidence was from 30 to 39 (20 patients, 40%). The youngest patient in this study was 24 years old and the oldest was 60 years old.

Of the 50 patients, majority of the patients, i.e., 21 (42%), had symptoms for more than 1 year, 15 patients (30%) had symptoms for 6 months–1 year, and 14 patients (28%) had symptoms for <6 months.

Majority of the patients, i.e., 23 (46%), presented with menorrhagia. The second most common group had post-menopausal bleeding (16 cases, 32%). There were 6 cases (12%) with polymenorrhagia and 5 patients (10%) with metrorrhagia.

Of the 50 patients, 28 cases (56%) were multipara, 19 cases (38%) were grand multi, and 3 cases (6%) were nulliparity.

Abnormal findings were seen in 23 patients (46%), while in the remaining 27 patients (54%), no abnormality was detected (negative hysteroscopic view) [Tables 1-5].

The most common abnormality was endometrial hyperplasia (10 cases, 20%), followed by endometrial polyps (7 cases, 14%). There were also 2 cases (4%) of submucous myomas, 3 cases (6%) of endometrial hypertrophy, and 1 case (2%) of endometritis.

The most common abnormality was endometrial hyperplasia (10 cases, 20%), followed by endometrial polyps (7 cases, 14%). There were also 2 cases (4%) of submucous myomas, 3 cases (6%) of endometrial hypertrophy, and 1 case (2%) of endometritis.

The most common abnormality was endometrial hyperplasia (10 cases, 20%), followed by endometrial polyps (7 cases, 14%). There were also 2 cases (4%) of submucous myomas, 3 cases (6%) of endometrial hypertrophy, and 1 case (2%) of endometritis.

Of the 30 normal cases (60%) reported, 5 cases had abnormal findings. The diagnosis of 4 cases of endometrial polyps and 1 case of submucous myoma was missed by endometrial histopathology.

Histopathology correctly diagnosed all cases of endometrial hyperplasia (10 cases, 20%), atrophic endometrium (4 cases, 8%), endometritis (1 case, 2%), and irregular ripening (1 case, 2%) with 100% accuracy.

Both hysteroscopy and curettage were accurate when an abnormality was diagnosed, giving a specificity of 96.15 and positive predictive value (PPV) of 95.65 (for both).

The ability to diagnose a lesion (sensitivity) was more with hysteroscopy in comparison to curettage (91.66 vs. 79.16), while a negative diagnosis was less wrongly made with hysteroscopy (false-negative ratio: 8.33% vs. 20.83%).

Of the 50 patients who underwent hysteroscopy and dilatation and curettage, 41 patients (82%) had the same tissue diagnosis in both hysteroscopy and curettage. Hysteroscopy revealed more information than curettage in 6 cases (12%), and curettage had more information in only 3 cases (6%).

Five cases who presented with post-menopausal bleeding were on hormone replacement therapy.

Complications among Patients Noted Postoperatively

- Vomiting: 10 cases
- Bleeding: 2 cases
- Infection: 0
- Perforation: 0.

There was no procedure-related mortality in this study.

DISCUSSION

In the present study, “a clinical study of diagnostic hysteroscopy in abnormal uterine bleeding and its histopathological correlation,” diagnostic hysteroscopy was performed in 50 consecutive cases of AUB and its correlation with histopathological findings was sought.

The age group in this study was between 20 and 60 years, and the maximum incidence was between 30 and 39 years. Panda *et al.*^[2] found that the maximum age incidence was between 35 and 45 years in range between 25 and 70 years. In Gianninoto *et al.*^[3] series, the age range was 38–80 years and the most common incidence was between 30 and 45 years. van Trotsenburg *et al.*^[4] reported the maximum age incidence between 41 and 50 years.

Table 1: Age incidence

Age group	Number of patients	Percentage
20–29	2	4
30–39	20	40
40–49	18	36
50–60	10	20

Table 2: Duration of symptoms

Duration	Number of patients	Percentage
<6 months	14	28
6 m–1 year	15	30
>1 year	21	42

Table 3: Clinical presentation

Presentation	Number of patients	Percentage
Menorrhagia	23	46
Polymenorrhea	6	12
Metrorrhagia	5	10
Post-menopausal bleeding	16	32

Table 4: Parity

Parity	Number of patients	Percentage
Nulliparous	3	6
Multiparous	28	56
Grand multi	19	38

Table 5: Findings at hysteroscopy

Findings	Number of patients	Percentage
Normal	27	54
Endometrial hyperplasia	10	20
Endometrial polyps	7	14
Submucous myoma	2	4
Endometrial atrophy	3	6
Endometritis	1	2

The most common presenting complaint in this series was menorrhagia (46%), followed by post-menopausal bleeding (32%) and polymenorrhea (12%). Panda *et al.*^[2] series had 60% cases of menorrhagia, followed by polymenorrhagia and metrorrhagia.

In this study, abnormal findings on hysteroscopy were found in 23 patients (46%), while in the remaining 27 patients (54%), no abnormality was detected.

The following Table 6 compares normal and abnormal findings in hysteroscopy in various series:

Of the 23 cases with abnormal findings on hysteroscopy, the most commonly seen was endometrial hyperplasia (10 cases, 20%), followed by endometrial polyps (7 cases, 14%) and submucous myoma (2 cases, 4%). Panda *et al.*^[2] found endometrial hyperplasia in 28.3%; Wamsteker^[5] found endometrial polyp in 19%, endometrial hyperplasia in 12.2%, and submucous myoma in 7.8%; van Trotsenburg *et al.*^[4] observed myomas and polyps in 14%; and de Wit *et al.*^[6] reported myomas in 21% and polyps in 14.4%.

Hysteroscopy diagnosed all cases of endometrial hyperplasia, polyps, and myomas with a specificity of 100%. Sheth *et al.*^[7] reported 81.8% accuracy in the diagnosis of polyps and myomas, while Garuti *et al.*^[8] reported 95.4% specificity in the diagnosis of polyps.

In the present study, hysteroscopy made a false-positive diagnosis of endometritis in 1 case and missed the diagnosis of 1 case each of endometrial atrophy and endometritis.

The accuracy of hysteroscopy in this study was 94% and that of endometrial histopathology was 88%.

A comparison of the accuracy with other similar studies is given Table 7:

A statistical analysis of the accuracy obtained by various authors and of the present study shows that there is no significant difference between the values.

Statistical Analysis of Sensitivity and Specificity of Hysteroscopy

There is no significant difference between sensitivity and specificity obtained in this study and that obtained by various other authors. This confirms the validity of hysteroscopy done in the present study.

A comparison of sensitivity and specificity of D and C obtained in the present study with those obtained by other authors shows no significant difference between the obtained values.

In the present study, the results of hysteroscopy and dilatation and curettage were in agreement in 82% of patients; hysteroscopy revealed more information than curettage in 12% and curettage revealed more information than hysteroscopy in 6% of patients [Tables 8-10].

This is comparable to another similar study which shows that panoramic hysteroscopy is better than curettage in the evaluation of AUB.

Summary

- Fifty patients who presented with AUB underwent panoramic hysteroscopy and subsequent dilatation and curettage
- Cured endometrium was sent for histopathological examination
- Age group of the patients ranged from 20 to 60 years, and the most common age group was 30–39 years (40%)
- Most of the patients (42%) had symptoms for more than 1 year, and the most common presenting symptom was menorrhagia (46%) and post-menopausal bleeding (32%)
- Hysteroscopy reported 27 patients (54%) as negative view and 23 patients (46%) as abnormal view
- Endometrial hyperplasia (20%) was the most common abnormality, followed by endometrial polyp (14%)
- The sensitivity, specificity, negative predictive value (NPV), and PPV for hysteroscopy were 91.66%, 96.15%, 92.59%, and 95.65%, respectively, and for D and C were 79.16%, 96.15%, 83.33%, and 95.65%, respectively
- The most consistent finding has been the detection of endometrial hyperplasia, endometrial polyp, and submucous myomas with 100% accuracy using hysteroscopy
- By hysteroscopy, there were 2 false-negative results: 1 case each of endometrial atrophy and endometritis and a false positive result of 1 case of endometritis

Table 6: Normal and abnormal findings at hysteroscopy in various series

Author (year)	Number of cases	Normal (%)	Abnormal (%)
Wamsteker (1984)	199	41.5	58.5
Gimpelson and Rappold (1988)	276	60	40
Loffer (1989)	91	48.66	51.44
Sheth (1990)	51	44	56
Parasnis (1992)	96	73.95	26.05
Neumann (1994)	85	55.2	44.8
Panda (1999)	66	46.6	53.4
Trotsenburg (2000)	819	66	34
Garuti (2001)	1500	61.8	38.2
Gianninoto (2003)	512	25	75
de Wit AC (2003)	1045	54.2	45.8
Present series	50	54	46

Table 7: Comparison of accuracy of hysteroscopy findings

Author	Accuracy	Misinterpretation
Baggish (1979)	87.5	12.5
Barbot (1980)	84	16
Sheth (1990)	82	18
Parasnis (1992)	92	8
Panda (1999)	92.69	7.31
Present series	94	6

Test used: F test $P=1>0.05$ NS

Table 8: Comparison of validity factors- hysteroscopy

Author	Sensitivity	Specificity
Loverro (1996)	98	95
Garuti (2001)	94.2	88.8
Loffer (1989)	98	100
Parasnis (1992)	92	100
Panda (1999)	92.5	78.78
Present series	91.66	96.15

Test used: F test $P=0.2688>0.05$ NS

Table 9: Comparison of validity factors - dilatation and curettage

Author	Sensitivity	Specificity
Loverro (1996)	79.2	95
Garuti (2001)	78	94
Loffer (1989)	65	100
Parasnis (1992)	76	100
Present series	79.16	96.15

Test used: F test $P=0.9962>0.05$ NS

Table 10: Panoramic hysteroscopy versus curettage

Results	Gimpelson and Rappold (1988)	Gimpelson (1984)	present series
Panoramic hysteroscopy equal to curettage	79	73	82
Hysteroscopy greater than curettage	18	24	12
Hysteroscopy less than curettage	3	3	6

Test used: F test $P=1>0.05$ NS

- Histopathology of endometrium missed 4 cases of endometrial polyps and 1 case of submucous myoma and gave a false-positive report of 1 case of endometrial atrophy
- D and C correctly diagnosed all cases of endometrial hyperplasia (10 cases), endometrial atrophy (4 cases), endometritis (1 case), and irregular ripening (1 case)
- In the present study, in 82% of patients, the results of

hysteroscopy and curettage were in agreement

- Hysteroscopy revealed more information than curettage in 12% and curettage revealed more information than hysteroscopy in 6% of cases
- Complications among patients noted postoperatively Vomiting: 10 cases, bleeding: 2 cases, infection: 0, and perforation: 0
- There was no procedure-related mortality in this study.

CONCLUSION

- This study confirms that hysteroscopy is superior to curettage in evaluating patients with AUB
- Hysteroscopy is a safe, reliable, and quick procedure in the diagnosis of cases with AUB with high sensitivity, specificity, and NPV
- The concern of today's gynecologist while evaluating AUB is not to miss a significant cancerous lesion. The chances that such a lesion would be missed are rare, if we stick to the criteria for negative hysteroscopic view, and usually, no further investigation may be necessary.

It would be prudent to obtain endometrial tissue for histopathological examination, especially in peri- or post-menopausal patients in spite of negative hysteroscopic view.

REFERENCES

- Jones HW 3rd, Rock JA. Operative hysteroscopy. In: TeLinde's Operative Gynecology. 11th ed. Ch. 18. Philadelphia, PA: Wolters Kluwer; 2015. p. 307-36.
- Panda A, Parulekar SV, Gupta A. Diagnostic hysteroscopy in abnormal uterine bleeding and its histopathological correlation. J ObstGyn India 1999;175:74-6.
- Gianninoto A, Morana C, Campione C. Diagnostic hysteroscopy in abnormal uterine bleeding. Five-years' experience. Minerva Ginecol 2003;55:57-61.
- van Trotsenburg M, Wieser F, Nagele F. Diagnostic hysteroscopy for the investigation of abnormal uterine bleeding in premenopausal patients. Contrib Gynecol Obstet 2000;20:21-6.
- Wamsteker K. Hysteroscopy in the management of abnormal uterine bleeding in 199 patients. In: Siegler AM, Lindemann HJ, editors. Hysteroscopy: Principles and Practice. Philadelphia, PA: JB Lippincott; 1984. p. 128-131.
- de Wit AC, Vleugels MP, de Kruif JH. Diagnostic hysteroscopy: A valuable diagnostic tool in the diagnosis of structural intra-cavitary pathology and endometrial hyperplasia or carcinoma? six years of experience with non-clinical diagnostic hysteroscopy. Eur J Obstet Gynecol Reprod Biol 2003;110:79-82.
- Sheth SS, Nerurkar NM, Mangeshkar PS. Hysteroscopy in abnormal uterine bleeding. J Obstet Gyn India 1990;40:451.
- Garuti G, Sambruni I, Colonnelli M, Luerti M. Accuracy of hysteroscopy in predicting histopathology of endometrium in 1500 women. J Am Assoc Gynecol Laparosc 2001;8:207-13.

How to cite this article: Padmaja P, Deepa P. Clinical Study of Diagnostic Hysteroscopy in Abnormal Uterine Bleeding and its Histopathological Correlation. Int J Sci Stud 2019;7(5):81-85.

Source of Support: Nil, **Conflict of Interest:** None declared.

A Study of Catheter Ablation versus Medical Management in Post-Myocardial Infarction Scar Ventricular Tachycardia Patients

C Mamatha Reddy¹, Bingi Srinivas²

¹Assistant Professor, Department of Cardiology, Kakatiya Medical College, Mahatma Gandhi Memorial Hospital, Warangal, Telangana, India,
²Assistant professor, Department of Medicine, Kakatiya Medical College, Mahatma Gandhi Memorial Hospital, Warangal, Telangana, India

Abstract

Introduction: Sudden cardiac death accounts for approximately 50% of all cardiac deaths, representing an estimated annual incidence ranging from 250,000 to 350,000 cases in the United States.

Materials and Methods: The objective of this study is to compare patients amiodarone plus substrate-based ventricular tachycardia (VT) ablation to amiodarone (usual therapy) for all-cause mortality, including cardiac arrest and sustained VT, in patients with recurrent VT post-myocardial infarction who have survived a life-threatening VT/ventricular fibrillation event (that is, AVID/CASH/CIDS criteria) but cannot afford an implantable defibrillator.

Results: The study group was divided into RFA YES (ablated for recurrent VT and on amiodarone) and RFA NO group (only on amiodarone).

Key words: Catheter ablation, Mortality, Tachycardia

INTRODUCTION

Sudden cardiac death (SCD) accounts for approximately 50% of all cardiac deaths, representing an estimated annual incidence ranging from 250,000 to 350,000 cases in the United States. The pathophysiologic mechanism for sudden death in the majority of these patients is thought to be ventricular tachycardia (VT) related to coronary artery disease (CAD), which can then degenerate to ventricular fibrillation (VF). Patients who survive an initial episode of VT/VF are prone to an extremely high incidence of recurrent life-threatening events (~25% at 1 year). Even in patients without a history of VT/VF, the presence of CAD and left ventricular (LV) dysfunction confers a 2-year mortality rate of 22%. If VT is inducible at electrophysiological testing, the 2-year mortality is ~30%.

MATERIALS AND METHODS

Objective

The objective of this study is to compare patients amiodarone plus substrate-based VT ablation to amiodarone (usual therapy) for all-cause mortality, including cardiac arrest and sustained VT, in patients with recurrent VT post-myocardial infarction (MI) who have survived a life-threatening VT/VF event (that is, AVID/CASH/CIDS criteria) but cannot afford an implantable defibrillator.

Endpoints

Primary endpoint

The primary endpoint of this study is freedom from all-cause mortality, sustained VT and cardiac arrest, at 24 months.

Secondary endpoints

The secondary endpoints in this study are as follows:

1. Proportion of subjects that die within 30 days or die by 24 months
2. Total number of ventricular arrhythmic events compared between the two treatments
3. Differences in LV ejection fraction (EF) between paired measurements recorded at baseline and

Access this article online



www.ijss-sn.com

Month of Submission : 06-2019
Month of Peer Review : 07-2019
Month of Acceptance : 08-2019
Month of Publishing : 08-2019

Corresponding Author: Dr. Bingi Srinivas, Flat no 301, Balaji residency, OPP OLD RTA office, Nayeemnagar, Hanmakonda, Warangal 506009, Telangana, India

6 months, 12 months for each patient will be used to test for significant differences between the two treatments.

Study Design

This was a prospective observational study.

Setting

Tertiary Cardiac Center.

Study Duration

The study was from December 2011 to December 2013 (24 months).

Number of Patients

Fifty patients with post-MI scar VT were participated in the study.

The study group is post-MI patients who have survived a recent VT/VF episode, thereby mandating implantable cardioverter-defibrillator (ICD) implantation. However, these patients are unable to afford an ICD and thus would receive medical therapy with chronic amiodarone therapy. This study will compare chronic amiodarone therapy alone and catheter ablation + chronic amiodarone therapy.

Follow-up will be conducted in regular intervals over a 24-month period.

Inclusion Criteria

Candidates will be included in the study of all of the following conditions apply.

1. ≥ 18 and ≤ 85 years of age
2. History of a remote MI (≥ 1 month)
3. Survival of a ventricular arrhythmic event (VT/VF) that would mandate placement of an ICD
4. Patient cannot afford an ICD and thus has been planned for treatment with amiodarone.

Exclusion Criteria

Candidates will be excluded from the study if any of the following conditions apply.

1. Patients with NYHA Class IV congestive heart failure
2. Presence of an LV thrombus
3. Contraindication to anticoagulation
4. Inability to access the endocardium due to mechanical mitral and aortic valve
5. Life expectancy < 1 year for any medical condition.

Methods

Ablation procedure

- Patient anesthesia will be administered according to standard electrophysiology (EP) laboratory protocol. Arterial and venous access will be achieved

through cannulation of the right and/or left femoral arteries and veins as determined by the treating electrophysiologist.

- EP study will be performed using up to triple ventricular extrastimuli from the right ventricular or LV in standard fashion. Before VT is deemed non-inducible, the following stimulation attempts must be performed: (i) Stimulation at ≥ 2 ventricular sites (e.g., right ventricular [RV] apex + RV outflow tract, or RV apex + LV), (ii) stimulation at ≥ 2 drive cycle lengths, and (iii) triple extrastimuli. Of course, if VT is inducible early in the stimulation protocol, the remaining protocol does not need to be completed if deemed inappropriate from a safety perspective.
- Twelve-lead electrocardiograms will be obtained for all inducible ventricular arrhythmias. An inducible sustained VT is defined as a monomorphic VT lasting > 15 s or requiring termination with pacing or cardioversion.
- To minimize the chance of post-procedural pulmonary edema, the fluid status (I/O, left atrial pressure if a transseptal sheath is employed, etc.) must be carefully monitored. Furthermore, a Foley urinary catheter is strongly recommended for patients with an LVEF $< 25\%$ or a clinical history of Class III congestive heart failure. Hemodynamic support and type of sedation are at the discretion.

RESULTS

- Over the course of 24 months, 50 patients of post-MI with scar VT enrolled.
- The study group was divided into RFA YES (ablated for recurrent VT and on amiodarone) and RFA NO group (only on amiodarone).
- All patients whose VT was scar related and consequent on a previous MI were included in the study. Patients were not enrolled within 30 days of a MI.
- Patients are followed at 3, 6, 9, 12, 18, and 24 months along with ER room presentation.
- The mean age of the patients was 53 years and 96% were male.
- MI was localized to inferior wall MI in 52% and 48% anterior wall MI.
- Of 50 patients with post-MI scar VT – 16% presented with palpitations, 14% with syncope, 14% shortness of breath, and 6% with congestive heart failure.
- The qualifying index arrhythmia was sustained monomorphic VT in 95%, inducible VT in 5%.
- About 5% of them were in NYHA Class I, 37% in NYHA Class II, and 8% in NYHA Class III at the initial presentation.
- The baseline EF was 39%.

- Patients were being treated with antiarrhythmic drug amiodarone, and most patients received antiplatelet drugs, beta-blockers, and angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers and statins.
- The two groups were well balanced with respect to baseline demographic and clinical characteristics.

Analysis

- Twenty-four underwent percutaneous and 12 surgical revascularizations before VT ablation. Following revascularization, patients were only enrolled following further documentation of spontaneous or inducible VT.
- Before radiofrequency ablation, all patients were investigated to exclude dynamic ischemic contributors to their arrhythmias including coronary angiography in 100%, echocardiogram in 100%, and functional assessments of ischemia in 20%. Twenty-two patients were enrolled under ablation group and during the ablation procedure, only one had pericardial effusion without tamponade, which was managed conservatively; one had an exacerbation of congestive heart failure requiring prolonged hospitalization and cardiac resynchronization therapy pacemaker was placed in this patient. One patient was ablated twice and presented with recurrent VT; ICD was placed for this patient. Three patients in drug group (RFA NO group) were crossover to ablation group (RFA YES group) due to recurrent episodes of VTs.
- All surviving patients completed the 2-year follow-up except the two who were in RFA NO group one lost to follow-up and other preferred ICD.
- The mean duration of follow-up was 22.5 (range, 0–26). During follow-up, all patients received antiarrhythmic drug amiodarone, and most patients received antiplatelet drugs, beta-blockers, and ACE inhibitors or angiotensin receptor blockers.
- In 2 years of follow-up, number of episodes of VT recurrences, EFs in both groups compared with baseline, mortality is compared between groups.
- At 3 months, 6 patients (22%) of those who did not undergo RFA (only on amiodarone, RFA NO group) presented with VT which was higher than those with RFA YES group and is statistically significant.
- During 6 months of follow-up, 7 patients (25.9%) in RFA NO group and 1 (4.5%) patient from RFA YES group had VT episodes ($P = 0.059$).
- During 12 months of follow-up, 5 (18.5%) patients in RFA NO group and 3 patients (13.6%) in RFA YES group had VT episodes ($P = 0.715$).
- During 24 months of follow-up, 5 (20%) patients in RFA NO group and 1 patient (4.5%) in RFA YES group had VT episodes ($P = 0.194$).

Mortality

- There were totally four deaths. One patient died of hepatic encephalopathy, one had SCD, one causes of death unknown, and one with CHF.
- There was one death in RFA YES group. Three deaths in RFA NO group ($P = 0.611$).

Ejection Fraction

- In RFA YES group, comparing baseline EF with EF at 12 months ($P = 0.05$), with EF at 24 months ($P = 0.935$), and EF at 12 months–24 months ($P = 0.004$).
- In RFA NO group, comparing baseline EF with EF at 12 months ($P = 0.229$), EF at 24 months ($P = 0.049$), EF at 12 months–24 months ($P = 0.003$).
- These results show that there is preserved EF in RFA YES group and no such preservation of EF in RFA NO group.
- Our study was initiated to objectively examine the use of substrate ablation in patients with a previous MI who were unable to afford an ICD for the secondary prevention of sudden death and chosen ablation as alternative mode of treatment which is cost effective.
- As compared with the RFA NO group, patients in the ablation group had a significant reduction in the number of VT episodes and preserved EF during the subsequent 2-year follow-up, and ablation procedure is safe.

DISCUSSION

- VT is a common complication of ischemic heart disease, with significant associated morbidity and mortality. The use of antiarrhythmic medications (AADs) to suppress the occurrence/recurrence of VT/VF in high-risk patients has been mostly disappointing. In large clinical trials, most AADs have not only proved to be inefficacious but also to actually increase mortality.^[1-7]
- The one potential exception appears to be amiodarone: One study suggests some mortality benefit (GESICA), while others suggest that amiodarone provides significant antiarrhythmic benefits without a change in mortality (EMIAT, CAMIAT, and SCD-HeFT). However, even the use of amiodarone is plagued with multiple organ toxicities, ranging from pulmonary fibrosis to hepatitis, and thyroid dysfunction.^[8]
- An important alternative to such questionably efficacious antiarrhythmics is the ICD, which can accurately and effectively detect and terminate VT/VF, resulting in a significant mortality benefit in both the primary and secondary prevention of SCD.^[9]
- Yet, despite these beneficial results, ICD implantation cannot be considered a cure for VT. Spontaneous VT episodes are associated with increased mortality

even if arrhythmia is treated with ICD. In addition, it is common for patients to experience painful high-voltage shocks secondary to recurrent ventricular arrhythmias or to lose consciousness before the delivery of therapy. Moreover, the considerable cost of ICDs severely limits their availability in the developing world – where public and/or private health insurance systems are rudimentary at best, and where the incidence of CAD is 4 times higher than that of the developed world – highlighting the urgency of establishing an alternative therapy for post-MI patients with ventricular arrhythmias that are both accessible and effective.

- One such option may be catheter ablation of ventricular arrhythmias.
- Catheter ablation of VT currently has an important role in the treatment of incessant VT and reduction of the number of episodes of recurrent VT.
- Conventional mapping techniques require ongoing tachycardia and hemodynamic stability during the procedure. However, in many patients with scar-related VT, non-inducibility of clinical tachycardia, poor induction reproducibility, hemodynamic instability, and multiple VTs with frequent spontaneous changes of morphology preclude tachycardia mapping.
- To overcome these limitations, new strategies for mapping and ablation in sinus rhythm (SR) – substrate mapping strategies – have been developed and are currently used by many centers. The previous studies of catheter ablation performed using a single catheter approach based on conventional activation mapping and pacing techniques, frequently associated with concomitant administration of antiarrhythmic drugs can offer a reasonable rate of success over the long term in patients presenting with recurrent hemodynamically tolerated VT following an MI. It has been shown that the overall sudden death and cardiac death rates reported are comparable to those achieved in patients treated exclusively by an ICD.
- A study was done by O'Donnell *et al.* radiofrequency ablation for post-infarction VT, report of a single-center experience of 112 cases largest consecutive series to date of radiofrequency ablation in the treatment of post-infarction VT patients were studied the mean follow-up period was 61 months.
- During follow-up, VT recurred in 25 patients: 22 after a failed procedure, two following a modified result, and one following a complete success. Twenty-five patients died: 13 of progressive cardiac failure and four of presumed arrhythmic causes, three after a failed procedure, and one following a modified result. There were no procedure-related deaths. Procedural complications occurred in seven patients.
- The results of our study are comparable to Donnell's

series in reducing VT recurrences, but our study has less procedural complications and less overall mortality. About 81% of the cases were performed using only conventional catheters and mapping techniques. In 11% the “CARTO” electroanatomical (Biosense Webster, Diamond Bar, CA, U.S.A.) and in 5% the “Ensite 3000” non-contact and our study with substrate modification technique by CARTO and Navix Thermocool catheter this is the limitation to compare the results.

- The catheter approach to substrate modification relies on electroanatomical mapping systems that create a high fidelity representation of the endocardium, allowing for the reconstruction and electronic manipulation of an endocardial cast of the ventricular chamber that carefully delineates the normal and abnormal tissues.
- This is based on the observation that during normal SR, there are distinguishing characteristics of the endocardial electrogram (EGM) of normal and abnormal tissue: Abnormal tissue manifests a lower voltage amplitude, prolonged EGM duration, and the presence of late and fractionated potentials.
- Marchlinski *et al.* reported in a seminal study that using a substrate-mapping strategy, catheter-based RF ablation lesions directed in a linear fashion were effective in controlling scar-related drug-refractory unstable VT. Marchlinski was acutely successful in eradicating or modifying VT in seven of nine patients with a recurrence in <20%.
- Furthermore, using this high-density electroanatomical mapping, (1) this strategy can be utilized to localize the arrhythmogenic substrate in the majority of patients with a history of MI and sustained ventricular tachyarrhythmias and (2) RF ablation using an irrigated tip ablation catheter can be effectively and safely used to modify the arrhythmogenic substrate to render VT non-inducible even in the presence of multiple VT morphologies.
- Further study of Irrigated Radiofrequency Catheter Ablation Guided by Electroanatomic Mapping for Recurrent VT after MI, the multicenter Thermocool VT Ablation Trial by Stevenson *et al.* showed that catheter ablation is a reasonable option to reduce episodes of recurrent VT in patients with prior MI, even when multiple and/or unmappable VTs are present.
- Catheter ablation of stable VT before defibrillator implantation in patients with coronary heart disease (VTACH): A multicenter randomized controlled trial by Prof Karl Heinz Kuck (VTACH) study was a prospective, open, and randomized controlled trial, undertaken in 16 centers in four European countries. Patients aged 18–80 years. One hundred and ten patients were randomly allocated in a 1:1 ratio to receive catheter ablation and an ICD (ablation group, $n = 54$) or ICD alone (control group, $n = 56$ was

followed up for at least 1 year. The primary endpoint was the time to the first recurrence of VT or VF.

- Mean follow-up was 22.5 months. Time to recurrence of VT or VF was longer in the ablation group (median 18.6 months [lower quartile 2.4 and upper quartile not determinable]) than in the control group (5.9 months [IQR 0.8–26.7]). At 2 years, estimates for survival free from VT or VF were 47% in the ablation group and 29% in the control group.
- Complications related to the ablation procedure occurred in two patients; no deaths occurred within 30 days after ablation. Fifteen device-related complications requiring surgical intervention occurred in 13 patients (ablation group, four; control group, nine). Nine patients died during the study (ablation group, five; control group, four).
- VTACH interpreted that prophylactic VT ablation before defibrillator implantation seemed to prolong time to recurrence of VT in patients with stable VT, previous MI, and reduced LVEF.
- The favorable results of Stevenson *et al.* studies prompted the initiation of substrate mapping and ablation in SR to halt VT trial (SMASH-VT), a prospective randomized clinical trial to objectively assess the clinical utility of substrate ablation of scar-related VT.
- This trial was a randomized-controlled trial examining the role of substrate mapping and RF ablation in the primary prevention of ICD shocks in patients presenting with clinically life-threatening VT/VF. That is, patients with a history of MI, who survive an episode of VT/VF are at high-risk for recurrent VT and thus treated with ICDs (in essence, these patients meet AVID/CIDS/CASH criteria). In normal clinical practice, these patients are not routinely treated with adjuvant medications due to their proarrhythmic potential and side effects. In addition to an ICD and routine clinical care, these patients were additionally randomized in SMASH-VT to substrate-based catheter ablation. This catheter ablation group underwent electroanatomic mapping to delineate the endocardial infarct margins (CARTO, Biosense Webster, Inc.). Substrate modification was then performed targeting the exit sites of induced VTs and/or late potentials within the scar using standard or irrigated radiofrequency ablation catheters.
- As published in late 2007 (Reddy *et al.*, NEJM, 357:2657), the 30-day post-ablation mortality was zero, and there was no significant change in ventricular function or functional class during follow-up. During an average follow-up of 22.5 ± 5.5 months, appropriate defibrillator therapy (anti-tachycardia pacing and shocks) occurred in 21 control (33%) and 8 ablation (12%) patients ($P = 0.007$ by the log-rank test). Of

these, appropriate defibrillator shocks alone occurred in 20 control (31%) and 6 ablation (9%) patients ($P = 0.003$). Mortality was not increased in the ablation arm (control 17%, ablation 9%; $P = 0.29$); indeed, there was a trend to decreased mortality in the ablation arm.

- Thus, the SMASH-VT study revealed that adjuvant substrate-based catheter ablation is feasible and use of a saline-irrigated RF ablation catheter for this ablation strategy is safe, and this strategy decreases subsequent ICD therapies in post-MI patients receiving defibrillators for the secondary prevention of sudden death.
- The favorable results of SMASH-VT and VTACH, Stevenson *et al.* combined with considerable technical and scientific improvements in catheter ablation of scar-related VT, also raise the possibility that the therapeutic benefit of ablation, in post-MI patients who have survived a ventricular arrhythmic event but are unable to afford an ICD.
- Our study intended to evaluate the efficacy of catheter ablation in post-MI patients who have survived a ventricular arrhythmic event and would be initiated on chronic amiodarone therapy due to an inability to afford ICD therapy.
- In our study, the 30-day post-ablation mortality was zero, and there was a significant preservation in ventricular function during follow-up in ablated patients.
- During an average follow-up of 22.5 ± 5.5 months, at 3 months, 6 patients (22%) of those who did not undergo RFA (only on amiodarone RFA NO group) presented with VT which was higher than those with RFA YES group and is statistically significant.
- During 6 months of follow-up, 7 patients (25.9%) in RFA NO group and 1 (4.5%) patient from RFA YES group had VT episodes ($P = 0.059$). During 12 months of follow-up, 5 (18.5%) patients in RFA NO group and 3 patients (13.6%) in RFA YES group had VT episodes ($P = 0.715$). During 24 months of follow-up, 5 (20%) patients in RFA NO group and 1 patient (4.5%) in RFA YES group had VT episodes ($P = 0.194$).
- Mortality was not increased in the ablation group; indeed, there was a trend to decreased mortality in the ablation group ($P = 0.611$).
- Our results are comparable with SMASH-VT and VTACH, and Stevensons *et al.* in reducing the VT recurrences and mortality.

CONCLUSIONS

- At present, radiofrequency ablation for ischemic VT is considered by many only as an adjunct to an ICD in patients with intractable or highly symptomatic VT.
- Our study has shown radiofrequency catheter ablation of patients with highly symptomatic, sustained, monomorphic post-infarction VT which can be

performed with high success rate and low procedural complication rate. The procedure can be successfully applied to a wide spectrum of patients including multiple morphologies of VT and hemodynamically unstable VT.

- With the results demonstrated in this study, procedural success of ablation could obviate the need for ICD implantation.
- These findings may expand the role of radiofrequency ablation, making it the therapy of first choice in a growing proportion of patients who cannot afford ICD, with ICDs reserved as the treatment for failed ablation procedures or for prophylactic indications.
- A definite statement of whether catheter ablation and antiarrhythmic drug (amiodarone) treatment can be used as an alternative to ICD in this subgroup of patients and, however, cannot be made until firmly proven by a dedicated study.

REFERENCES

1. Cardiac Arrhythmia Suppression Trial (CAST) Investigators. Preliminary report: Effect of encainide and flecainide on mortality in a randomized

trial of arrhythmia suppression after myocardial infarction. *N Engl J Med* 1989;321:406-12.

2. Cardiac Arrhythmia Suppression Trial II Investigators. Effect of the antiarrhythmic agent moricizine on survival after myocardial infarction. *N Engl J Med* 1992;327:227-33.
3. Coplen SE, Antman EM, Berlin JA, Hewitt P, Chalmers TC. Efficacy and safety of quinidine therapy for maintenance of sinus rhythm after cardio version. A meta-analysis of randomized control trials. *Circulation* 1990;82:1106-16.
4. Moosvi AR, Goldstein S, VanderBrug Medendorp S, Landis JR, Wolfe RA, Leighton R, *et al.* Effect of empiric antiarrhythmic therapy in resuscitated out-of-hospital cardiac arrest victims with coronary artery disease. *Am J Cardiol* 1990;65:1192-7.
5. Stanton MS, Prystowsky EN, Fineberg NS, Miles WM, Zipes DP, Heger JJ, *et al.* Arrhythmogenic effects of antiarrhythmic drugs: A study of 506 patients treated for ventricular tachycardia or fibrillation. *J Am Coll Cardiol* 1989;14:209-15.
6. IMPACT Research Group. International mexiletine and placebo antiarrhythmic coronary trial: Report on arrhythmia and other findings. *J Am Coll Cardiol* 1984;4:1148-63.
7. Teo KK, Yusuf S, Furberg CD. Effects of prophylactic antiarrhythmic drug therapy in acute myocardial infarction. An overview of results from randomized controlled trials. *JAMA* 1993;270:1589-95.
8. Jafari-Fesharaki M, Scheinman MM. Adverse effects of amiodarone. *Pacing Clin Electrophysiol* 1998;21:108-20.
9. Hohnloser SH. Implantable devices versus antiarrhythmic drug therapy in recurrent ventricular tachycardia and ventricular fibrillation. *Am J Cardiol* 1999;84:56-62.

How to cite this article: Reddy CM, Srinivas B. A Study of Catheter Ablation versus Medical Management in Post-Myocardial Infarction Scar Ventricular Tachycardia Patients. *Int J Sci Stud* 2019;7(5):86-91.

Source of Support: Nil, **Conflict of Interest:** None declared.

Observational, Concurrent Study to Assess Safety and Efficacy of Glycopyrronium and Arformoterol Home Nebulization in High-risk, Symptomatic Acute Exacerbation of Chronic Obstructive Pulmonary Disease Cases: SYMPTOM Study

Salil Bendre¹, S Katiyar²

¹Senior Consultant, Department of Chest Medicine, KLS Memorial Hospital, Mumbai, Maharashtra, India, ²Senior Consultant, Department of Pulmonology and Respiratory Medicine, Apollo Spectra Hospital, Kanpur, Uttar Pradesh, India

Abstract

Background: Chronic obstructive pulmonary disease (COPD) is one of the most important reasons for hospitalization worldwide with high 30-day readmission rates. Although the prognostic significance of early readmission is not fully understood, they are often associated with poor outcomes including high mortality rates of 4%–19% at 30 and 365 days, respectively. Similarly, in acute exacerbations of COPD (AECOPD) cases receiving emergency department care, current status on lung function and cardiovascular comorbidities are considered as best predictors for both 30- and 90-day COPD readmission rates. Dual bronchodilator strategy with long-acting muscarinic antagonist (LAMA)/long-acting beta-agonists (LABA) is therefore recommended by GOLD (2019) in the postdischarge phase following an acute exacerbation.

Aim: To further assess the clinical impact of dual bronchodilators including glycopyrronium and arformoterol as home nebulization in the post-discharge phase of AECOPD, the current postapproval, observational study was conducted.

Materials and Methods: An observational, concurrent, and non-inferiority study with glycopyrronium and arformoterol home nebulizing solutions on patients with moderate and severe COPD was conducted at two centers in India. An estimated sample size of 40 patients involving moderate and severe COPD cases was factored for per-protocol analyses with $P < 0.05$ considered as statistically significant. A concurrent study analysis for the follow-up visit was conducted as per the principles of International Conference of Harmonization for Good clinical practice and Declaration of Helsinki while ensuring confidentiality during access of patient support registration sheets.

Results: Per protocol analyses for consecutive 46 cases from two centers receiving Nebulized glycopyrronium (25 mcg) and arformoterol (15 mcg), as separate formulations are given as admixed solution with follow-up visit for at least 4 weeks was carried out. Baseline demographics for the overall group showed exacerbation history (46, 100%), hospitalization for AECOPD (21, 45.6%); ED visit (25, 54.3%), forced expiratory volume in one second (FEV_1) 1.2 ± 0.6 L/min; FEV_1/FVC $64.8\% \pm 10.6$; reversibility $8.4\% \pm 11.8$; CAT 34.6 ± 2.3 ; and vibrating mesh nebulizer (46, 100%). The mean predose FEV_1 (Δ) at the end of 4 weeks for overall, moderate and severe COPD cases were observed as of $9.6 \pm 3.1\%$, $11.8\% \pm 3.1$, and $8.4\% \pm 1.6$, respectively ($P < 0.0001$). Similarly, the mean CAT(Δ) score at the end of 4 weeks was observed as of 18.1 ± 0.69 , 20.6 ± 0.69 , and 18.26 ± 0.6 for overall, moderate and severe COPD cases, respectively ($P < 0.0001$). The intergroup differences for rescue medication use for a lone case with severe COPD (1, 2.04%) complied with the suggested non-inferiority margin between the groups. There were no other treatment-emergent adverse events or serious adverse events that warranted treatment modification or withdrawals in both groups.

Conclusion: Glycopyrronium and arformoterol home nebulization with Vibrating mesh nebulizer (VMN) offers bronchodilation that is clinically significant with successful use of the drugs as “Rescue Medication” in post-discharge high-risk symptomatic AECOPD cases.

Key words: Acute exacerbation of chronic obstructive pulmonary disease, Arformoterol, Glycopyrronium, Home nebulization, High risk COPD, Vibrating mesh nebulizer

Access this article online



www.ijss-sn.com

Month of Submission : 07-2019
Month of Peer Review : 07-2019
Month of Acceptance : 08-2019
Month of Publishing : 08-2019

Corresponding Author: Dr. Salil Bendre, Department of Chest Medicine, KLS Memorial Hospital, Mumbai, Maharashtra, India.
E-mail: studysymptom@gmail.com

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is one of the most important reasons for hospitalization worldwide with 1 in 5 patients readmitted within 30 days. Notwithstanding, the various reasons for the readmission rate including patient adherence to device and formulation use, clinical comorbidities for hypertension, cardiovascular disease (CVD), bronchiectasis, Type 2 diabetes, and high-risk status for prior exacerbations play a pivotal role in above readmission rates for acute exacerbations of COPD (AECOPD) cases. Although the prognostic significance of early readmission is not fully understood, they are often associated with poor outcomes including high mortality rates of 4%–19% at 30 and 365 days, respectively.^[1]

Similarly, in AECOPD cases receiving emergency department (ED) care were often associated higher readmission rates due to the inappropriate therapy received at most of these centers. In a 1-year long retrospective study conducted among AECOPD cases receiving ED care, current status on lung function and cardiovascular comorbidities are considered as best predictors for both 30- and 90-day COPD readmission rates were the best predictors for both 30- and 90-day COPD readmission rates in these cases. Only 50% of the ED group patients received bronchodilators, oral steroids, and antibiotics inclusively, and the need for oral steroids to treat AECOPD predicted future 90-day COPD readmissions in the ED group ($P < 0.003$).^[2]

The 2008 Canadian Thoracic Society guidelines recommend that patients with AECOPD be treated with combined, increased doses of inhaled, short-acting beta-agonists, and an anticholinergic to improve dyspnea and pulmonary function. However, their use as long-term maintenance therapy may be fraught with several challenges including cardiac side effects or tachycardia that may be detrimental particularly in patients with cardiac comorbidities.^[3,4] Moreover, in patients with moderate to severe AECOPD, oral or parental corticosteroids for 7–14 days are recommended. The treatment of AECOPD with systemic corticosteroids has been shown to improve airflow limitations, decrease treatment failure rates, and decrease the risk of relapse.^[5] The GOLD guidelines in this line recommend the use of corticosteroids as maintenance therapy only in cases with elevated sr. eosinophils (≥ 300 cells/ μ L) due to the risk of pneumonia and immunosuppression leading to TB reactivation. In the postdischarge phase following an acute exacerbation, dual bronchodilator strategy with LAMA/LABA is therefore recommended in such cases by GOLD guidelines.^[6]

In most of the high-risk or severe COPD cases, the poor inspiratory flow rate observed is often associated

with related noncompliance toward conventional devices.^[7] In ambulatory patients of COPD, again, poor inspiratory flow rates (<45 L/min) were observed for about 20% cases.^[8] Low peak inspiratory flow rate (PIFR) (<60 L/min), especially in post-discharge settings following an exacerbation, was observed in nearly 31.7% of the patients.^[9]

In a systematic review of randomized controlled trials implementing AECOPD rehospitalization reduction interventions failed to find clinical trials targeting a 30-day readmission outcome, especially when the rehospitalization rates have been as high as 58.4%.^[1] In most of the cases NIV plays a significant role in hypercapnic COPD while delivering oxygen or short-acting bronchodilators including short-acting muscarinic antagonist (SAMA)/short-acting beta2-agonists (SABA) combinations for patient a tune to tidal breathing.

In this line, glycopyrrolate 25 mcg and arformoterol (15 mcg) nebulizing solutions remain as the only US FDA approved formulations for use in clinical practice that may be nebulized in home settings with new generation advanced ultra-compact, noiseless, portable vibrating mesh nebulizers (VMNs) further improving the patient compliance and adherence to therapy that is vital for long-term beneficial outcomes. In both the cases, the long-term studies involving nebulized glycopyrronium and arformoterol have successively highlighted the safety profile of these formulations even when coprescribed with ancillary bronchodilators including beta2-agonists or anticholinergics.^[10]

Aim

To further assess the real-world use and clinical impact of nebulized glycopyrronium 25 and arformoterol 15 mcg given as separate formulation when delivered through new-generation active VMNs in high-risk COPD cases on 30-day relapse or readmission rates, the current observational, concurrent clinical study was planned.

MATERIALS AND METHODS

An observational, concurrent, noninferiority clinical study i.e. SYMPTOM study on Glycopyrronium and Arformoterol Nebulizing solutions for High risk COPD was conducted after obtaining approval from an Independent Institutional Ethics committee with registration in the Clinical Trial Registry of India (Clinical Trial Registry of India CTRI/2019/07/020144). Consecutive patient records for High risk COPD with above formulations that utilized Spirometric assessment of Lung function and CAT symptom score for Moderate

to Severe COPD cases were collated. A concurrent study analyses for the follow-up visit was conducted as per the principles of International Conference of Harmonization for Good clinical practice and Declaration of Helsinki while ensuring confidentiality of patient identifiers before analyses. Patient support provided was accessed from the Patient access registration sheets.

The inclusion criteria included Post discharge cases of Acute Exacerbation of COPD (AECOPD) following ED visit or hospitalization; GOLD defined COPD cases with history of ≥ 1 exacerbation in past year with smoking or nonsmoking risk factors; and patients willing for follow-up visit while receiving glycopyrronium 25 mcg and arformoterol 15 mcg nebulizing solutions admixed and delivered as one nebulization twice a day for at least 4 weeks were assessed and analyzed.

The exclusion criteria included patients with < 1 follow-up visit to be excluded from the analyses; personal history of bronchial asthma; patients with history on use of oxygen therapy > 12 h/day; patients with any history of unstable disease and/or recent hospitalization due to COPD before 6 weeks of study observation.

The study endpoints included: Inter-group differences for percentage patients requiring additional anticholinergics and beta2-agonist dosages in hospitalized and outpatient cases of moderate or severe COPD; prebronchodilator forced expiratory volume in one second (FEV₁) improvement at 4 weeks; common adverse events ($> 1\%$) at 4 weeks; and change in CAT score at 4 weeks.

Safety variables were assessed as treatment-emergent adverse event (TEAE) rate at 4 weeks with severity classification as mild, moderate or severe. In case of any of these serious adverse events (SAEs), appropriate notification records on notification to the National Coordination Centre, PvPI (CDSCO) utilizing Suspected Adverse Drug Reaction Reporting form on pvpi@ipcindia.net was also assessed for analyses.

Statistical considerations with an estimated sample size of 40 patients involving moderate and severe COPD cases with dropout rate of 25% were factored for analyses with $P < 0.05$ considered as statistically significant. The sample size for a non-inferiority study was based on the assessment of primary endpoint. Percentage patients requiring rescue medication use for exertional or acute symptoms in both arms for a proportion size difference of 20% at the end of 4 weeks. Based on NI margin of 10%, the current sample size was calculated assuming 80% power to detect a difference in two arms with a two-sided alpha of 5%.

RESULTS

The intent to treat and per-protocol analyses for 49–46 cases, respectively, receiving nebulized glycopyrronium (25 mcg) and arformoterol (15 mcg) with follow-up visit for at least 4 weeks were carried out. Baseline demographics included high-risk COPD, i.e., patients with at least one prior history of exacerbation in the past year [Table 1]. In all of the cases, glycopyrronium (25 mcg) and arformoterol (15 mcg) were admixed and inhaled as one inhalation twice a day using a VMN following hospitalization or ED visit for AECOPD.

Clinical records with follow-up data for at least 4 weeks receiving nebulized bronchodilators exclusively during the continuation phase (on 3rd day of discharge or 7th day of moderate exacerbation) following completion of steroid course were included in the analyses as per protocol analyses. Post-discharge cases of ED or hospitalized cases receiving SAMA/SABA background therapy were also included in the analyses.

Efficacy variables for FEV₁ and CAT score

A significant improvement in FEV₁ and CAT score at the end of 4 weeks was observed as the mean change of $9.6 \pm 3.1\%$ [Figure 1] and 18.1 ± 0.69 , respectively ($P < 0.0001$).

Table 1: Baseline demographics for overall group with moderate or severe COPD

Parameters	N (%)
Per protocol analysis set	46
Mean Age (Years)	64 \pm 16.9
Gender	
Male	28 (57.1)
Female	21 (42.8)
Mean Weight (kg)	56 \pm 12.2
Airway obstruction	
FEV ₁ (%)	44.1 \pm 16.2
FEV ₁ (L/min)	1.2 L/min \pm 0.6
FEV ₁ /FVC (%)	64.8 \pm 10.6
Reversibility	8.4 \pm 11.8
CAT	34.6 \pm 2.3
Risk factors	
Hospitalization history	21 (45.6)
ED visit history	25 (54.3)
Current/Ex-smoker	
Cig/day	17 \pm 5.5
Years	13.6 \pm 7.2
Treatment arms	
Moderate COPD (FEV ₁ \geq 50%)	12 (24.5)
Severe COPD (FEV ₁ $<$ 50%)	37 (75.5)
Comorbidities	
Hypertension	30 (61.2)
ASCVD	2 (4.1)
Type 2 diabetes	7 (14.2)

COPD: Chronic obstructive pulmonary disease, FEV₁: Forced expiratory volume in one second, CVD: Cardiovascular disease

Moderate COPD

The mean change in FEV₁ and CAT score showed significant improvement with glycopyrronium 25 and arformoterol 15 mcg nebulization given twice a day as maintenance therapy at the end of 4 weeks [Figure 2 and 3].

Severe COPD

The mean change in FEV₁ and CAT score showed significant improvement with glycopyrronium 25 and arformoterol 15 mcg nebulization given twice a day with VMN as maintenance therapy at the end of 4 weeks [Figure 4 and 5].

The intergroup differences for pre-bronchodilator FEV₁ and CAT score improvement in the moderate and severe COPD groups are highlighted in Table 2. The efficacy variables including intergroup differences for FEV₁ improvement in the moderate and severe groups were not significant ($P = \text{NS}$)

The intergroup differences for rescue medication use for a lone case with severe COPD (1, 2.04%) complied with the suggested non-inferiority margin between the groups.

Safety Analyses

In a lone case of severe COPD with baseline FEV₁ 20% and history of one exacerbation in the last year, patient-

Table 2: Intergroup differences for FEV₁ and CAT score change between moderate and severe COPD at 4 weeks

Mean change at 4 weeks	Moderate COPD (Mean $\Delta \pm \text{SE}$)	Severe COPD (Mean $\Delta \pm \text{SE}$)	P value
FEV ₁ (%)	11.8% \pm 3.1	8.4% \pm 1.6	$P = \text{NS}$
CAT score	20.6 \pm 0.69	18.26 \pm 0.6	$P < 0.05$

COPD: Chronic obstructive pulmonary disease, FEV₁: Forced expiratory volume in one second

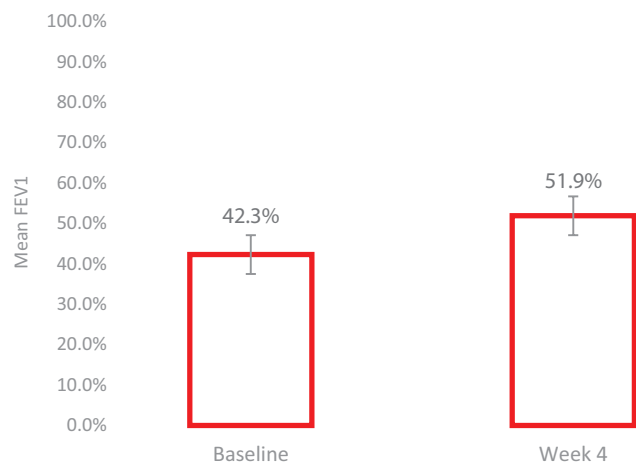


Figure 1: Mean FEV₁ in Overall group with Moderate or Severe COPD at four weeks (* $P < 0.0001$ vs. baseline)

reported exertional symptoms or dyspnea that warranted additional dosage of glycopyrronium 25 mcg and arformoterol 15 mcg as a rescue medication with further continuation as one inhalation 4 times a day before de-escalation to twice daily dosage in the next few weeks. The event resolved without any sequelae or further events that required any additional therapy. There were no other TEAEs or SAEs that warranted treatment modification or withdrawal in either of the patients with moderate or severe COPD.

DISCUSSION

This real-world, observational, concurrent, noninferiority study highlights the clinical efficacy and safety of nebulized glycopyrronium in AECOPD cases when coadministered with arformoterol.

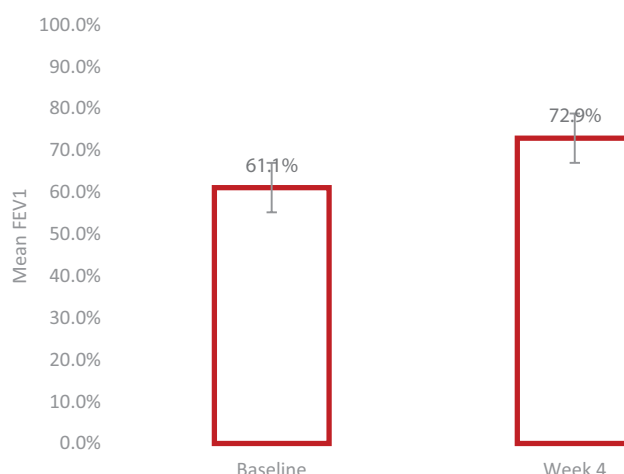


Figure 2: Mean FEV₁ in Moderate COPD group at four weeks (* $P < 0.0001$ vs. baseline)

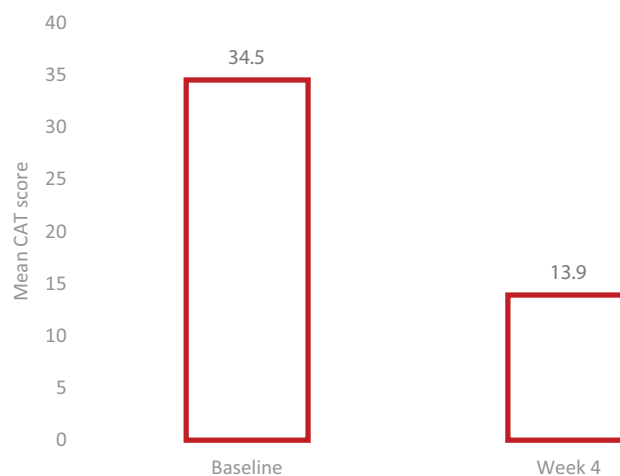


Figure 3: Mean CAT score for Moderate COPD group at four weeks (* $P < 0.0001$ vs. baseline)

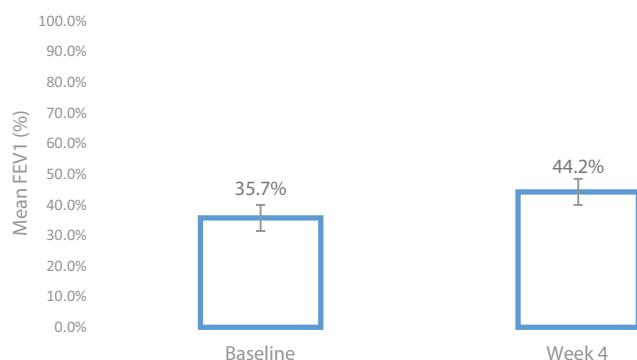


Figure 4: Mean FEV₁ in Severe COPD group at four weeks (*P < 0.0001 vs. baseline)

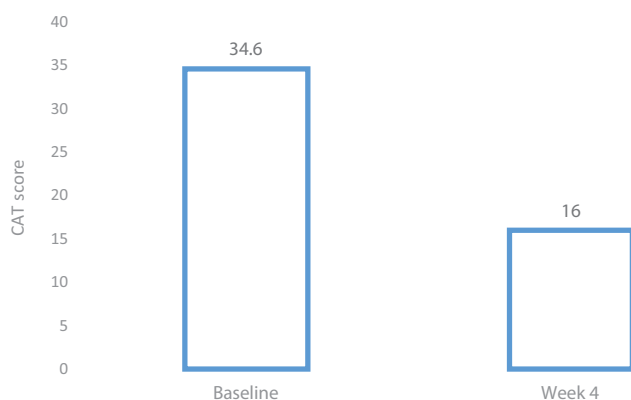


Figure 5: Mean CAT score for Severe COPD group at four weeks (*P < 0.0001 vs. baseline)

The study met the primary endpoint of non-inferiority for intergroup differences between moderate and severe COPD for FEV₁ improvement and 30-day rescue medication for any exacerbation requiring rescue medication.

This is the first study to demonstrate the 30-day readmission or exacerbation rate in high-risk COPD cases with moderate or severe exacerbation for patients receiving nebulized LAMA/LABA or glycopyrronium 25 mcg and arformoterol 15 mcg, one inhalation twice a day as maintenance delivered by VMN. Small volume nebulizers including VMNs offer compact, convenient, portable, noiseless device option for likely improved patient compliance and adherence with simple tidal breathing that is vital especially in the patients hospitalized due to severe exacerbation who demonstrate low PIFR in the post-discharge phase. Several studies have highlighted the stability and feasibility of dry powder inhaler inhalation in patients with PIFR of 90 L/min, however, in a prospective, observational study by Sharma,^[9] most of the cases demonstrated much lower values of 71 ± 22.12 L/min in the post-discharge phase following an acute exacerbation.

The complexity and dexterity of inhalation therapy with pressurized metered-dose inhaler (pMDI) involving

patient hand mouth coordination, lack of priming, breath-holding or emptying of respiratory airways before inhalation often precludes the high rate of inhalation errors as demonstrated by Cho-Reyes^[11] that is often relevant despite the availability and use of spacers. Even the use of SMI requires an accurate priming and breathing technique with longer inhalation and holding period as compared to conventional pMDIs. In general, patients that commit errors during inhalation therapy hiring, tend to be older, more debilitated and to have greater severity of disease due to multiple comorbidities including cardiac risk factors of hypertension and/or CVD as demonstrated in the current study. In elderly patients, unintentional nonadherence to inhalation therapy often comes from cognitive impairment, hearing or visual loss, and other physical disabilities, such as arthritis and tremors resulting in poor coordination, which significantly affect their ability to understand and follow the suggested treatment. In this line, the recent introduction and availability of new generation advanced nebulizers including VMNs have resulted in patients and their caregivers to be increasingly satisfied with nebulized drug delivery, in terms of symptom relief, ease to use, and improved quality of life.^[12]

European Research Society Guidelines^[13] recommend the use of nebulization strategy in obstructive airway disease patients with severe airflow limitation (acute exacerbation), frequent users of rescue medications and patients unable to use or coordinate or carry spacers along with pMDIs that may be of clinical relevance especially in patients with Severe asthma or ACO who are more prone to exacerbations. GOLD^[6] also recommends nebulizers to be used in specific populations, such as patients with inspiratory flow rates as low as 30 L/s or patients with poor hand-eye coordination while advocating the clinical role and use of LAMA/LABA in such cases requiring ED visit or hospitalization. The current study is first in its kind to demonstrate the clinical feasibility and practicality of LAMA/LABA involving glycopyrronium and arformoterol admixture in real-time before nebulization through a hand-held device for patients in post-discharge phase following hospitalization or ED visit for AECOPD.

In the current study, there was a lone case (1, 2.04%) that reported exertional symptoms of dyspnea that were resolved with physician-administered strategy of home nebulization with nebulized glycopyrronium and arformoterol given as four dosages in a day for a week. The patient subsequently completed the follow-up visit with no use of any additional dosages in the 2nd, 3rd, and 4th week, respectively. The safety analyses reported compares favorably with the clinical trials

reported by Ferguson^[10] and Hanania.^[14] In a 1-year long-term study on nebulized glycopyrronium 50 mcg BID administered for high-risk COPD with cardiac risk factors ($n = 1087$), the clinical impact and safety of LAMA mono- and combination therapy with LABAs (42%) were assessed. The TEAEs reported were comparable to placebo arm with persistent symptoms or dyspnea reported in 4.5% (27/620 cases). Similarly, Hanania^[14] reported dyspnea of 6.5% (35/541 cases) with formoterol nebulization administered as 20 mcg twice a day inhalation for moderate to severe COPD in a multicentric, randomized, and controlled clinical trial involving 1071 cases.

CONCLUSION

Severe exacerbation represents an important milestone in COPD topography, often associated with declining lung function, increased exacerbation, and mortality rate due to systemic inflammation and comorbidities that warrants the use of cardio – “safe” bronchodilators including glycopyrronium and arformoterol.

Nebulized glycopyrronium and arformoterol with VMN offers bronchodilation as demonstrated by improvement in FEV₁ and reduction in CAT score that is clinically significant in moderate or severe COPD cases with successful use of the drugs as “Rescue Medication” for likely translational impact on patient compliance, adherence, and quality of life.

ACKNOWLEDGMENTS

None.

DISCLOSURES

The study was supported by patient support program for Vibrating mesh nebulizer supply to patients with acute exacerbations of chronic obstructive pulmonary disease.

REFERENCES

1. Jacobs DM, Noyes K, Zhao J, Gibson W, Murphy TF, Sethi S, *et al.* Early hospital readmissions after an acute exacerbation of chronic obstructive pulmonary disease in the nationwide readmissions database. *Ann Am Thorac Soc* 2018;15:837-45.
2. Guerrero M, Crisafulli E, Liapikou A, Huerta A, Gabarrús A, Chetta A, *et al.* Readmission for acute exacerbation within 30 days of discharge is associated with a subsequent progressive increase in mortality risk in COPD patients: A Long-term observational study. *PLoS One* 2016;11:e0150737.
3. Bartels W, Adamson S, Leung L, Sin DD, van Eeden SF. Emergency department management of acute exacerbations of chronic obstructive pulmonary disease: Factors predicting readmission. *Int J Chron Obstruct Pulmon Dis* 2018;13:1647-54.
4. Zhou F, Chandra K, Sohi D, Robertson C, Fraser J, Scoville J, *et al.* Do guidelines influence emergency department staff behaviours and improve patient outcomes? Evaluation of a multifaceted intervention for the implementation of local acute exacerbations of chronic obstructive pulmonary disease guidelines. *Cureus* 2018;10:e3588.
5. O'Donnell DE, Hernandez P, Kaplan A, Aaron S, Bourbeau J, Marciniuk D, *et al.* Canadian thoracic society recommendations for management of chronic obstructive pulmonary disease-2008 update-highlights for primary care. *Can Respir J* 2008;15 Suppl A:1A-8A.
6. Global Initiative on Chronic Obstructive Lung Disease. Pocket Guide to COPD Diagnosis, Management, and Prevention. A Guide for Health Care Professionals. GOLD; 2019 Report. Available from: <https://www.goldcopd.org/wp-content/uploads/2018/11/GOLD-2019-v1.7-FINAL-14Nov2018-WMS.pdf>. [Last accessed on 2019 Jul 28].
7. Santus P, Radovanovic D, Cristiano A, Valenti V, Rizzi M. Role of nebulized glycopyrrolate in the treatment of chronic obstructive pulmonary disease. *Drug Des Devel Ther* 2017;11:3257-71.
8. Duarte AG, Tung L, Zhang W, Hsu ES, Kuo YF, Sharma G, *et al.* Spirometry measurement of peak inspiratory flow identifies suboptimal use of dry powder inhalers in ambulatory patients with COPD. *Chronic Obstr Pulm Dis* 2019;6:246-55.
9. Sharma G, Mahler DA, Mayorga VM, Deering KL, Harshaw O, Ganapathy V, *et al.* Prevalence of low peak inspiratory flow rate at discharge in patients hospitalized for COPD exacerbation. *Chronic Obstr Pulm Dis* 2017;4:217-24.
10. Ferguson GT, Goodin T, Tosiello R, Wheeler A, Kerwin E. Long-term safety of glycopyrrolate/eFlow CS in moderate-to-very-severe COPD: Results from the glycopyrrolate for obstructive lung disease via electronic nebulizer (GOLDEN) 5 randomized study. *Respir Med* 2017;132:251-60.
11. Cho-Reyes S, Celli BR, Dembek C, Yeh K, Navaie M. Inhalation technique errors with metered-dose inhalers among patients with obstructive lung diseases: A systematic review and meta-analysis of U.S. Studies. *Chronic Obstr Pulm Dis* 2019;6:267-80.
12. Usmani OS. Choosing the right inhaler for your asthma or COPD patient. *Ther Clin Risk Manag* 2019;15:461-72.
13. Boe J, Dennis JH, O'Driscoll BR, Bauer TT, Carone M, Dautzenberg B, *et al.* European respiratory society guidelines on the use of nebulizers. *Eur Respir J* 2001;18:228-42.
14. Hanania NA, Sethi S, Koltun A, Ward JK, Spanton J, Ng D, *et al.* Long-term safety and efficacy of formoterol fumarate inhalation solution in patients with moderate-to-severe COPD. *Int J Chron Obstruct Pulmon Dis* 2019;14:117-27.

How to cite this article: Bendre S, Katiyar S. Observational, Concurrent Study to Assess Safety and Efficacy of Glycopyrronium and Arformoterol Home Nebulization in High-risk, Symptomatic Acute Exacerbation of Chronic Obstructive Pulmonary Disease Cases: SYMPTOM Study. *Int J Sci Stud* 2019;7(5):92-97.

Source of Support: Patient support program, **Conflict of Interest:** None declared.

Comparison of Academic Performance of 2nd MBBS Students Participating in Quiz Versus Nonparticipants: A Retrospective Analysis

Koli Paresh Girdharlal¹, Shetty Yashashri C², Singh Vishal³

¹Senior Resident, Department of Pharmacology and Therapeutics, Seth GS Medical College and KEM Hospital, Parel, Mumbai, Maharashtra, India, ²Associate Professor, Department of Pharmacology and Therapeutics, Seth GS Medical College and KEM Hospital, Parel, Mumbai, Maharashtra, India, ³Junior Resident, Department of Pharmacology and Therapeutics, Seth GS Medical College and KEM Hospital, Parel, Mumbai, Maharashtra, India

Abstract

Introduction: Pharmacology quiz participants undergo training by their teachers on pharmacology which is much more rigorous than routine pharmacology teaching program. Effect of this training for pharmacology quiz on the performance of students in the 2nd year MBBS exams, i.e., terminal, preliminary, and university exam has not been evaluated.

Methodology: Study was a retrospective analysis of scores of three exams (1st term, 2nd term, and prelim) conducted in 2nd-year MBBS student in the department of pharmacology of four batches. Participants were students who had given their names for participation in the quiz and had undergone pre-quiz training and selected candidates were among the participants who got selected to take part in the final quiz. Participants were trained for the quiz. Rest of the students were considered as nonparticipants. Equal number of topper nonparticipants was chosen based on number of selected students. Marks between the groups were compared with paired and unpaired *t*-test, Mann-Whitney *U*-test, and Wilcoxon Signed-rank test. *P* < 0.05 was considered statistically significant.

Results: Out of a total of 728 students, 147 were participants, 131 participated but not selected, and 16 got selected, 581 were nonparticipants, 16 toppers were selected. The theory, practical and combined marks of participants and selected students were higher than nonparticipants and not selected students, respectively. Practical and combine marks of topper nonparticipants were higher than the selected students at baseline, but in 3rd term the difference was not significant (*P* > 0.05).

Conclusion: Quiz-based teaching in pharmacology enhances performance in pharmacology.

Key words: Contest, Exam, Learning, Teaching methods

INTRODUCTION

A quiz program is a test of knowledge between individuals and teams, as a form of entertainment. The quiz format provides motivation not only for participants but also for the audience, because it provides four kinds of gratification and appeals: (1) Self-rating appeal: On a primary level, it serves as a tool of self-assessment of intellectual status

or subject knowledge in relation to the others; (2) social interaction: Questions can encourage social interaction because they can be discussed within the team and at audience level; (3) excitement appeal: The appeal of winning a prize or being rated as superior among peers; and (4) educational appeal: Quizzes serve as educational tools by encouraging thinking and learning.^[1]

Applying collaborative and cooperative learning theories, group quizzes serve as effective means of education. Quizzes engage participants in collaborative learning by helping them harness joint intellectual effort and group processing. They also promote positive interdependence and motivate participants for cooperative learning. In addition, they improve recall of information, generate discussion, and prompt those with no knowledge (even among audience) to learn.^[1]

Access this article online	
 www.ijss-sn.com	Month of Submission : 06-2019
	Month of Peer Review : 07-2019
	Month of Acceptance : 08-2019
	Month of Publishing : 08-2019

Corresponding Author: Shetty Yashashri C, Department of Pharmacology and Therapeutics, Seth GS Medical College and KEM Hospital, Parel, Mumbai, Maharashtra, India.

The role of teaching quality cannot be ignored in recent brilliant scientific advances. One of the major challenges of teaching is finding an approach to increase students' level of understanding and learning. Various teaching techniques have resulted in different outcomes.^[2]

It is documented that students preserve about 20% of items taught during a 45-min lecture, but the active participation of students in the learning process would increase the level of students' understanding. Quizzes and assignments, as teaching aid equipment, can provide appropriate feedback and error correction for students during educational courses.^[2,3]

Active participation in the educational processes, they would acquire the desired education, and by attaining knowledge, attitudes, and necessary expertise, they achieve certain professional skills to serve the community.^[2]

Pharmacology is a paraclinical subject taught in 2nd-year MBBS in India. There are few students who participate in quiz program. The students usually participate in many local, regional, state, national, and international level pharmacology quizzes. These are the type of students who are inherently motivated and want to learn and achieve more. However, many a times, we feel they are better academic achievers than their counterparts as they are willing to venture and explore different type of intellectual learning and evaluation. A puzzle-based pedagogy, when compared to traditional lecture-based teaching, has effectively enhanced the performance of students on standard course-specific assessments when evaluated by quiz and test scores in physiology and anatomy.^[3]

Pharmacology quiz participants undergo training by their teachers on pharmacology which is much more rigorous than routine pharmacology teachings program.

Department of Pharmacology and Therapeutics, Seth GSMC, Mumbai, had been conducting pharmacology quiz since 2001. This activity was started as intent to create interest in the subject of pharmacology. There are different methods to teach pharmacology, but generally pharmacology as a subject is felt tough by students, and very few students excel in this subject. There are various factors which can lead to their better performances, so we thought quiz could be one of the factors. Effect of training in pharmacology quiz on the performance of students in the 2nd-year MBBS exams (1st terminal, 2nd terminal, and prelims exam) has not been evaluated. We planned this study to find and compare the pharmacology exam scores of students who participated in the quiz and got selected for the final quiz versus those who did not.

METHODOLOGY

This study was a retrospective analysis of marks (scores) of 2nd MBBS students of August 2012–2016 batches. The data is under the Department of Pharmacology and Therapeutics, and the respective permission of Departmental Head and Institutional Ethics Committee (IEC) was sought to access the data. Confidentiality and privacy of data was maintained.

Definition of the Terms used in the Study

(1) Participators: Students who have given their names for participation in the quiz and cleared all the elimination round and received training for final quiz competition, (2) nonparticipators: Students who have never participated in pharmacology quiz and have not received any pre-quiz training, (3) selected: Students who got selected in the final quiz and took part in the quiz, (4) participated but not selected: Students who participated and got pre-quiz training but did not get selected for the final quiz, and (5) topper nonparticipators: Students who had not participated in the quiz but were class topper when an average of 1st and 2nd term marks was considered.

The list of students participating in the quiz and the four selected students list was available in the department of pharmacology. Their respective scores of 1st terminal, 2nd terminal, and 3rd term (preliminary) exams were also available with the department of pharmacology. The batch for consideration was August 2012–2016. Between years 2013 and 2017, five batches of students had participated in the pharmacology quiz. Data of one of the batches were not included in the analysis due to missing/incomplete data of quiz participating students. The data were retrospectively analyzed in the next 2 months. This was a single-center retrospective study conducted in the Department of Pharmacology of Seth GS Medical College and KEM Hospital. Exemption from Ethics Committee Review was sought from IEC.

The student's name was anonymized and coded so that the evaluator was blinded during analysis. Confidentiality and privacy of the students was maintained.

Archived data of marks of students in 1st terminal examination, 2nd terminal examination, and preliminary examinations were noted down in the Microsoft Excel sheet. Marks of written theory exam, practical exam and theory viva were noted down. Multiple choices questions, short answer questions, and long answer questions were the domain in which affective, cognitive, and psychomotor skills were tested in theory exams. Spots, prescription writing, criticism of fixed-dose combination, rationality/irrationality of prescription, grand and pharmacy viva,

Table 1: Association between percentage marks for an average of 1st and 2nd term marks (baseline) to 3rd term for participators, nonparticipators, selected, not selected, participated but not selected students and topper nonparticipators

Groups	Mean	SD	Median	IQR	P value
1 st and 2 nd term average percentage marks (baseline) in theory					
Participators	57.43	9.75	57	51–65	<0.0001*
Non-participators	45.66	12.94	46.25	37.5–54.5	
Selected	64.56	8.81	65.75	60.13–69.13	<0.0001*
Not selected	47.65	13.08	48.25	39.5–56.5	
Selected	64.56	8.81	65.75	60.13–69.13	<0.0001*
Participated but not selected	56.57	9.54	56	50.50–63.50	
Selected	70.03	2.71	70	60.13–69.13	0.015*
Topper nonparticipators	64.56	8.81	65.75	67.63–72	
3 rd term percentage marks in theory					
Participators	64.26	8.68	64.38	57.5–70.63	<0.0001*
Nonparticipators	54.79	11.08	55.63	48.13–63.13	
Selected	71.88	8.09	73.75	67.81–77.19	<0.0001*
Not selected	56.36	11.12	57.5	49.38–64.38	
Selected	71.88	8.09	73.75	67.81–77.19	<0.0001*
Participated but not selected	63.33	8.31	63.75	57.5–70	
Selected	71.88	8.09	73.75	67.03–77.66	0.061
Topper nonparticipators	66.91	9.87	68.44	62.81–72.66	
1 st and 2 nd term average percentage marks (baseline) in practical					
Participators	66.80	8.17	67.50	61.75–72	<0.0001*
Nonparticipators	57.78	12.06	59.25	51.06–65.5	
Selected	72.10	5.92	71.09	68.56–78.03	<0.0001*
Not selected	59.30	11.90	60.81	52.66–67.25	
Selected	72.10	5.92	71.09	68.56–78.03	<0.0001*
Participated but not selected	66.15	8.19	66.63	61.13–71.50	
Selected	72.10	5.92	71.09	68.56–78.03	0.047*
Topper nonparticipators	76.48	4.18	76	73.72–77.97	
3 rd term percentage marks in practical					
Participators	65.78	9.16	66.5	60–72.6	<0.0001*
Nonparticipators	55.70	10.69	56.25	49–62.5	
Selected	72.20	7.97	73.85	66.25–76.25	<0.0001*
Not selected	57.42	11	57.5	50–65.72	
Selected	72.20	7.97	73.85	66.25–76.25	<0.0001*
Participated but not selected	65	9.01	66.25	59.9–72.5	
Selected	72.20	7.97	73.85	64.38–76.25	0.305
Topper nonparticipators	70	6.62	71.88	65.94–73.75	
1 st and 2 nd term average percentage marks (baseline) in theory+practical					
Participators	61.60	7.98	61.89	56.67–67.11	<0.0001*
Nonparticipators	51.05	11.72	52.28	44.14–59.11	
Selected	67.91	6.96	68.06	63.14–73.36	<0.0001*
Not selected	52.83	11.72	54.11	46.17–60.83	
Selected	67.91	6.96	68.06	63.14–73.36	<0.0001*
Participated but not selected	60.83	7.78	61.11	56.11–66.72	
Selected	67.91	6.96	68.06	63.14–73.36	0.029*
Topper nonparticipators	72.90	2.52	72.64	70.47–74.24	
3 rd term percentage marks in theory+practical					
Participators	64.77	8.15	65.42	58.75–70.54	<0.0001*
Nonparticipators	55.09	10.10	55.83	48.67–62.5	
Selected	71.98	7.31	73.5	68.12–76.45	<0.0001*
Not selected	56.71	10.30	57.5	50.42–63.78	
Selected	71.98	7.31	73.5	68.12–76.45	<0.0001*
Participated but not selected	63.88	7.82	64.58	58.33–69.58	
Selected	71.98	7.31	73.50	67.6–76.77	0.102
Topper nonparticipators	67.94	8.19	68.37	65.57–72.71	

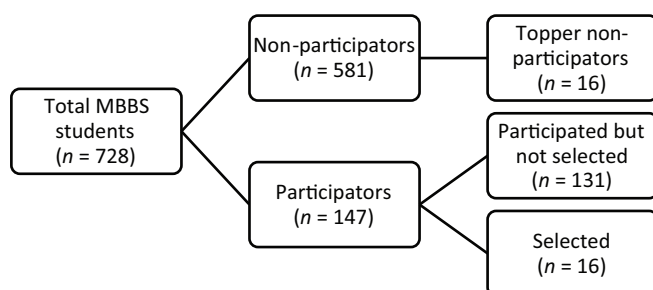
*Significance with $P < 0.05$ using Mann–Whitney U -test. IQR: Interquartile range

and objective structured clinical examination/objective structured practical examination along with oral and vocabulary skills are tested in practical exam. A total score of students in theory and practical exam was

considered for statistical analysis. Baseline score (average of 1st and 2nd terminal examination marks) was assessed between participators and nonparticipators, selected and non-selected students, selected, and participated but not

Table 2: Within the group paired data comparison of the average of 1st and 2nd term marks (baseline) with 3rd term marks

Exam	Groups	1 st and 2 nd term average percentage marks (baseline)		3 rd term percentage marks		P value
		Mean	SD	Mean	SD	
Theory	Participants	57.44	9.76	64.26	8.68	<0.001*
	Nonparticipants	45.67	12.95	54.05	12.71	0.001#
	Selected	64.57	8.82	71.88	8.10	0.012*
	Not selected	47.66	13.09	55.74	12.55	<0.001#
	Participated but not selected	56.57	9.54	63.33	8.31	<0.001*
	Topper nonparticipants	70.04	2.72	66.92	9.87	0.185
Practical	Participants	66.80	8.18	65.79	9.16	0.112
	Nonparticipants	57.79	12.07	54.95	12.43	0.001#
	Selected	72.10	5.93	72.20	7.97	0.944
	Not selected	59.31	11.90	56.78	12.49	<0.001#
	Participated but not selected	66.15	8.20	65.01	9.02	<0.001*
	Topper nonparticipants	76.48	4.19	70.00	6.63	0.002*
Combined	Participants	61.60	7.99	64.77	8.14	<0.001*
	Nonparticipants	51.06	11.72	54.35	11.89	0.001#
	Selected	67.92	6.96	71.99	7.31	0.050*
	Not selected	52.83	11.73	56.08	11.85	<0.001#
	Participated but not selected	60.83	7.78	63.89	7.83	<0.001*
	Topper nonparticipants	72.90	2.52	67.95	8.20	0.017*

* $P < 0.05$ by Paired t-test, # $P < 0.05$ by Wilcoxon signed-rank test**Figure 1: Number of students in individual groups as defined in the methodology**

selected students and topper nonparticipants with selected students.

Statistics

Descriptive statistics were applied to all the data using Microsoft Excel and IMB SPSS v25. Unpaired and paired *t*-test, Mann–Whitney *U*-test, and Wilcoxon Signed-rank test were applied for between the group analysis. $P < 0.05$ was considered as statistically significant.

RESULTS

Data of a total of 728 students was analyzed in the study.

Out of 728 students, 581 were nonparticipants, 147 students participated in the quiz training, and out of these 131 had participated but were not selected for the final quiz [Figure 1]. A total of 16 students got selected in 4 years of quiz, i.e., four students per year; thus, 16 toppers from non-participant group were chosen for the comparison.

A total of 712 students were not selected (combination of non-participants [$n = 581$] and participated but not selected [$n = 131$]). Sixteen topper non-participant students were selected from non-participant group who had highest marks at the baselines (i.e., average of 1st and 2nd term exams).

Percentage marks of participants when compared to non-participants were significantly different ($P < 0.05$) for theory and practical at baseline (1st and 2nd term) and 3rd term [Table 1]. Similar association was seen between selected and non-selected students and between selected and participated but not selected students.

Baseline marks in theory of selected students were significantly higher ($P < 0.05$) compared to topper non-participants. However, the same difference was not statistically significant ($P > 0.05$) in the 3rd term theory exam.

Baseline marks in practical of topper non-participants were significantly higher ($P < 0.05$) compared to selected students but the difference was not significantly different ($P > 0.05$) in 3rd term practical marks.

Combined baseline theory and practical marks of topper nonparticipants were significantly higher ($P < 0.05$) compared to selected students, but in 3rd term the same difference was not statistically significant ($P > 0.05$).

On paired data analysis [Table 2] between average marks of 1st and 2nd term with prelim exam marks it was found that there was a statistically significant ($P < 0.05$) increase in

theory marks of participators, non-participators, selected, not selected, and participated but not selected students. Combined marks of participators, non-participators, selected, not selected, and participated but not selected students to increased in prelim compared to 1st and 2nd term marks. In practical exams, there was a significant decrease in marks of nonparticipators, not selected, and participated but not selected and topper nonparticipators. There was no difference in marks between the 1st and 2nd term and prelim exam for participators and selected students. There was no difference in theory marks of topper nonparticipators, and practical marks of participators and selected students.

DISCUSSION

This study was planned to find an association of training in pharmacology quiz on the performance of the students in 2nd-year MBBS exams.

It was found that theory, practical, and combined marks of participators and selected students were higher than nonparticipators and not selected students, respectively.

At baseline theory marks of selected students were higher than the topper nonparticipators but in 3rd term the difference was not significant. Practical marks of topper nonparticipators were higher than the selected students at baseline which in 3rd term became not significantly different. Similarly, combine marks of topper nonparticipators was higher than the selected students at baseline, but in 3rd term the difference was not significant. This shows that participating and getting selected in the quiz have a positive impact on the practical and combined marks of the students and scores become better at the end of 3rd term exam.

Quiz based learning involves additional training apart from traditional teaching methods. Quiz training involves much more extensive reading, understanding deeper concepts of pharmacology, variant reading including case based, crossword solving, dose calculation, match the following, true or false, structure–activity relationship, drug discovery in terms of origins of medicines, and history of pharmacology. All these combined leads to improvement in student's understanding and interest in pharmacology.

The reason for the improvement in marks of the students at the end of 3rd term exam maybe because of better understanding of the subject and increasing efforts by the students, which can make them achieve more in final university examination. Selected students are highly motivated and already good in the exams as seen in their baseline scores. Hence, the reason for the less mean

difference in the scores of selected students could be that improvement in scores of good students is more difficult than improvement in marks of average students. Reduction in marks of topper non-participators could be due to their learning only through traditional lecture methods which may not be enough to improve or even maintain their already good scores.

A study indicated that quizzes could serve as collaborative/cooperative learning methods. Such sessions during scientific conferences not only entertain the participants by engaging them but they also help participants brush up on their knowledge, improve recall of information, and prompt participants to learn.^[1]

In a 2013 study by Zamini *et al.* study it was found that taking frequent quizzes is not associated with higher final scores than regular training techniques. Previous studies have shown that the effects of frequent examinations and quizzes on science teaching and learning can have favorable effects in the earlier detection of the students' errors and in raising and maintaining high standards of learning attainment. Quizzes and assignments, as teaching aid equipment, can provide appropriate feedback and error correction for students during educational courses. The quiz is a tool for encouraging and monitoring the progress of students, especially when they are taken frequently. It may also have desirable effects such as improving academic achievement, reducing anxiety, augmenting the student-professor communication, and decreasing the study time for the final exam. Conversely, in some cases, it can increase the students' anxiety, and in other cases may have poor or negative effects on the learner's performance.^[2]

A 2013 study on Iranian Dentistry students showed that scores of the final examinations were significantly higher among students in the quiz group and the combination method of teaching compared to the traditional lecture method group.^[4]

There are studies which have shown that quizzes have no effect on the student's performance. Harter and Harter in a 2014 study found that adding online quizzes in a semester long introductory economics course did not increase student performance on multiple-choice questions on the final exam nor did it increase students' overall course grades.^[5,6] This is contradictory to what we found in the study. This can be a possibility as there are multiple factors playing role in final mark score.

A 2013 study by Orr and Foster concluded that students who take pre-exam quizzes tend to be more successful in exams and students of all abilities benefit from participating in pre-exam quizzing.^[7] Another 2013 study indicated that quizzes

could serve as collaborative/cooperative learning methods and quizzes during conferences would entertain participants, brush up their knowledge, and prompt them to learn.^[1]

In a study done on nursing students, pre-test results showed no significant difference in their achievement scores. However, in the immediate achievement post-test and the retention test, the students in the quiz group scored significantly better than those in the lecture group. A satisfaction questionnaire showed that the game format was well liked and accepted by students as a more satisfying teaching method.^[8] A pre-lecture quiz also leads to more questions asked by the students and increase in number of students who come in the class reading the study material.^[9] Approximately a third of high- and medium-performing students and one-fifth of low-performing students can make large improvements in their exam grades with quizzes.^[10] The formative online quizzes did enhance summative exam performance and that the online quizzes were valid predictors of exam performance.^[11] Students who elect to use online quizzes performed better in summative examinations.^[12] Puzzle-based pedagogy, when compared to traditional lecture-based teaching, can effectively enhance the performance of students on standard course-specific assessments, even when the assessments only test a limited conceptual understanding of the material.^[3]

Limitations of our study are that we were not able to analyze data of one batch of students due to unavailability of the complete data, which could have made our study findings more robust due to larger sample size. As it was a retrospective study, many factors influencing the scores could not be studied.

CONCLUSION

Quiz based training in pharmacology enhances performance. This can be one of the methods for teaching pharmacology.

REFERENCES

1. Gavaravarapu SM. Group quiz: A tool for nutrition education and self-assessment. *J Nutr Educ Behav* 2013;45:380-2.
2. Zamini G, Khadem Erfan MB, Rahmani MR, Khodavaisy MS, Davari B. Effects of frequent announced parasitology quizzes on the academic achievement. *Iran J Parasitol* 2013;8:617-21.
3. Stetzik L, Deeter A, Parker J, Yukech C. Puzzle-based versus traditional lecture: Comparing the effects of pedagogy on academic performance in an undergraduate human anatomy and physiology II lab. *BMC Med Educ* 2015;15:107.
4. Lahijani MS, Kateb HR. The effect of PBL and film showing, frequent quizzes and lecture-based method on short-term performance of dentistry students. *J Med Educ* 2004;4. Available from: <http://www.journals.sbm.ac.ir/jme/article/view/826>. [Last accessed on 2019 May 28].
5. Hadsell L. The effect of quiz timing on exam performance. *J Educ Bus* 2009;84:135-41.
6. Harter CL, Harter JF. Teaching with technology: Does access to computer technology increase student achievement? *East Econ J* 30:507-14. Available from: <https://www.jstor.org/stable/40326144>. [last accessed on 2019 jun 06].
7. Orr R, Foster S. Increasing student success using online quizzing in introductory (majors) biology. *CBE Life Sci Educ* 2013;12:509-14.
8. Aljezawi M, Albashtawy M. Quiz game teaching format versus didactic lectures. *Br J Nurs* 2015;24:86, 88-92.
9. Marcell M. Effectiveness of regular online quizzing in increasing class participation and preparation. *Int J Scholarsh Teach Learn* 2016;2:7-17.
10. Dalfen SR, Fienup DM, Sturmey P. Effects of a contingency for quiz accuracy on exam scores. *Behav Anal Pract* 2018;11:106-13.
11. Dobson JL. The use of formative online quizzes to enhance class preparation and scores on summative exams. *Adv Physiol Educ* 2008;32:297-302.
12. Kibble J. Use of unsupervised online quizzes as formative assessment in a medical physiology course: Effects of incentives on student participation and performance. *Adv Physiol Educ* 2007;31:253-60.

How to cite this article: Koli PG, Shetty YC, Singh V. Comparison of Academic Performance of 2nd MBBS Students Participating in Quiz Versus Nonparticipants: A Retrospective Analysis. *Int J Sci Stud* 2019;7(5):98-103.

Source of Support: Nil, **Conflict of Interest:** None declared.

A Unique Case of Acquired Capillary Hemangioma in Adult

Nithisha Tegginamatha¹, Sandhya Baskar², Neethu Narayana Rao², Remya Joseph Parappallil²

¹Professor, Department of Ophthalmology, Rajarajeswari Medical College and Hospital, Bengaluru, Karnataka, India, ²Junior Residents, Department of Ophthalmology, Rajarajeswari Medical College and Hospital, Bengaluru, Karnataka, India

Abstract

Adult capillary hemangioma is a rare clinical entity. We report a typical case presentation of capillary hemangioma in adult. A 55-year-old male presented with a history of hyperpigmentation of the complete left half of the face and right lower half of face since birth. He started developing nodules from age 25 which gradually increased. On examination, non-tender and hyperpigmented multiple nodular swellings present on the face involving the left side. Visual acuity in the left eye is the perception of light, projection of rays positive, and right eye is 6/9. Capillary hemangioma of the adult is a rare condition whose pathophysiological process is still unclear.

Key words: Acquired capillary hemangioma, Adult capillary hemangioma, Vascular tumor

INTRODUCTION

Most capillary hemangioma is congenital in nature. Acquired cases are very rare. To the best of our knowledge, only eight such cases have been reported in literature. We report the case of a 55-year-old male with acquired capillary hemangioma of the left half of the face and right lower half of face. Capillary hemangioma is a benign vascular tumor composed of proliferating endothelial cells within fibrous tissue in a normal location. It is the most common vascular tumor in infancy. It usually presents within the 1st few weeks or months of life.^[1]

CASE REPORT

A 55-year-old male presented with loss of vision in the left eye followed by a history of trauma in the childhood. History of hyperpigmentation of the complete left half of the face with the right lower half of face since birth started developing nodules from age 25 and gradually

increased. Ocular examination including visual acuity, anterior and posterior examination, and b scan was done. Non-tender and hyperpigmented multiple nodular swellings on the face involving the left side and lower half of right side. Visual acuity in the right eye is 6/9 and left eye is the perception of light and projection of rays negative.

The left eye has dilated congested episcleral vessels, macular corneal opacity with bleeding spot at 10'o clock position, calcification at 4'o clock–6'o clock position and vascularization at 12'o clock position. The right eye has dilated episcleral vessels. Fundus was normal in the right eye. B scan showed tractional retinal detachment in the left eye.

DISCUSSION

Acquired capillary hemangioma of the eyelid and periorcular region is a very rare phenomenon.^[2] The exact etiology is not known. It has been associated with hormonal changes and increased estrogen levels during puberty and pregnancy.^[3] Overexpression of angiogenic growth factors, including vascular endothelial growth factor (VEGF), has been associated with capillary hemangioma. Cosmesis, visual obstruction, and bleeding are the main reasons for seeking treatment.^[4] The pathogenesis of infantile hemangioma remains unclear, although two

Access this article online



www.ijss-sn.com

Month of Submission : 06-2019
Month of Peer Review : 07-2019
Month of Acceptance : 08-2019
Month of Publishing : 08-2019

Corresponding Author: Sandhya Baskar, Department of Ophthalmology, Rajarajeswari Medical College and Hospital, Bengaluru, Karnataka, India.

theories dominant current thought. The first theory suggests that hemangioma endothelial cells arise from disrupted placental tissue imbedded in fetal soft tissues during gestation or birth.^[5] A second theory arose from the discovery of endothelial progenitor and stem cells in the circulation of patients with hemangioma.^[6] Genetic errors in growth factor receptors have also been shown to affect the development of hemangioma.^[7] Nonsurgical interventions include the use of corticosteroids, which accelerate the regression of the lesion. Intralesional corticosteroids (triamcinolone) are used for small, well-localized hemangioma while systemic corticosteroids for large or multiple hemangiomas.^[8] Recombinant interferon-alpha (2a or 2b), vincristine, cyclophosphamide, imiquimod, and antiangiogenic agents such as bevacizumab are the other drugs found to be effective in life-threatening hemangiomas.^[9,10] Systemic propranolol has also been used successfully. The exact mechanism of action is not known, but vasoconstriction, decreased expression of VEGF, and induction of apoptosis of capillary endothelial cells are supposed to cause regression of the lesion.^[10] Surgical resection is recommended in cases where conservative therapy has failed, and where the hemangioma is blocking the airway or vision or is bleeding.^[9,10] Pre-operative imaging, including magnetic resonance (MR) imaging, MR angiography, and angiogram is necessary to identify the feeding vessels. Low-level radiotherapy can speed the regression of the mass by creating micro embolisms in the tumors. Carbon dioxide, argon, Nd: YAG laser, and flash-lamp pumped-dye laser have also been used in the treatment.^[10] There is, however, no standard treatment modality for the hemangioma.

CONCLUSION

Adult capillary hemangioma does not involute like their infantile counterparts. Ophthalmologists should be aware of the ocular complications of this tumor. Early recognition and timely diagnosis and treatment may prevent amblyopia and cosmetic disfigurement.

REFERENCES

1. Bang GM, Setabutr P. Periocular capillary hemangiomas: Indications and options for treatment. *Middle East Afr J Ophthalmol* 2010;17:121-8.
2. Hemangioma Investigator Group, Haggstrom AN, Drolet BA, Baselga E, Chamlin SL, Garzon MC, *et al.* Prospective study of infantile hemangiomas: Demographic, prenatal, and perinatal characteristics. *J Pediatr* 2007;150:291-4.
3. Leroux K, den Bakker MA, Paridaens D. Acquired capillary hemangioma in the lacrimal sac region. *Am J Ophthalmol* 2006;142:873-5.
4. Mulliken JB, Fishman SJ, Burrows PE. Hemangiomas and other vascular tumors. In: Wells SA, editor. *Current Problems in Surgery: Vascular Anomalies*. Boston: Mosby; 2000. p. 529-51.
5. North PE, Waner M, Brodsky MC. Are infantile hemangiomas of placental origin? *Ophthalmology* 2002;109:633-4.
6. Richter GT, Friedman AB. Hemangiomas and vascular malformations: Current theory and management. *Int J Pediatr* 2012;2012:645678.
7. Steeples LR, Bonshek R, Morgan L. Intralesional bevacizumab for cutaneous capillary haemangioma associated with pregnancy. *Clin Exp Ophthalmol* 2013;41:413-4.
8. Pushker N, Bajaj MS, Kashyap S, Balasubramanya R. Acquired capillary haemangioma of the eyelid during pregnancy. *Clin Exp Ophthalmol* 2003;31:368-9.
9. Calicchio ML, Collins T, Kozakewich HP. Identification of signaling systems in proliferating and involuting phase infantile hemangiomas by genome-wide transcriptional profiling. *Am J Pathol* 2009;174:1638-49.
10. Yu Y, Flint AF, Mulliken JB, Wu JK, Bischoff J. Endothelial progenitor cells in infantile hemangioma. *Blood* 2004;103:1373-5.

How to cite this article: Tegginamatha N, Baskar S, Rao NN, Parappallil RJ. A Unique Case of Acquired Capillary Hemangioma in Adult. *Int J Sci Stud* 2019;7(5):104-105.

Source of Support: Nil, **Conflict of Interest:** None declared.

Facial Nerve Schwannoma – A Diagnostic and Surgical dilemma: A Case Report

T Santhi¹, S Vivek²

¹Additional Professor, Department of Otorhinolaryngology, Government T. D. Medical College, Alleppey, Kerala, India, ²Senior Resident, Department of Otorhinolaryngology, Government T. D. Medical College, Alleppey, Kerala, India

Abstract

Facial nerve schwannomas are rare facial nerve tumors that can arise anywhere along the course of the nerve where Schwann cells are present. The clinical presentation and symptoms differ not only due to the location of tumor but also due to the neighboring anatomical structures it involves. Delay in diagnosis can increase the morbidity of the condition for the patient. Surgical excision is the definitive treatment and often it can be challenging to the surgeon. Our case demonstrates an unusual presentation of this relatively uncommon tumor that mimicked cholesteatoma causing lower motor neuron facial palsy which turned out to be a facial schwannoma later by biopsy.

Key words: Facial nerve, Facial palsy, Schwann cells, Schwannoma, Tympanic segment

INTRODUCTION

Facial nerve schwannomas are rare benign tumors which take its origin along the facial nerve. They can arise anywhere along the path of the facial nerve from the cerebellopontine angle to its extratemporal peripheral divisions. They constitute only 0.8% of the mass lesions within the petrous bone.^[1]

Facial schwannomas have diverse patterns of presentation. This can be attributed mainly to the varied location of the tumor and its closeness to the auditory apparatus.^[2] The surgical approach is primarily decided by the site of the tumor, its extent, and the involvement of the surrounding structures.

CASE REPORT

A 60-year-old diabetic female patient presented to the ear, nose, and throat outpatient department with complaints of recurrent episodes of bilateral ear discharge for the past

15 years which subsided with medications in each episode. For 4 months she had profuse left ear discharge, vertigo and progressive hard of hearing on the left side. She also noticed a recent onset of deviation of the angle of mouth to the right side on attempted smiling and difficulty in eye closure on the left side.

On otoscopy, both tympanic membranes had central perforations. The middle ear mucosa was found to be congested on both sides. The Rinne test was found to be negative for 256 Hz, 512 Hz, and 1024 Hz in both ears with the Weber test lateralized to the right side. The fistula test was negative bilaterally.

House-Brackmann grading of the lower motor neuron (LMN) facial palsy was Grade IV on the left side.^[3]

On otomicroscopy, discharge was cleaned from both ears, and a smooth pale yellowish mass was seen lying on the promontory protruding through the central perforation in the left middle ear along with mucopurulent discharge. The left ear swab yielded mixed bacterial growth on culture.

Hearing loss was found to be 65 dB on the right side and 50 dB on the left side, which were of conductive type.

High-resolution computed tomography (HRCT) of the temporal bone revealed soft-tissue opacification

Access this article online



www.ijss-sn.com

Month of Submission : 06-2019
Month of Peer Review : 07-2019
Month of Acceptance : 08-2019
Month of Publishing : 08-2019

Corresponding Author: Dr. S Vivek, Karottumadathil House, Opp Mount Sinai Hospital, Thodupuzha, Kerala, India

of the left middle ear, mastoid air cells, and antrum with deossification of the ossicles and with blunting of scutum suggestive of Chronic otitis media (COM) with cholesteatoma. On administration of contrast, no significant enhancement of this soft tissue was noted. Provisional diagnosis of a secondary acquired cholesteatoma was made.

The patient was hospitalized and started on intravenous antibiotics (injection ciprofloxacin and injection metronidazole) along with injection dexamethasone and other supportive measures. She was put on insulin for control of blood sugar. The patient was posted for left-sided mastoid exploration under general anesthesia. The mastoid antrum was approached through the post aural route. Mastoid air cells were few. The antrum was found to be contracted and filled with granulation tissue. The aditus was widened. The tympanomeatal flap was elevated. The posterosuperior meatal wall was curetted out. Soft-tissue mass was seen arising from the inferior surface of the tympanic segment of the facial nerve partially obscuring the view of remnant incus. Malleus handle was found to be foreshortened and was displaced anteriorly by the soft tissue. The same was carefully dissected from the sheath of the facial nerve. Decompression of the tympanic segment of the facial nerve was done. Granulation tissue was noted in the middle ear extending to the aditus. The attic wall was partially eroded. Hence, a canal wall down mastoidectomy was done. The mastoid cavity was smoothened. No traces of cholesteatoma were found in the middle ear and mastoid. The harvested temporalis fascia graft was tucked into the middle ear and was draped over the facial ridge and smoothened cavity. The postoperative period was uneventful. Histopathology report was that of a

schwannoma [Figure 1]. The postoperative period was uneventful. But the facial nerve palsy still persists after 6 months of follow up.

DISCUSSION

Facial schwannomas are uncommon benign tumors that can affect any age group. However, its incidence rises between the 3rd and 6th decade of life. The incidence is equal in both males and females.^[4]

The first reported case was in 1931 described by Schmidt, following that approximately 500 cases of facial nerve schwannoma have been published.^[4,5]

Facial nerve schwannoma often presents insidiously, and its presentation depends upon the site and extent of the lesion. Facial weakness is the most common presenting complaint often preceded by facial twitching.^[6] Facial schwannoma has been found as a causative factor in about 5% of patients suffering from Bell's palsy.^[7] The presenting symptoms in facial schwannomas can be categorized into three broad categories (a) symptoms related to facial nerve dysfunction, (b) hearing loss and (c) facial neuralgias.^[8] The hearing loss in these cases can be either conductive or sensorineural (cochlear or retrocochlear) in type. Retrocochlear type of hearing loss may be a presenting symptom of intracanalicular tumors. Aural polyp with ear discharge may be seen when the tumor arises from the mastoid portion of the facial nerve.^[6] Otalgia is a relatively uncommon presentation.

Audiological and vestibular function testing, Brainstem evoked response audiometry (BERA), HRCT scan of temporal bone, and magnetic resonance imaging (MRI) should be included in the diagnostic armamentarium of facial schwannomas. Radiological investigations help to identify the presence and assess the extent of the tumor. The role of MRI and computed tomography (CT) scan is complementary to each other.^[9] A high-resolution bone-targeted CT scan of the temporal bone is considered superior to MRI. Facial nerve enlargement indicates neoplastic change.^[2] The facial canal is best located by CT scan, and MRI demonstrates tumor size and extent. The diagnosis may be clinched by an intact facial canal on CT and high-signal intensity on T2-weighted MRI,^[10] while cholesteatoma appears as low intensity on T1-weighted imaging and high intensity on T2-weighted imaging. The facial nerve tumor in the internal acoustic meatus causes the radiological widening of the meatus which poses a diagnostic challenge in differentiating the tumor from the acoustic

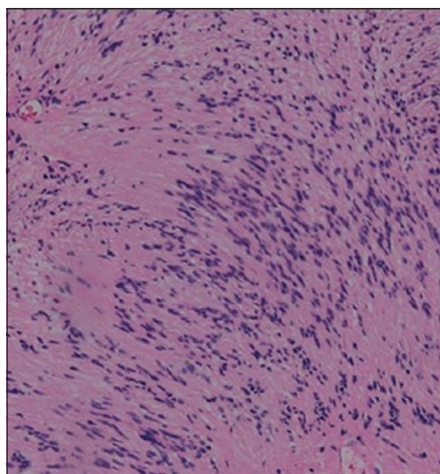


Figure 1: Microphotograph showing features of schwannoma with spindle-shaped cells having wavy-elongated nuclei with pointed ends. Both Antoni A (cellular) and Antoni B (hypocellular) patterns are seen



Figure 2: High-resolution computed tomography scan showing homogeneous soft-tissue mass filling the left middle ear. (a) Axial and (b) Coronal views

neuroma. Electroneurography can serve as a valuable tool in assessing the prognosis of post-operative facial palsy. Electromyography quantifies the residual motor function of the nerve and predicts the success of nerve repair.^[2]

Surgical excision is the preferred treatment. However, the timing for surgical intervention is controversial. Immediate surgical intervention is required in cases with progressive facial nerve palsy or paralysis, for large cerebellopontine angle tumors causing brainstem compression or hydrocephalus, and an invasion of inner ear structures by the tumor.^[11] However, patients without facial dysfunction pose the greatest surgical challenge because postoperatively patient almost always lands up in facial nerve palsy. Some authors have advocated a wait-and-watch policy in patients with normal facial nerve function and to intervene surgically when facial dysfunction happens.^[12,13] Those who are against this idea believe that delaying surgery makes the surgical approach difficult with more chances of post-operative complications and poor recovery of facial nerve function.^[2,14,15]

Surgical management primarily depends upon the site and extent of the tumor. The preservation of useful hearing should also be borne in mind before operating. Intracranial neuromas are mainly managed through middle fossa craniotomy in patients with useful hearing and translabyrinthine or transpetrosal route for patients without a useful hearing.^[2,11] Tumors on the tympanic or mastoid portion of the nerve can be managed by a transmastoid operation followed by a tympanoplasty. Tympanoplasty should be performed in patients with a serviceable hearing.^[2] In case of large tumors involving multiple segments, transmastoid and transtemporal approaches are combined where intracranial-intratemporal anastomosis is required.^[16]

House–Brackmann Grade III palsy is often the best possible outcome a patient can have regardless

of the timing of surgery or the type of nerve reconstruction.^[15,17]

Stereotactic radiosurgery is a new promising treatment modality. There exist only a few reports regarding its use in facial nerve tumors, unlike acoustic neuroma. However, the number of patients treated by this treatment option is increasing nowadays.^[18]

Both cholesteatoma and schwannoma appear as a homogeneous mass in the middle ear [Figure 2]. In this case, MRI was not done. MRI along with HRCT can give a better clue as to the nature of the lesion. This patient had an unusual presentation of chronic otitis media with LMN facial nerve palsy, mimicking a complication of acquired cholesteatoma clinically and radiologically. Histopathology alone helped to clinch the diagnosis correctly.

CONCLUSION

Cholesteatomas are commonly associated with long-standing chronic otitis media. A high clinical index of suspicion should be entertained when a patient with chronic otitis media presents with an LMN facial nerve palsy, and other differential diagnoses should be considered before any intervention.

REFERENCES

1. Rosenblum B, Davis R, Camins M. Middle fossa facial schwannoma removed via the intracranial extradural approach: Case report and review of the literature. *Neurosurgery* 1987;21:739-41.
2. Yamaki T, Morimoto S, Ohtaki M, Sakatani K, Sakai J, Himi T, *et al.* Intracranial facial nerve neurinoma: Surgical strategy of tumor removal and functional reconstruction. *Surg Neurol* 1998;49:538-46.
3. House JW, Brackmann DE. Facial nerve grading system. *Otolaryngol Head Neck Surg* 1985;93:146-7.
4. Rainsbury JW, Whiteside OJ, Bottrill ID. Traumatic facial nerve neuroma following mastoid surgery: A case report and literature review. *J Laryngol Otol* 2007;121:601-5.
5. McClelland S 3rd, Dusenbery KE, Higgins PD, Hall WA. Treatment of a facial nerve neuroma with fractionated stereotactic radiotherapy. *Stereotact Funct Neurosurg* 2007;85:299-302.
6. Pillsbury HC, Price HC, Gardiner LJ. Primary tumors of facial nerve. *Laryngoscope* 1983;93:1045-8.
7. Latack JT, Gabrielsen TO, Knake JE, Kemink JL, Graham MD, Gebarski SS, *et al.* Facial nerve neuromas: Radiologic evaluation. *Radiology* 1983;149:731-9.
8. Horn KL, Crumley RL, Schindler RA. Facial neurilemmomas. *Laryngoscope* 1981;91:1326-31.
9. Saada AA, Limb CJ, Long DM, Niparko JK. Intracanalicular schwannoma of the facial nerve: A manifestation of neurofibromatosis Type 2. *Arch Otolaryngol Head Neck Surg* 2000;126:547-9.
10. Vlahos L, Yiotakis J, Gouliamos A, Kotoulas G, Adamopoulos G. Localized mastoiditis simulating a facial nerve schwannoma on MRI. *J Laryngol Otol* 1994;108:1008-9.
11. Angeli SI, Brackmann DE. Is surgical excision of facial nerve schwannomas always indicated? *Otolaryngol Head Neck Surg* 1997;117:S144-7.
12. King TT, Morrison AW. Primary facial nerve tumors within the skull. *J Neurosurg* 1990;72:1-8.

13. Lipkin AF, Coker NJ, Jenkins HA, Alford BR. Intracranial and intratemporal facial neuroma. *Otolaryngol Head Neck Surg* 1987;96:71-9.
14. Saleh E, Achilli V, Naguib M, Taibah AK, Russo A, Sanna M, *et al.* Facial nerve neuromas: Diagnosis and management. *Am J Otol* 1995;16:521-6.
15. Symon L, Cheesman AD, Kawauchi M, Bordi L. Neuromas of the facial nerve: A report of 12 cases. *Br J Neurosurg* 1993;7:13-22.
16. Draf W, Samii M. Intracranial-intratemporal anastomosis of the facial nerve (author's transl). *Laryngol Rhinol Otol (Stuttg)* 1980;59:282-7.
17. Liu R, Fagan P. Facial nerve schwannoma: Surgical excision versus conservative management. *Ann Otol Rhinol Laryngol* 2001;110:1025-9.
18. Mackle T, Rawluk D, Walsh RM. Atypical clinical presentations of vestibular schwannomas. *Otol Neurotol* 2007;28:526-8.

How to cite this article: Santhi T, Vivek S. Facial Nerve Schwannoma – A Diagnostic and Surgical dilemma: A Case Report. *Int J Sci Stud* 2019;7(5):106-109.

Source of Support: Nil, **Conflict of Interest:** None declared.

A Rare Incidence of Solitary Extramedullary Plasmacytoma of Nasal Cavity

Harridas Manickam, C L Tang

Department of Otorhinolaryngology, Hospital Sibul, Sarawak, Malaysia

Abstract

Extramedullary plasmacytoma (EMP) is a rare neoplasm characterized by monoclonal proliferation of plasma cells. They originate in either bone – solitary osseous plasmacytoma, or in soft tissue – EMP. EMP represents <1% of all head and neck malignancies. The nasal cavity and nasal septum are the common sites of occurrence. This is a report of EMP in a 47-year-old gentleman. He presented with a 3-month history of the left nasal blockage and epistaxis. Examination revealed a large reddish to blackish mass of the left nasal cavity. The first biopsy, however, showed benign sinonasal polyps. Biopsy was repeated in view of suspicious clinical and computed tomography features. Histopathology from the second biopsy reported as EMP, confirmed by immunohistochemical techniques. The patient underwent bone marrow aspirate and trephine, skeletal survey, and laboratory investigations was performed to exclude multiple myeloma. Radiotherapy was initiated.

Key words: Benign sinonasal polyp, Extramedullary plasmacytoma, Multiple myeloma

INTRODUCTION

Extramedullary plasmacytoma (EMP) is an uncommon plasma cell neoplasm which occurs in soft tissue. It shows a preference for the upper respiratory tract, especially the nasal cavity and paranasal sinus (PNS). It corresponds to <10% of all plasmacytic tumors,^[1] representing <1% of all head and neck tumors^[2] and <0.5% of tumors of the aerodigestive tract.^[3] It typically arises in submucosal soft tissues of the upper respiratory tract and it is destructive with a tendency to local recurrence.

The clinical symptoms: Tumor or local edema in 80%, nasal obstruction in 35%, epistaxis in 35%, localized pain in 20%, proptosis in 15%, rhinorrhea in 10%, regional lymphadenopathy in 10%, and paralysis of the VI cranial nerve in 5% of cases.^[2,4] To exclude multiple myeloma (MM) or plasmacytoma of the bone, a systemic work-up and follow-up of the patient are mandatory, including serum protein electrophoresis, urinalysis for the Bence-Jones protein, skeletal survey, and bone marrow biopsy.

The treatment of choice for EP is surgery and radiation therapy (RT) with a dose of 40–50 Gy over a 4-week period, the disease is highly radiosensitive.^[1,5]

Overall, most studies report high local control rates of approximately 80–100% with moderate doses.^[6]

CASE REPORT

A 42-year-old male underlying schizophrenia, presented with epistaxis over the left nostril for 3 months associated with nasal blockage. On physical examination, cranial nerve was intact, there was no external deformity. Nasoendoscope showed a dark reddish, well-lobulated mass occupying whole left nasal cavity [Figure 1], unable to visualize the origin of the mass. The right nostril was clear and bilateral for no mass seen. There were no neck nodes palpable. Biopsy was taken and reported as benign sinonasal polyp. Computed tomography (CT) PNS done and showed enhancing mass arising from the left nasal cavity measuring (4.7 × 3.6 × 4.8cm). Superiorly, the mass extended into the left anterior ethmoidal cells and frontal recess, left orbital wall intact, laterally into left maxillary ostium, and obliterates left ostiomeatal complex. Medially, it caused septal deviation to the right, inferiorly, until the level hard palate, with inferoposterior margin of the mass compresses onto the left torus tubarius. Anteriorly, the mass protruded into the left nostrils. Posteriorly, the mass extends to the posterior left ethmoidal air cells, obliterates

Access this article online



www.ijss-sn.com

Month of Submission : 06-2019
Month of Peer Review : 07-2019
Month of Acceptance : 08-2019
Month of Publishing : 08-2019

Corresponding Author: Dr. Harridas Manickam, Department of Otorhinolaryngology, Hospital Sibul, Sarawak, Malaysia.

the sphenothmoidal recess [Figures 2 and 3]. Biopsy was repeated under geometric algebra due to suspicious mass and reported as EMP as CD 138 positive cells with kappa light chain restriction. The patient was referred to medical team and a systemic work-up to exclude MM performed.

Renal profile was normal, blood profile shows no evidence of bone marrow infiltration by malignancy or plasma cell myeloma. Serum and urine protein electrophoresis shows IgA kappa paraproteinemia of 5.7 g/dL in the beta zone with no immunoparesis. Serum and urine free light chain showed no light chain detected. Bone marrow needle biopsy and skeletal survey were negative. CTNTAP showed no evidence of lesion/mass in the thorax or abdomen. Thus, a diagnosis of extramedullary nasal plasmacytoma was made.

The patient received radiotherapy with a radiation dose of 40 Gy in 15 fractions. The tumor reduces in size post-radiotherapy and currently under surveillance follow-up

with nasoendoscope and CT scan. At present, 2-month post-radiotherapy, nasoendoscope showed the nasal mass remains the same size [Figure 4].

DISCUSSION

EMP is a rare neoplasm characterized by monoclonal proliferation of plasma cells outside bone marrow. It is defined as a soft tissue plasma cell tumor occurring in the absence of systemic signs of MM, such as bone osteolytic lesions, plasma cell infiltration in bone marrow, lytic bone lesion, or serum or urine myeloma protein (M-component). The most frequently affected areas in the upper aerodigestive tract are the nasal cavity or PNS (43.8%), followed by nasopharynx (18.3%), oropharynx (17.8%), and larynx (11.1%) due to its rich lymphatic tissue.^[7]

Due to its presentation in the submucosa of the aerodigestive tracts, it is suggested that the etiology of

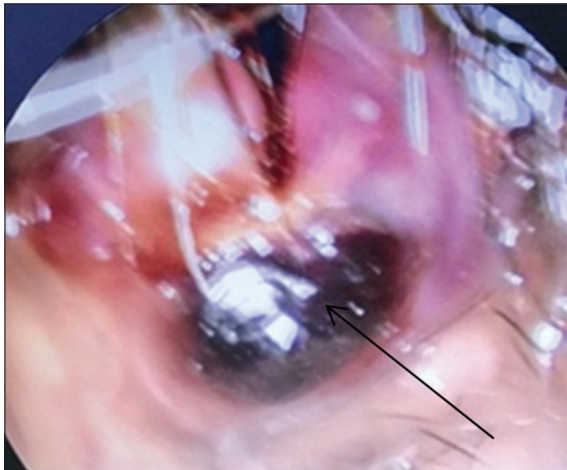


Figure 1: Nasoscopy shows the left anterior nasal occupied with mass in red color – black arrow (before radiotherapy)



Figure 2: Computed tomography paranasal sinus shows homogenous enhancing mass (black arrow) arising from the left nasal cavity extends into the left maxillary ostium, anterior ethmoidal air cells, and frontal recess



Figure 2: Computed tomography scan axial view showing homogenous mass (black arrow) filling up the left nasal cavity. Orbital wall intact

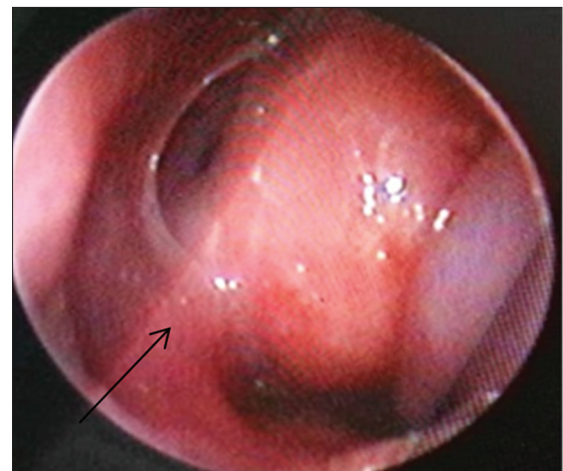


Figure 4: Nasoscopy shows the left nasal mass confined over the inferior turbinate – black arrow (post-radiotherapy)

EMP may be related to chronic stimulation caused by inhaled irritants or viral infection.^[4] The most common clinical findings are as follows: Blocked nose, soft tissue mass (fleshy, yellowish-grey to dark red sessile, polypoid, or pedunculated), epistaxis, nasal discharge, pain, more rarely cranial nerve palsy, and neck lymphadenopathy.

The diagnosis of EMP depends on clinical suspicion such as unilateral nasal mass and biopsy to exclude other nasal tract malignancy. The differential diagnosis includes other nasal tract malignancies such as inverted papilloma, pleomorphic adenoma, squamous cell carcinoma, adenocarcinoma, adenoid cystic carcinoma, melanoma, esthesioneuroblastoma, rhabdomyosarcoma, lymphoma, sinonasal undifferentiated carcinoma, and Wegener granulomatosis.

In this case, the initial biopsy shows that inflammatory polyps could be due to superficial punch biopsy. Deeper biopsy under general anesthesia subsequently showed EMP. Deep biopsy should be performed because the tumor is submucosal and the mucosal lining can become thicker due to an inflammatory reaction. In cases, where clinical appearance is suspicious, a repeated biopsy is required.

A study using immunohistochemical methods confirmed the plasmatic nature of the cells with cell markers, for example, CD 138, which indicates the necessity of performing an evaluation for a differential diagnosis from other cancers such as melanoma, undifferentiated carcinoma, and pituitary adenoma.^[8]

In all case of EMP, a systemic work-up including blood profile, renal and liver function, serum and urinary protein electrophoresis, serum immunoglobulin level, skeletal survey, and bone marrow examination must be performed to exclude a systemic disease such as MM.

RT is the treatment of choice in EMP localized in the head and neck, not extending through the floor of the anterior and middle cranial fossae and into the orbit. The British Society for Hematology recommends initial radiation treatment with 40 Gy in 20 fractions with a 2 cm margin for tumors smaller than 5 cm and 50 Gy in 25 fractions for larger tumors, whereas the role of surgery is usually limited to biopsy and to excision of residual disease.^[1,5] The prognosis for patients with EMP is 5-year survival rates between 30 and 82% and 10-year rates 50–90%.

Chemotherapy is considered only in patients with tumors larger than 5 cm, high-grade tumors, refractory and/or relapsed disease, and in case of progression to MM.^[5,9]

The rate of conversion of EMP to MM is lower than other plasma cell neoplasms, such as SPB, with rates reported to be

between 11 and 33% over 10 years.^[9] Hence, it is recommended that patients receive regular follow-up after diagnosis of EMP due to the relatively high risk of conversion.

Myeloma guidelines by the Italian Association of Medical Oncology (AIOM)^[10] suggest the first screening 45–60 days after radiotherapy by serum examinations, then every 3 months for the 1st year, subsequently, every 6 months by serum, radiological, and bone marrow examinations, if necessary. Due to the high risk of conversion, D'Aguillo *et al.*^[9] proposed a regular screening for MM every 6 weeks for the first 6 months after diagnosis of EMP and then periodically, but without a specific timing. For these reasons, we propose a follow-up protocol consisting of nasal endoscopy and serum examinations every 3 months, and imaging study with magnetic resonance imaging (MRI) 3 months after radiotherapy and subsequently every 6 months/year for 5 years; after 5 years, we propose serum examinations and nasal endoscopy every 6 months and MRI every year. We recommend a biopsy only in cases of clinical and instrumental suspicion of recurrence.

In our patient, the location of tumor involving only the left anterior ethmoidal air cells and frontal recess. The left orbital wall is still intact with no tumor extension intraorbitally led us to performed only radiotherapy which the size of tumor significantly reduced. Currently patient under 3 monthly Otorhinolayngology follow up post radiotherapy and nasoendoscopy shows the mass significantly reduce in size as [Figure 4] with further systemic workout shows no multiple myeloma.

CONCLUSION

EMP is a rare, aggressive tumor that mainly affects the submucosa of the nasal cavity and PNS. This tumor can remain in the area of the early lesion, advance to neighboring areas, or even spread. The otorhinolaryngologist must identify the lesion and refer the patient for hematologic monitoring; moreover, a multidisciplinary approach is required to differentiate between localized disease and blood dyscrasias with a poor prognosis, such as MM. Treatment with radiotherapy is effective because the tumor is radiosensitive, and surgery may occasionally be used to complement the treatment. Controlled clinical trials are needed to establish a definitive treatment of choice for the management of these patients. The patient should always be monitored for a long period of time.

REFERENCES

1. Fernandes AM, Podovani JA, Maniglia JP. Plasmocitoma extramedular de nasofaringe: Relato de um caso e revisão da literatura. Rev Bras

- Otorrinolaringol 1998;64:296-8.
2. Koppersmith RB. Extramedullary Plasmacytoma of the Head and Neck. Available from: <http://www.bcm.edu/oto/grand/32896.html>. [Last accessed on 2019 Jun 14].
3. Granato L, Petitto JW, Prospero JD. Plasmocitoma extramedular do aparelho respiratório apresentação do caso. Rev Bras Otorrinolaringol 1977;43:214-23.
4. Kapadia SB, Desai U, Cheng VS. Extramedullary plasmacytoma of the head and neck. A clinicopathologic study of 20 cases. Medicine (Baltimore) 1982;61:317-29.
5. Batsakis JG, Medeiros JL, Luna MA, El-Naggar AK. Plasma cell dyscrasias and the head and neck. Ann Diagn Pathol 2002;6:129-40.
6. Sasaki R, Yasuda K, Abe E, Uchida N, Kawashima M, Uno T, *et al.* Multi-institutional analysis of solitary extramedullary plasmacytoma of the head and neck treated with curative radiotherapy. Int J Radiat Oncol Biol Phys 2012;82:626-34.
7. Alexiou C, Kau RJ, Dietzfelbinger H, Kremer M, Spiess JC, Schratzenstaller B, *et al.* Extramedullary plasmacytoma: Tumor occurrence and therapeutic concepts. Cancer 1999;85:2305-14.
8. Creston JE, Creek W. The otolaryngologic manifestations of multiple myeloma. Laryngoscope 1978;88:1320-32.
9. D'Aguillo C, Soni RS, Gordhan C, Liu JK, Baredes S, Eloy JA, *et al.* Sinonasal extramedullary plasmacytoma: A systematic review of 175 patients. Int Forum Allergy Rhinol 2014;4:156-63.
10. Pinotti G, Proserpio I, Brighen S, Chini C, Mangiacavalli S, Olivares C, *et al.* Linee Guida Mieloma. In: Linee Guida AIOM. Italian Association of Medical Oncology-AIOM; 2015.

How to cite this article: Manickam H, Tang CL. A Rare Incidence of Solitary Extramedullary Plasmacytoma of Nasal Cavity. Int J Sci Stud 2019;7(5):110-113.

Source of Support: Nil, **Conflict of Interest:** None declared.