

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

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Abstract

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

Methods: A total of 60 patients aged 3-6 years with ASA Grade I-II were enrolled in this study. They were randomized to receive either ropivacaine (0.1% - 1 ml/kg) or ropivacaine with clonidine (0.1% - 1 ml/kg with 1 mcg/kg) in caudal analgesia. Hemodynamic parameters heart rate (HR), systolic blood pressure (SBP) and diastolic blood pressure (DBP), and oxygen saturation (SpO₂) were recorded during and after the procedure. The duration of analgesia and sedation score was noted in the post-operative period.

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

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

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

INTRODUCTION

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

but regional anesthesia is the cornerstone of modern anesthesia.

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

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

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

Ropivacaine has been extensively used for regional anesthesia in adult and older children⁵ due to its wider margin of safety than bupivacaine with lower potential for central nervous and cardiovascular side effects. Ropivacaine has greater sensory and fewer motor effects, and this could allow rapid mobilization after surgery^{6,7} when compare to bupivacaine. Recent studies have showed that reducing the concentration of ropivacaine would provide an additional margin of safety as well as reduces the incidence of the unwanted motor blockade.⁸ Addition of adjuvants such as epinephrine, opioids, ketamine, and alpha 2 agonist prolongs the duration of caudal analgesia.⁹⁻¹¹ Opioids have the risk of delayed respiratory depression.

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

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

METHODS

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

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

All children of both the groups were pre-medicated with 0.5 mg/kg of midazolam orally. In the operating room, monitors were attached, and the baseline reading of heart rate (HR), systolic blood pressure (SBP) and diastolic blood pressure (DBP), oxygen saturation (SpO₂) were recorded. Inhalational induction was done with 8% sevoflurane in oxygen, and intravenous access was secured. Fentanyl 2 mcg/kg was administered intravenously for analgesia. The airway was maintained using a face mask, laryngeal mask airway, or endotracheal tube according to anesthesiologist choice, and the anesthesia was maintained with 1-2% sevoflurane in O₂-N₂O.

After induction, the children were placed in the lateral decubitus position the caudal space was identified, and the appropriate drug was injected as per the group using a 23 G Hypodermic needle. Total volume is being constant at 1 ml/kg in both the groups. After placing a caudal block, the patient was turned supine. The anesthesia was maintained with 1-2% sevo in a mixture of 66% N₂O and 33 % O₂. The surgical incision was made 5 min after caudal placement of the drug, and the duration of the surgery was noted. Intravenous fluids (isolyte-P) were administered according to body weight and the fasting status. Intra operative continuous monitoring of HR, SBP, DBP, SpO₂ was undertaken throughout the surgical procedure, and the record was made at 10 min interval until the end of the surgery and subsequently was monitored for 2, 4, 6, 8, 10, 12, and 24 h in the post-operative period.

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

Respiratory depression was defined as a decrease in SpO₂ to <93% and was treated with oxygen by mask 6 L/min. Hypotension was defined as a decrease in mean arterial blood pressure to <30% from the baseline and was treated with a bolus of 10 ml/kg crystalloid. Bradycardia was defined as HR <15% from the baseline and was treated with 10 mcg/kg of atropine. The sedation score was graded as 0 for awake, 1 for mild (arousable by voice), 2 for moderate (response to physical shake), and 3 for severe (unarousable). The sedation score was noted every 15 min up to 2 h in post-anesthesia care unit.

RESULTS

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

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

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

DISCUSSION

We conducted this prospective, randomized study in an attempt to evaluate whether administration of clonidine to a commonly administered balanced anesthetic regimen

improves the post-operative analgesia in pediatric patients undergoing lower abdominal surgeries.

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

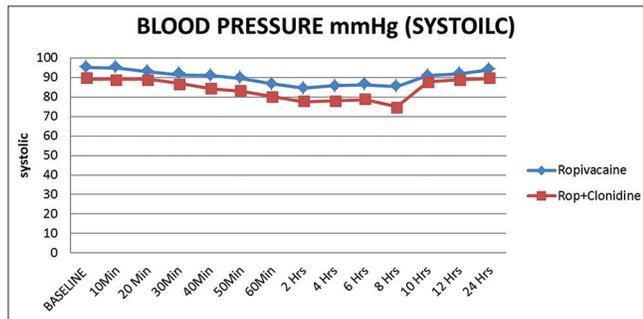
Table 1: FLACC scale

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

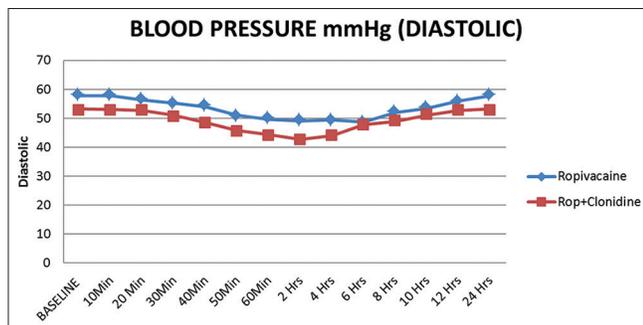
Score 0: No pain, 1-3: Mild pain, 4-7: Moderate pain, 8-10: Severe pain, FLACC: Face, Legs, Cry, Consolability

Table 2: Demographic data

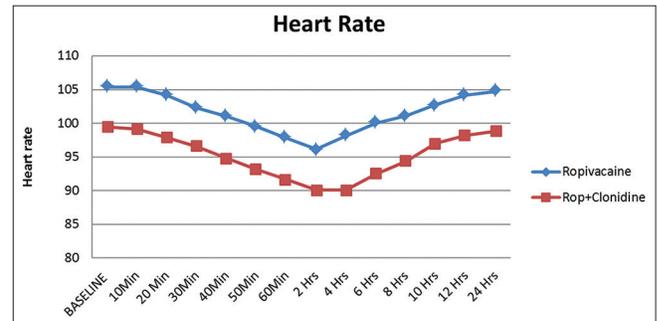
Parameters	Group R (n=30)	Group RC (n=30)
Age (years)	4.37±1.47	4.90±1.58
Gender		
M%/F%	67/33	80/20
Weight (kg)	17±5.19	18.63±4.61
Duration of surgery (mins)	37±10.55	31.83±16



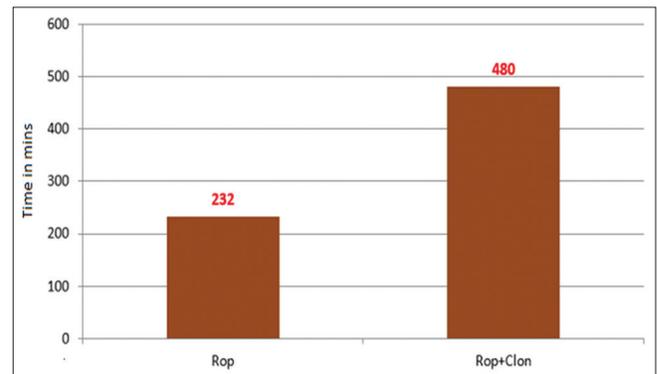
Graph 1: Mean systolic blood pressure



Graph 2: Mean diastolic blood pressure



Graph 3: Mean heart rate



Graph 4: Mean duration of analgesia

Table 3: Sedation score

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

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

Clonidine, an α_2 agonist, has been used as additive to local anesthetics, e.g., Bupivacaine. It has been widely used as an adjuvant to local anesthetics to enhance the quality of analgesia in the post-operative period. So, from the above studies, we decided to take clonidine as a caudal additive

along with ropivacaine with better safety profile. The dose of clonidine was based on the study conducted in the pediatric population though no ideal dose of clonidine via the caudal route is yet recommended. A volume of 1 ml/kg was chosen for both the groups because only sub-umbilical surgeries were included in the study. The sub-umbilical surgeries require T_{10} and below levels for analgesia.

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

In our study, a mixture of 0.1% ropivacaine with 1 mcg/kg of clonidine has been used to improve the duration and quality via the caudal route. Different doses of ropivacaine along with clonidine 1-2 mcg/kg has been studied in children for a single shot caudal epidural so as to enhance the quality of analgesia in the post-operative period. Ivani *et al.*, state that addition of clonidine 2 mcg/kg to ropivacaine 0.1% provides an increase in duration of analgesia when compared with plain ropivacaine 0.2%. In 2010, Bajwa *et al.*, found that the mean duration of analgesia was 8.5 h with 0.25% plain ropivacaine and 13.4 h with ropivacaine and clonidine 2 mcg/kg which was significantly prolonged. In 2012, Manickam *et al.*, found that mean duration of analgesia was 243.37 min with 0.1% ropivacaine and 590.25 min with 0.1% of ropivacaine with 1 mcg/kg clonidine and 388.25 min with 0.2% ropivacaine. In our study, we found that caudal ropivacaine alone provides an excellent analgesia in the early post-operative period, with the effect lasting a few hours (232 min) of caudal placement of drug. However, the addition of clonidine prolongs the mean duration of analgesia for 480 min. The addition of clonidine prolongs the duration of analgesia due to several mechanism. The anti-nociceptive action is due to the direct suppression of the spinal cord nociceptive neurons. Clonidine also cross the blood brain barrier and interacts with α_2 adrenoreceptors at spinal and supra-spinal sites to provide analgesia. It also suppresses the neurotransmission in peripheral sensory Adelta and C fibers. It acts on $\alpha_2\beta$ adrenoreceptors located at the peripheral vascular smooth muscles causes vasoconstriction.

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

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

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

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

CONCLUSION

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

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