Original Article

Efficacy of clonidine as an adjuvant to ropivacaine for caudal analgesia in children undergoing subumbilical surgery

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Abstract

Context: The use of clonidine as an adjuvant to ropivacaine in different concentrations through the caudal space has been shown to improve the analgesic efficacy of local anesthetics.

Aims: The purpose of our study was to compare the efficacy of ropivacaine 0.1% with clonidine 1 mcg/kg to that of plain 0.1% and 0.2% ropivacaine for caudal analgesia in children.

Settings and Design: Prospective, double blind, randomized controlled trial.

Materials and Methods: Sixty children in the age group of 1–6 years undergoing subumbilical surgeries were included in the study. Group A received 1 ml/kg of 0.1% ropivacaine, group B received 1 ml/kg of 0.1% ropivacaine with clonidine 1 mcg/kg, and group C received 1 ml/kg of 0.2% ropivacaine.

Results: The mean duration of analgesia was 243.7 ± 99.29 min in group A, 590.25 ± 83.93 min in group B, and 388.25 ± 82.35 min in group C. The duration of analgesia was significantly prolonged in group B compared to groups A and C with the *P value* of 0.001. At 8 h, all the 20 children in group A had received the first rescue analgesic compared to 18 children in group C and 3 children in group B. The duration of motor blockade after extubation was 30.6 ± 7.8 min and was noted only in group C. Only 1 child in group B received two rescue medications compared to 15 (75%) children in group A and 8 (40%) children in group C. None of the groups were treated for bradycardia or hypotension and no significant sedation was noted.

Conclusions: Clonidine 1 mcg/kg with ropivacaine 0.1% prolongs the duration and quality of analgesia compared to plain ropivacaine 0.1% and 0.2% without any significant sedation.

Key words: Caudal analgesia, clonidine, ropivacaine

Introduction

Caudal epidural block remains the standard of care for providing postoperative analgesia in children. The search for the ideal adjuvant and a local anesthetic with wide margin of safety, minimal motor blockade, and prolonged period of analgesia continues till date.[1-4] Ropivacaine produces a greater differential blockade with less toxic effects,[5] but moderate concentrations of ropivacaine (0.25–0.375%) cause unwanted motor blockade in the initial postoperative period.[6-8] We undertook the study to assess the efficacy of ropivacaine 0.1% with the addition of clonidine (1 mcg/kg) to that of ropivacaine 0.1% and 0.2% in providing analgesia following single-shot caudal epidural block in children.

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Materials and Methods

The study was a prospective, double-blind, randomized, controlled trial. The sample size was based on the previous studies.[9,10] The calculation revealed that 15 subjects per group were needed to detect a difference in the duration of analgesia as small as 1.5 times the standard deviation with the power of 0.8 and significance level of 0.05. The sample size was increased by 30% (20 per group) to account for the skew deviations of the variables in the study.

After approval of the institutional ethics committee and written informed consent from parents, children in the age group of 1–6 years under ASA status I and II, scheduled for subumbilical surgeries were enrolled in the study. Children with bleeding disorders, neuromuscular diseases, bony abnormalities of the spine, and infection at the site

of caudal analgesia were excluded from the study. Sixty children were randomly allocated in to three groups: group A, group B, and group C based on picking lots from a sealed bag. All children received 0.5 mg/kg of midazolam orally as premedication 30 min prior to induction of anesthesia. The intraoperative monitors included electrocardiogram, pulse oximetry, noninvasive blood pressure, and end tidal carbon dioxide Inhalational induction was done with 8% sevoflurane in oxygen and intravenous access was secured. Fentanyl 2 mcg/kg was administered intravenously for analgesia. Anesthesia was maintained with 1–2% sevoflurane in oxygen–nitrous oxide (1:3) mixture. The airway was maintained using a face mask, laryngeal mask airway, or endotracheal tube. Maintenance of the airway was left to the decision of the anesthesiologist. No additional fentanyl was given.

After induction of anesthesia, 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 22G needle. The preparation of drug was done by one anesthesiologist and the caudal block was performed by another. The latter also monitored the intraoperative variables and scores. Group A received 1 ml/kg of 0.1% ropivacaine, group B received 1 ml/kg of 0.1% ropivacaine with clonidine 1 mcg/ kg, and group C received 1 ml/kg of 0.2% ropivacaine. The surgical incision was made 5 min after caudal placement of the drug and the duration of surgery was noted. The intraoperative hemodynamic and respiratory parameters were monitored and documented every 5 min till awakening. The duration of anesthesia was noted in all the three groups. The pain score and motor block were noted at extubation. The degree of motor blockade was assessed by Bromage scale every 10 min and the time taken for complete recovery of motor blockade was recorded. The heart rate, blood pressure, respiratory rate, pain score, and sedation score were assessed in the postoperative period for 2 h. Pain score was assessed using face, legs, activity, cry, consolability (FLACC) scale [Table 1] and was noted at 0, 1, 2, 3, 4, 5, 6, 8, 10, 12, and 24 h postoperatively. The follow-up in PACU and ward for FLACC scale was noted separately by the anesthesiologist in the PACU and a nurse in the ward who were blinded.

The time from caudal placement of drug to the first recording of a FLACC scale > 3 was taken as the duration of analgesia. Rescue analgesia was provided with paracetamol suppository 40 mg/kg whenever the pain score was recorded as >3. The number of rescue analgesic doses required for 24 h were also noted. Respiratory depression was defined as a decrease of SpO_2 to <93%. Hypotension was defined as mean arterial blood pressure 30% less than the baseline value and was treated with a bolus of 10 ml/kg crystalloid. Bradycardia was defined as heart rate less than 15% from the base line value. The sedation score was graded as 0 for awake, 1 for mild (arousable by voice), 2 for moderate (arousable to pain), and 3 for unarousable. The sedation score was assessed every 15 min and documented for 2 h in the PACU. The data collected were tabulated and analyzed using appropriate statistical tests by a statistician.

Results

The age, weight, and the duration of surgery in the study groups were compared using the independent *t*-test. The type of surgery was compared between the three groups using the Pearson's chi-square test. The study groups were comparable with respect to age, weight, and duration of surgery [Table 2]. The type of surgery was similar in all the three groups [Table 3]. The duration of analgesia between the groups was compared using the Analysis of Variance (ANOVA) test. The mean duration of analgesia was 243.7 ± 99.29 min in group A, 590.25 ± 83.93 min in group B, and 388.5 ± 82.35 min in group C. The duration of analgesia was significantly prolonged in group B compared to groups A and C with the *P* value of 0.001 [Figure 1]. The motor scores at extubation were compared using the Pearson's chi-square test. The motor blockade at extubation was observed in all the children of group C with a duration of 30.6 ± 7.8 min [Table 4] and none of

Table 1: FLACC Score

Parameter	0	1	2
Face	No expression	Occasional grimace	Frequent to constant quivering chin
Legs	Normal position or relaxed	Uneasy restless, tense	Kicking or legs drawn up
Activity	Lying quiet	Squirming, shifting back and forth,tense	Arched, 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, activity, cry, consolability

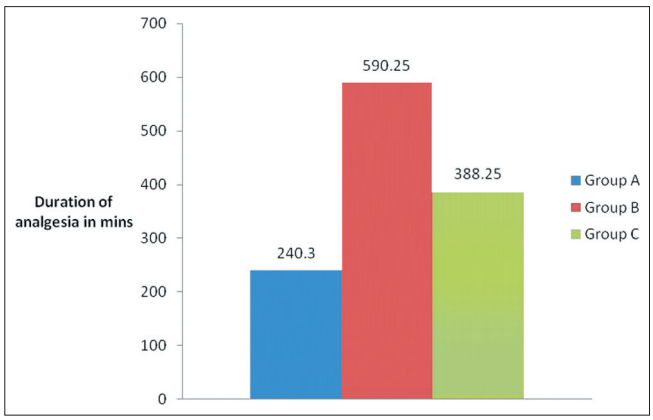

Figure 1: The mean duration of analgesia in the three groups

the children had motor blockade in group A and group B. The pain score was compared using the Pearson's chi-square test. There was a significant difference in the pain score of children in group B at 2, 4, 6, and 8 h postoperatively when compared to group A and group C. At 8 h, only 3 children in group B had pain score more than 3 compared to 18 children in group C and all 20 children in group A [Table 5]. The requirement of rescue medications was compared between the three groups using Pearson's chi-square test and it was found to be significant with group B receiving less number of analgesics, followed by group C and group A. One child in group B received two rescue medications compared to group A, in which 15 (75%) children received two rescue medications, followed by group C where 8 (40%) children received two rescue medications [Figure 2].

The mean heart rate and blood pressure at 0, 5, 10, 15, 30, 45, 60, and 75 min in the intraoperative period between groups were compared using the ANOVA test. The mean heart rate and blood pressure were lower in group B at different time intervals compared to group A and group C with a *P* value of 0.02 [Figures 3 and 4]. None of the children in group B were treated for hypotension and bradycardia as per the criteria defined in our study. Three children in group B and two children in group C had a sedation score of 1. None of the children had sedation score more than 1 in the PACU.

Table 2: Demographic data and duration of surgery in the three groups expressed as mean with standard deviation

	Group A (n = 20)	Group B (n = 20)	Group C (n = 20)
Age (years)	3.62 ± 1.5	3.77 ± 1.5	3.4 ± 1.5
Weight (kg)	12.70 ± 2.63	13.90 ± 2.93	13.29 ± 2.75
Duration of surgery (min)	58.75 ± 23.94	59.35 ± 21.29	61.50 ± 20.59

Table 3: Type of surgeries in the three groups

Type of surgery	Group A	Group B	Group C
Circumcision	6	4	3
Urethroplasty	2	1	4
Hernioplasty	4	5	4
Hypospadias Correction	3	4	3
Hydrocele repair	5	6	6

Table 4: Motor blockade in different groups expressed as number of patients

Motor score	Group A	Group B	Group C
0	20	20	0
1			1
2			9
3			10
Duration of motor blockade (min)			30.6 ± 7.8

Table 5: Pain score more than 3 at different time intervals prior to rescue medication

Number of patients with pain score>3 at	Group A (n = 20)	Group B (n = 20)	Group C (n = 20)
2 h	1	0	0
4 h	9	0	1
6 h	10	1	12
8 h	0	2	6
10 h	0	12	1
12 h	0	5	0

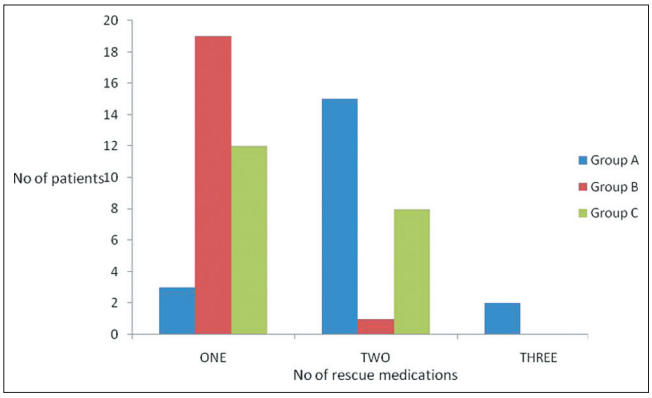

Figure 2: The number of rescue medications received by children in different groups

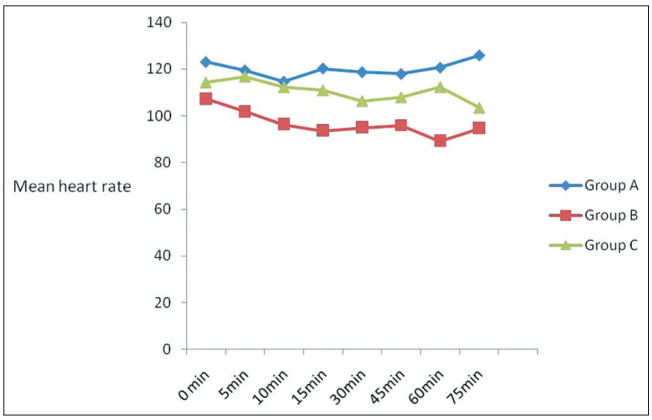

Figure 3: The mean heart rate at different time intervals in the intraoperative period

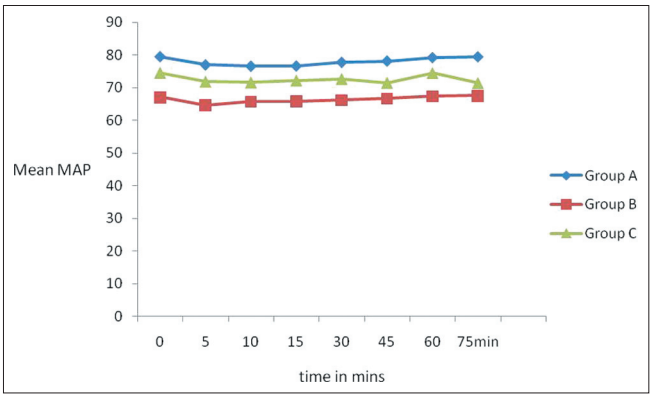

Figure 4: The mean arterial pressures at different time intervals in the intraoperative period

Discussion

The minimum concentration of ropivacaine, under general anesthesia, required to provide caudal analgesia in children is reported as 0.11%.[11] Use of ropivacaine 0.1% is not as effective as 0.2% ropivacaine in terms of duration and quality of analgesia in the postoperative period following single-shot caudal epidural block in children under going subumbilical surgeries.[10,12,13] Clonidine has been used widely as an adjuvant to local anesthetics to enhance the quality of analgesia in the postoperative period.[2,3] We hypothesized that addition of clonidine at 1 mcg/kg to 0.1% ropivacaine would enhance the quality of analgesia and prolong the duration of pain relief as compared to plain 0.1% ropivacaine while avoiding motor blockade that occurs with 0.2% ropivacaine. A volume of 1 ml/kg was chosen in all the three groups as only subumbilical surgeries were included, requiring T10 and below levels for analgesia.[14] The dose of clonidine was based on the studies in the pediatric population though no ideal dose of clonidine via the caudal epidural route is yet recommended.[2,3,15-18]

The different doses of ropivacaine along with clonidine 1–2 mcg/kg have been studied in children for single-shot caudal epidural to enhance the quality of analgesia in the postoperative period. Ivani *et al.*[9] reported an increased duration along with improved quality of analgesia with the addition of clonidine (2 mcg/kg) to ropivacaine 0.1% compared to plain 0.2% ropivacaine alone. Bajwa *et al.*[16] found that the mean duration of analgesia was 8.5 h with 0.25% plain ropivacaine and 13.4 h with 0.25% ropivacaine and clonidine 2 mcg/kg. In our study, the mean duration of analgesia was 590 min in the clonidine–ropivacaine group, which was significantly prolonged compared to plain 0.1% and 0.2% ropivacaine. The requirement of rescue medication was less in the clonidine–ropivacaine group. Luz *et al.*[13] compared ropivacaine 0.1% and 0.15% with bupivacaine 0.2% and concluded that ropivacaine was less effective in providing postoperative analgesia. Bosenberg *et al.*[10] compared the efficacy of caudal ropivacaine 1, 2, and 3 mg/ml and found the pain score at 4 h higher in 0.1% compared to 0.2 % and 0.3% ropivacaine. We found similar results in our study.

Khalil *et al.*[12] compared varying doses of ropivacaine in caudal anesthesia and found motor blockade with 0.2% ropivacaine in the early postoperative period. We also observed postoperative motor blockade in children who received 0.2% ropivacaine. The persistence of motor blockade in the postoperative period is undesirable in children. Though the blockade was observed only for a short duration, the advantage of using ropivacaine with better sensory and motor discrimination was lost with use of 0.2% ropivacaine and the duration of analgesia was also less compared to the ropivacaine–clonidine group.

Epidural administration of clonidine can cause bradycardia due to parasympathetic predominance and hypotension as a result of inhibition of preganglionic sympathetic fibres. Eisenach *et al.*[17] reported decrease in mean arterial pressure and heart rate within 15–30 min after injection of clonidine in the epidural space. In our study, the mean arterial pressure and heart rate in the clonidine group were less compared to plain ropivacaine. However, none of the children required intervention as the hemodynamic parameters were not below the defined criteria.

Lee *et al.*[19] noted significant sedation when 2 mcg/kg clonidine was added to caudal bupivacaine and concluded that the sedative effects in children reflected the improved quality of analgesia offered by clonidine. Various other studies have however shown the absence of significant sedation with use of clonidine at 2 mcg/kg in the caudal space.[9,16] In our study the children had only mild sedation which was not significant statistically.

To conclude, the addition of clonidine 1 mcg/kg to 0.1% ropivacaine provided increased duration and better quality of pain relief with no motor blocakade and sedation compared to plain 0.1% ropivacaine and 0.2% ropivacaine.

References

1. Tsui BC, Berde CB. Caudal analgesia and anaesthesia techniques in children. Curr Opin Anaesthesiol 2005;18:283-8.
2. Lonnqvist PA. Adjuncts to caudal block in children–Quo vadis? Br J Anaesth 2005;95:431-3.
3. Yildiz TS, Korkmaz F, Solak M, Toker K. Clonidine addition prolongs the duration of caudal analgesia. Acta Anaesthesiol Scand 2006;50:501-4.
4. Dobereiner EF, Cox RG, Ewen A, Lardner DR. Evidence-based clinical update: Which local anesthetic drug for pediatric caudal block provides optimal efficacy with the fewest side effects? Can J Anesth 2010;57:1102-10.
5. Zink W, Graf BM. The toxicity of local anesthetics: The place of ropivacaine and levobupivacaine Curr Opin Anaesthesiol 2008;21:645-50.
6. Koinig H, Krenn CG, Glaser C, Marhofer P, Wildling E, Brunner M. The dose-response of caudal ropivacaine in children. Anesthesiology 1999;90:1339-44.
7. Da Conceicao MJ, Coelho L, Khalil M. Ropivacaine 0.25% compared with bupivacaine 0.25% by the caudal route. Paediatr Anaesth 1999;9:229-34.
8. Da Conceicao MJ, Coelho L. Caudal anaesthesia with 0.375% ropivacaine or 0.375% bupivacaine in paediatric patients. Br J Anaesth 1998;80:507-8.
9. Ivani G, De Negri P, Conio A, Lonnqvist PA. Ropivacaine-clonidine combination for caudal blockade in children. Acta Anaesthesiol Scand 2000;44:446-9.
10. Bosenberg A, Thomas J, Lopez T. The efficacy of caudal ropivacaine

1, 2, 3 mg/ml for postoperative analgesia in children. Paediatr Anaesth 2002;12:53-8.
11. Deng XM, Xiao WJ, Tang GZ, Luo MP, Xu KL. The minimum local anesthetic Concentration of ropivacaine for caudal Analgesia in Children. Anesth Analg 2002;94:1465-8.
12. Khalil S, Lingadevaru H, Bolos M, Rabb M, Matuszczak M, Maposa D. Caudal regional anesthesia, ropivacaine concentration, postoperative analgesia, and infants. Anesth Analg 2006;102:395-9.
13. Luz G, Innerhofer P, Häussler B, Oswald E, Salner E, Sparr H. Comparison of ropivacaine 0.1% and 0.2% with bupivacaine 0.2% for single-shot caudal anaesthesia in children. Paediatr Anaesth 2000;10:499-504.
14. Schrock CR, Jones MB.The dose of caudal epidural analgesia and duration of postoperative analgesia. Paediatric Anaesth 2003;13:403-8.
15. Beer DA, Thomas ML. Caudal additives in children solutions or problems? Br J Anaesth 2003;90:487-98.
16. Bajwa SJ, Kaur J, Bajwa SK, Bakshi G, Singh K, Panda A. Caudal ropivacaine-clonidine: A better post-operative analgesic approach. Indian J Anaesth 2010;54:226-30.
17. Eisenach J, Detweiter D, Hood D. Haemodynamic and analgesic action of epidurally administered clonidine. Anesthesiology 1993;78:277-87.
18. Bernard SM, Kick O, Bonnet F. Comparison of intravenous and epidural clonidine for post operative patient controlled analgesia. Anesth Analg 1995;81:706-71.
19. Lee JJ, Rubin AP. Comparison of a bupivacaine –clonidine mixture with plain bupivacacaine for caudal analgesia in children. Br J Anaesth 1994;72:258-62.

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