

Efficacy of dexmedetomidine as an adjuvant to ropivacaine in pediatric caudal epidural block

ABSTRACT

Context: Caudal analgesia is a reliable and an easy method to provide intraoperative and postoperative analgesia for infraumbilical surgeries in pediatric population but with the disadvantage of short duration of action after single injection. Many additives were used in combination with local anesthetics in the caudal block to prolong the postoperative analgesia.

Aim: We compared the analgesic effects and side effects of dexmedetomidine added to ropivacaine in pediatric patients undergoing lower abdominal surgeries.

Settings and Design: Double-blinded randomized controlled trial.

Materials and Methods: Sixty patients (2-10 years) were evenly and randomly assigned into two groups in a double-blinded manner. After sevoflurane in oxygen anesthesia, each patient received a single caudal dose of ropivacaine 0.25% (1 ml/kg) combined with either dexmedetomidine 2 µg/kg in normal saline 0.5 ml, or corresponding volume of normal saline according to group assignment. Hemodynamic variables, end-tidal sevoflurane, and emergence time were monitored. Postoperative analgesia, requirement of additional analgesic, sedation, and side effects were assessed during the first 24 h.

Results: The duration of postoperative analgesia was significantly longer ($P = 0.001$) and total consumption of rescue analgesic was significantly lower in Group RD compared with Group R ($P < 0.05$). Group RD have better quality of sleep and prolonged duration of sedation ($P = 0.001$). No significant difference was observed in the incidence of hemodynamic changes or side effects.

Conclusion: Addition of dexmedetomidine to caudal ropivacaine significantly prolongs analgesia in children undergoing lower abdominal surgeries without an increase in the incidence of side effects.

Key words: Anesthetic techniques, regional, caudal; Anesthetics local, ropivacaine; Analgesia, paediatric, postoperative

Introduction

Caudal epidural block has become one of the most popular, safe, and commonly performed regional blocks in pediatric patients since its introduction into clinical practice by Campbell in 1933.^[1] The caudal epidural block could reduce the requirement of inhaled and intravenous (IV) anesthetic agents, attenuate the stress response to surgery, facilitate


a rapid, smooth recovery, and provide good immediate postoperative analgesia.^[2]

The main disadvantage of single-shot caudal injection is the short duration of analgesia even with the use of long-acting local anesthetics such as bupivacaine^[3] or ropivacaine.^[4] Prolongation of caudal analgesia could be accomplished using

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a caudal catheter or by the addition of various adjuvants such as epinephrine, opioids, ketamine, and α_2 -agonists.^[5-7] However, the former technique is not popular because of concern about infection.^[2,4]

Dexmedetomidine is an α_2 -agonist having an eightfold greater affinity for α_2 -adrenergic receptors than clonidine and much less α_1 effects. A major advantage of dexmedetomidine is its higher selectivity compared with clonidine for α_{2A} receptors which is responsible for the hypnotic and analgesic effects.^[8,9] Dexmedetomidine possesses anxiolytic, sedative, sympatholytic, and analgesic properties without respiratory depressant effect.^[10]

This prospective, randomized, double-blinded study was an attempt to compare analgesic effect, hemodynamic changes, and side effect of dexmedetomidine when added to ropivacaine in the caudal epidural block in pediatric patients undergoing lower abdominal surgery.

Materials and Methods

This study was conducted after getting approval from the Ethical Committee of the Institute and informed, written consent from parents. In this study, 60 patients, aged between 2 and 10 years, belonging to the American Society of Anesthesiologist (ASA) Grade I and II, undergoing lower abdominal surgery, were enrolled.

Exclusion criteria included parental refusal; history of developmental delay or mental retardation, which could make observational pain intensity assessment difficult; children with known allergy to local anesthetics; infection at the local site; children with coexisting medical illness, preexisting neurological disease, coagulation disorders, and anatomical abnormalities of spine and sacrum.

During preoperative visit, patient's age, weight, and baseline vital parameters were recorded. Detailed history, general physical and systemic examinations were done. Routine laboratory investigations such as hemoglobin, bleeding time, and clotting time were carried out for all patients. All patients were kept fasting as per institutional protocol (2 h for clear liquid and 6 h for semisolid and solid) and midazolam syrup 0.5 mg/kg body weight was given 30-45 min before surgery.

Randomization was done using a computer-generated list and all children were evenly assigned into two groups R (ropivacaine) and RD (ropivacaine plus dexmedetomidine). A person not participating in the study kept the computer-generated table of random numbers and prepared all

medications. According to the weight and randomizing table, the volume to be injected in the caudal block was prepared in syringes with labels indicating only the serial number of the patient.

On arrival of patient in the operating room, ASA standard monitor was attached and baseline parameters including heart rate (HR), blood pressure (BP), oxygen saturation (SpO₂), and respiratory rate (RR) were recorded. Induction of anesthesia was achieved with 8% sevoflurane in oxygen with spontaneous ventilation, IV line was secured with appropriate size cannula (22-gauge, 24-gauge) and ringer lactate was infused at a rate of 4 ml/kg/h and an appropriate-sized laryngeal mask airway (LMA) was inserted. After the LMA insertion, sevoflurane concentration was reduced to 3% with fresh gas flow of 3-4 l/min, patients were placed in left lateral decubitus position and under all aseptic precautions single-dose caudal block was performed using a 23-gauge short-beveled hypodermic needle according to the group assigned.

1. Group R received 0.25% ropivacaine 1 ml/kg + 0.5 ml normal saline.
2. Group RD received 0.25% ropivacaine 1 ml/kg + 2 µg/kg dexmedetomidine (in 0.5 ml volume).

The time at which caudal block was performed was noted and patients were turned to supine position. Anesthesia was maintained with sevoflurane in oxygen/air (50:50) mixture. The inhaled concentration of sevoflurane was adjusted to maintain hemodynamic changes <20% of baseline value. No other narcotics, analgesics, sedatives, or anti-emetics were administered intraoperatively. At the beginning of skin closure, sevoflurane was discontinued. After completion of surgery, during emergence from anesthesia, LMA was removed and the patient was transported to the Post Anesthesia Care Unit.

The onset of block was assessed by applying mechanical stimulus at surgical site after 5, 10, 15, and 20 min of the caudal block. The onset of the block is defined as the time in minutes between local anesthetic injection and the absence of motor response or absence of >20% increase in HR on application of mechanical stimulus. Skin incision was allowed after the onset of the block. Failure of caudal block was defined as any increase in HR more than 20% of the preincision values and presence of motor response at 20 min. Patients with failed caudal block were excluded from the study.

Vitals (HR, BP, SpO₂, and RR) were recorded before induction, just before and after skin incision and every 5 min for ½ h, and every 15 min for 1 h. The anesthesia time (the time

from induction of anesthesia to the end of surgery when the sevoflurane was discontinued), emergence time (the time from discontinuation of sevoflurane to opening the eyes on calling the patient's name), and a delayed anesthetic emergence (defined as >20 min elapsing from the end of surgery to exiting the operating theater) were also noted. Postoperative recording of vital parameters, assessment of postoperative pain using the pediatric observational face, legs, activity, cry, consolability (FLACC) pain scale^[11] with its 0-10 score range and postoperative sedation using Ramsay Sedation Scale^[12] were done every hour till 6 h, every 3 h till 12 h, and every 6 h till 24 h. The duration of adequate caudal analgesia (from the time of onset of the block to time at which FLACC score was 4 or more) was recorded, and syrup paracetamol 10 mg/kg was administered at FLACC pain score ≥ 4 , also total doses of rescue analgesic administered in observation period were recorded. Duration of motor block (from the time of onset of the block to time at which patient began to move his leg) was also recorded.

Adverse effects such as nausea, vomiting, respiratory depression, bradycardia, hypotension, and urinary retention were looked for, recorded, and treated accordingly. Postoperative respiratory depression was defined as a decrease in SpO₂ of <95% requiring supplementary oxygen. Fall in BP and HR by >20% from the preoperative value was defined as hypotension or bradycardia, respectively, and was treated by fluid bolus, ephedrine, or atropine, as necessary. Nausea and vomiting was treated with IV ondansetron.

The sample size ($n = 30$) was calculated to detect a 65% reduction in the analgesic requirement during the first 24 h from 75% in the ropivacaine group with $\alpha = 0.05$ and $\beta = 0.20$.^[13] The data obtained was tabulated and analyzed using the computer software (SPSS for Windows, Version 16.0. Chicago, SPSS Inc.). Results of continuous measurements were presented as mean (standard deviation [SD]) if not specified, and results of categorical measurements were presented in numbers or ratio. Student's *t*-test was used for numerical values and chi-square test used for categorical values. The value $P < 0.05$ was considered statistically significant.

Results

Out of the 60 attempted caudal blocks, none was perceived as being a failed attempt. Both groups were comparable with regard to age, weight, gender, type, and duration of surgery [Table 1]. No significant difference was observed in the end-tidal concentration of sevoflurane and emergence time [Table 1]. Intraoperative and postoperative hemodynamic changes

(HR and Mean Arterial Pressure) did not show statistically significant difference between the groups [Figure 1].

The mean (SD) of onset of the block was 14.5 (3.30) min in Group RD as compared to Group R 17.16 (3.13) min with a *P* value of 0.005 [Table 1]. Duration of analgesia recorded a median (95% confidence interval [CI]) of 390 (414.95-483.05) min in Group R as compared with 750 (771.08-926.92) min in Group RD with a *P* value of 0.001 [Table 2]. During the first 4 h after operation, all patients in both groups had adequate analgesia (FLACC score <4), then the number of patients with adequate analgesia declined rapidly in Group R as compared to Group RD and the difference was statistically significant. At 6 h postoperative, 60% of the patients in Group R achieved a FLACC score of ≥ 4 as compared to 0% patients in Group RD, whereas 60% of the patients in Group RD achieved a FLACC score of ≥ 4 at 18 h postoperative [Figure 2]. Mean (SD)

Table 1: Demographic profile of participants

Character	Mean \pm SD		P
	Group R	Group RD	
Age (years)	3.93 \pm 2.06	4.23 \pm 2.43	0.617
Weight (kg)	14.1 \pm 4.13	14.23 \pm 4.12	0.902
Gender (male)	93.33	93.33	—
Type of surgery			
Hemiotomy	23	26	0.978
Urethroplasty	3	1	
Circumcision	3	0	
Orchidectomy	1	0	
Orchidopexy	0	3	
Duration of surgery	33 \pm 7.26	33 \pm 7.26	0.999
End-tidal sevoflurane	2.4 \pm 0.7	2.6 \pm 0.7	0.98
Emergence time	12.9 \pm 7.2	9.1 \pm 3.4	0.111
Onset of block (min)	17.16 \pm 3.13	14.5 \pm 3.30	0.005*
Side effect			
Hypotension (%)	6.66	6.66	0.897
PONV (%)	10	6.66	

*Significantly different; SD: Standard deviation; PONV: Postoperative nausea and vomiting

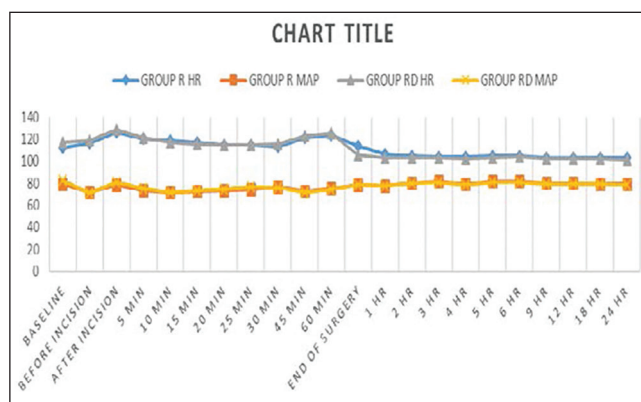


Figure 1: Hemodynamic parameter - trends of heart rate and mean blood pressure in both groups at different time intervals

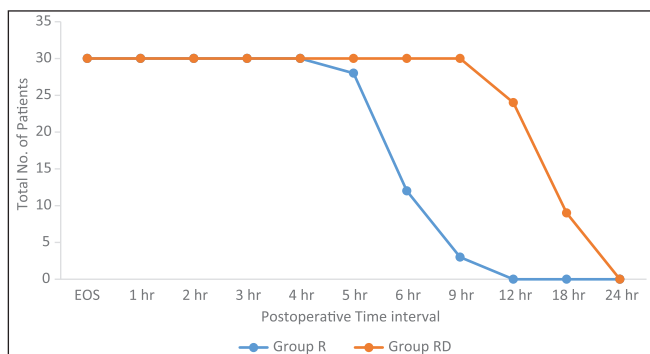


Figure 2: Face, legs, activity, cry, consolability pain score: Number of patients with adequate caudal analgesia (face, legs, activity, cry, consolability pain score <4) in both groups at different time intervals

time to first analgesic dose was significantly longer in the RD group 849 (208.7) min than in Group R 449 (19.2) min ($P = 0.001$). The total postoperative analgesic requirements for oral paracetamol were significantly less in the RD group during the observation period [Table 3]. Duration of motor block recorded a median (95% CI) of 75 (55.16-86.84) min in Group R as compared with 90 (72.34-101.66) min in Group RD with a P value of 0.1349 [Table 2].

The median (95% CI) duration of sedation recorded was significantly prolonged in Group RD 247.5 (214.53-267.47) min as compared with Group R 30 (32.008-45.5) min with a P value of 0.001 [Table 2]. Postoperative sedation scores between the two groups are shown in Table 4.

Ten percent patients in Group R and 6.66% patients in Group RD had vomiting. About 6.66% patients in both groups had clinically significant hypotension which responded well to fluid bolus [Table 1]. None of the patients in both the groups had clinically significant bradycardia, desaturation, or respiratory depression and urinary retention.

Discussion

Pain is perhaps the most feared symptom of disease, which a human being is always trying to alleviate and conquer since ages. Historically, children have been under treated for pain because of the wrong notion that they neither feel pain nor remembered the painful experiences to the same degree as an adult do. The concept of postoperative pain relief and its utilization in the pediatric age group has improved dramatically over the recent years.^[14]

Adequate postoperative analgesia provides pain relief and allows the patients to breathe and move freely to enhance early restoration of function. Till date, various methods have evolved for providing postoperative analgesia in children.^[3,4] Among the methods, caudal epidural block is the safest and

Table 2: Caudal block characteristic and sedation

Characteristic	Median (95% CI)		P
	Group R	Group RD	
Duration of analgesia (min)	390 (414.95-483.05)	750 (771.08-926.92)	0.001*
Duration of motor block (min)	75 (55.16-86.84)	90 (72.34-101.66)	0.1349
Duration of sedation (min)	30 (32.008-45.5)	247.5 (214.53-267.47)	0.001*

*Significantly different; CI: Confidence interval

Table 3: Requirement of analgesia during observation period

Number of doses	Group R (%)	Group RD (%)
0	2 (15)	6 (20)
1	2 (15)	24 (80)
2	12 (40)	0 (0)
3	12 (40)	0 (0)

Table 4: Ramsay Sedation Score during observation period

Time	Median (range)	
	Group R	Group RD
End of surgery	2 (1-3)	3 (2-3)
At 1 h	1 (0-2)	2 (2-2)
At 2 h	1 (0-1)	2 (2-2)
At 3 h	0 (0-0)	1 (0-2)
At 4 h	0 (0-0)	1 (0-2)
At 5 h	0 (0-0)	0 (0-1)
At 6 h	0 (0-0)	0 (0-0)

most reliable technique.^[2] Several studies have been reported about the caudal usage of opioids, ketamine, midazolam, neostigmine, α_2 -agonists, and other drugs in children to improve postoperative analgesia.^[5-7] Although the use of caudal opioids did prolong the duration of analgesia, it was also associated with side effects such as respiratory depression, pruritus, urinary retention, and nausea and vomiting.^[15,16] Hence, other drugs such as α_2 -agonists have been used to improve analgesia in the postoperative period while avoiding the side effects associated with usage of opioids.

Dexmedetomidine is a highly selective α_2 -adrenoceptor agonist and when added to local anesthetic agents enhances their effects without increasing the incidence of side effects.^[17] Its mechanism of action differs from clonidine as it possesses selectivity, especially for the A subtype of α_2 receptor, which causes it to be a much more effective sedative and analgesic agent than clonidine without undesirable cardiovascular effects from α_1 receptor activation even with higher doses.^[18] In addition, dexmedetomidine is a shorter-acting drug than clonidine and it is unique that its sedative effect can be reversed by atipamezole. Dexmedetomidine, although currently approved for IV use only, has been successfully used in neuraxial blocks in experimental and

clinical studies without neurological deficits encouraging its use by the epidural route.^[13,19-21] Nevertheless, there are still some concerns regarding its safety.^[22]

Compared to bupivacaine, ropivacaine is safer, has less motor blockade, less cardiovascular or neurological toxicity and similar duration of analgesia. It can be used safely for regional anesthesia and analgesia in pediatric ambulatory surgery.^[6,11,23,24]

In the present study, we administered dexmedetomidine 2 µg/kg along with ropivacaine 0.25% (1 ml/kg) caudally and observed that the duration of postoperative analgesia (FLACC <4) without the need rescue analgesic was significantly longer in group receiving ropivacaine-dexmedetomidine mixture (median [95% CI] 750 [771.08-926.92] min) than the group receiving ropivacaine alone (median [95% CI] 390 [414.95-483.05] min). These results are similar to those reported in a study conducted by Anand *et al.*^[14] They administered dexmedetomidine in a dose of 2 µg/kg as an adjuvant with 0.25% ropivacaine caudally, and observed that the duration of analgesia was significantly higher in the group receiving ropivacaine-dexmedetomidine mixture (median [95% CI]: 14.5 h [13.90-15.09]) than the group receiving ropivacaine alone (median [95% CI]: 5.5 h [4.97-6.03]). Similarly, El-Hennawy *et al.*^[8] administered dexmedetomidine and clonidine, both in a dose of 2 µg/kg as an adjuvant with 0.25% bupivacaine caudally. They found that the duration of analgesia was significantly higher in the group receiving bupivacaine-dexmedetomidine mixture (median [95% CI]: 16 h [14-18]) or bupivacaine-clonidine mixture (median [95% CI]: 12 h [3-21]) than the group receiving bupivacaine alone (median [95% CI]: 5 h [4-6]). Neogi *et al.*^[9] compared clonidine 1 µg/kg and dexmedetomidine 1 µg/kg as adjuncts to ropivacaine 0.25% for caudal analgesia in pediatric patients and found that mean (SD) duration of analgesia was 15.26 (0.86) h in dexmedetomidine group, which was significantly higher than both clonidine group 13.17 (0.68) h and ropivacaine group 6.32 (0.46) h.

In our study, we observed that the mean time to first rescue analgesic was significantly higher and total doses of rescue analgesic required during the observation period was significantly less in Group RD as compared to Group R. Similarly, Saadawy *et al.*^[13] also observed in their study that 77% of the children in the bupivacaine-dexmedetomidine (BD) group versus 10% in group bupivacaine did not require additional analgesia and total postoperative analgesic requirements for oral paracetamol were significantly less in the BD group ($P < 0.01$) during the first 24 postoperative hours.

The pre-, intra-, and post-operative hemodynamic variables [Figure 1] between the groups were comparable and were not statistically significant and therapeutic interventions were not required. No episodes of clinically significant postoperative complications such as postoperative nausea and vomiting, respiratory depression, urinary retention, pruritus, hypotension, and bradycardia were observed in both the groups [Table 1]. The results of our observations show that in addition to prolonged postoperative analgesia, dexmedetomidine has a favorable safety profile and stable hemodynamics, which are in concordance with the reports published by several other authors.^[8,12,17,25-28]

In our study, we observed no statistically significant difference in end-tidal sevoflurane concentration and emergence time between the groups which is in accordance with El-Hennawy *et al.*,^[8] however, Saadawy *et al.*^[13] and Anand *et al.*^[14] found significant reduction in end-tidal sevoflurane concentration and emergence time in group receiving dexmedetomidine.

Although rapid recovery without residual sedation is a major objective in outpatient adult surgery, a certain degree of sedation after pediatric surgery might represent a desired effect by the parents. A calm and sedated child during the early postoperative period could decrease the parent's anxiety.^[29] We observed statistically significant difference in duration of sedation of both groups ($P < 0.001$). RD group had significant sedation compared to R group, meaning that RD group children were asleep but easily arousable which is in concordance with results of various other studies.^[8,13,14]

Our results allow us to conclude that addition of dexmedetomidine (2 µg/kg) to caudal ropivacaine 0.25% at 1 ml/kg significantly prolonged analgesia after anesthetic recovery in children, undergoing lower abdominal surgeries without increasing the incidence of side effects.

Limitation

As for all additives in regional anesthesia, the true question is to compare the potential local effects to a systemic administration particularly when additives were used off-label. Lack of control group with IV dexmedetomidine did not allow us comment on the potential local effect of dexmedetomidine. Studies are required with IV dexmedetomidine as a control group to establish potential local effect of dexmedetomidine. Although we did not encounter even a single block failure, it will be safer and precise to conduct the procedure under ultrasound guidance.

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Conflicts of interest

There are no conflicts of interest.

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