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COMPARISON OF TWO DIFFERENT DOSES OF DEXMEDETOMIDINE AS AN ADJUVANT TO CAUDAL ROPIVACAINE FOR POST OPERATIVE ANALGESIA IN PAEDIATRIC INFRA-UMBILICAL SURGERIES

Anaesthesiology

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ABSTRACT

Background and aims: This study was undertaken to evaluate the optimal dose of dexmedetomidine added to caudal ropivacaine for postoperative prolongation of analgesia without any major adverse effects inchildren. **Material and Methods:** This was a prospective randomized double blinded study involving 74 children aged between 2 to 10 years of either sex, of ASA grade I and II undergoing elective infraumbilical surgeries. Group 1 received dexmedetomidine 1µg/kg along with 0.25% ropivacaine 1ml/kg caudally; and Group 2 received dexmedetomidine 2µg/kg along with 0.25% ropivacaine 1ml/kg for caudal anesthesia. **Results:** The mean duration of analgesia was significantly longer (p value = <0.0001) in group 2 (932.40± 53.98 mins) than group 1 (666.21 ± 35.81 mins). The total number of doses of rescue analgesics required and pain scores (p value = <0.05) were also less in group 2. **Conclusion:** Dexmedetomidine 2µg/kg as caudal adjuvant to 0.25%ropivacaine 1ml/kg significantly prolongs analgesia in children without any adverse effects as compared to dexmedetomidine 1µg/kg along with 0.25% ropivacaine 1ml/kg.

KEYWORDS

Caudal anaesthesia, dexmedetomidine, ropivacaine, postoperative analgesia

INTRODUCTION

Analgesic efficacy of single-shot caudal blocks which is by far the most commonly used regional block in pediatric practice,[1] is limited by half life of local anaesthetic employed. So, numerous attempts to prolong the analgesic effects of a single shot caudal block by combining a local anaesthetic with other additives has been studied by many investigators.

Dexmedetomidine is a highly selective alpha 2 adrenergic receptor agonist with a relatively high ratio of α2/α1-activity (1620:1). Although there are multiple studies regarding efficiency and safety of dexmedetomidine as caudal adjuvant to local anaesthetics for analgesia, but still there is no clarity about optimum dose to achieve a good quality postoperative analgesia without any undesirable side effects. A recent meta-analysis comprising six randomised control trials on caudal dexmedetomidine concluded that there are insufficient data regarding the effects of different doses of dexmedetomidine. [2] Hence, this study was undertaken to evaluate the efficient, yet safe dose of dexmedetomidine as caudal adjuvant for prolongation of analgesia in children.

The present study aims to compare the effect of dexmedetomidine in two different doses (1µg/kg and 2µg/kg) administered caudally in pediatric patients undergoing infra-umbilical surgeries under caudal epidural with 0.25% ropivacaine 1ml/kg with the objectives to compare the duration and quality of post-operative analgesia, postoperative sedation, any effects on haemodynamic profile or any other adverse effects observed.

Methods

This prospective randomized double blinded study was conducted after getting approval from Institutional Ethical Committee, although no CTRI registration was done. This study was carried out in 74 patients of age 2 to 10 years, of either sex belonging to ASA physical status I or II, posted for infra-umbilical surgeries like circumcision, herniotomy, urogenital and perineal surgeries after getting parental written informed consent. No major abdominal surgeries or orthopaedic surgeries were included. Excluding criteria were patient's / parents refusal and any contraindications to the caudal block. Preanesthetic checkup was done and parents were taught to perform their role in the study and the use of FLACC pain scale. Complete blood count, bleeding time, clotting time and urine routine examination were reviewed. All patients were kept fasting as per institutional protocol.

On arrival of patient to the operating room all standard monitors were attached like pulse oximetry, ECG and NIBP and baseline parameters were recorded. Intravenous line was secured with appropriate size cannula and Ringer Lactate infusion was started according to the Holiday and Segar's formula.[3] Induction of anesthesia was achieved with 8% Sevoflurane in Oxygen and N2O (50/50) with spontaneous ventilation. An appropriate sized LMA was inserted and after insertion sevoflurane concentration was reduced to 3% in O2: N2O mixture (1:1) till caudal block was performed. No muscle relaxants or endotracheal intubation were used as no major abdominal or orthopaedic surgeries were included.

All the patients were randomly divided into two groups of 37 patients using sealed opaque envelope method and the study drugs were prepared accordingly by an anaesthesiologist not involved in further study, whereas caudal block placement and intraoperative and postoperative data collection were performed by a separate anaesthesiologist to maintain double blinding. Dexmedetomidine 100 µg/ml preparation was used. The dosage were calculated according to the patient's weight, loaded using an insulin syringe rounded off to the closest unit and diluted to one ml with normal saline to maintain the total volume of drug similar for both groups for caudal block.

1. Group 1 patients received caudal anesthesia with 0.25% ropivacaine (1ml/kg) plus dexmedetomidine 1µg/kg diluted to 1 ml normal saline; and
2. Group 2 patients received caudal anesthesia with 0.25% ropivacaine (1ml/kg) plus dexmedetomidine 2µg/kg diluted to 1 ml normal saline.

The onset of block was assessed by applying atraumatic needle prick sensation at surgical site after 5, 10, 15, and 20 min of the caudal block. Before needle prick sevoflurane concentration was reduced to 1% and N2O was stopped and ensured that MAC on monitor was not more than 0.5. 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 heart rate on application of mechanical stimulus. Skin incision was allowed after the onset of the block and sevoflurane concentration was again increased. Failure of caudal block was defined as any increase in heart rate more than 20% of the preincision values

and/or presence of motor response at 20 min. Maintenance of anaesthesia was provided with sevoflurane (in N_2O:O_2 in 1:1 ratio) and its concentration adjusted to achieve haemodynamic changes less than 20% of baseline value. No other narcotic or analgesics were used intra operatively. After the completion of surgery, sevoflurane was discontinued and LMA was removed and patients were transferred to post anaesthesia care unit for observation.

Heart rate, mean arterial blood pressure and oxygen saturation were recorded before surgery, every 5 min after performing the caudal block till the end of surgery, every 15 min postoperatively in recovery room and after that every hour till 6 hours and every 3 hours till 24 hours after surgery. All these parameters were recorded by the same anaesthesiologist who performed caudal block. The occurrence of intra-operative hypotension requiring fluid bolus and bradycardia requiring atropine was recorded. A decrease in mean arterial pressure >30% was defined as hypotension and was treated with intravenous fluids/injection ephedrine. A decrease in HR >30% was considered as bradycardia and was to be treated with injection atropine 0.01 mg/kg. After emergence from anaesthesia postoperative pain was assessed using FLACC scale, using the pediatric observational face, legs, activity, cry, consolability pain score.[4] With its 0-10 score range, each patient's pain intensity was assessed at the end of surgery and then every 4 hours for 24 hours after operation. If the FLACC pain score was 4 or more injection Paracetamol 10mg/kg intravenous was administered. Duration of analgesia from the time of performing caudal injection to the time at which FLACC score was 4 or more was also recorded. Sedation was assessed using 4-point objective score based on eye opening[5,6] 0 = spontaneous eye opening (awake), 1 = eye opening in response to verbal command (drowsy, mild sedation), 2 = eye opening in response to physical stimulus like earlobe tug or shaking shoulders (asleep, moderate sedation), 3 = eye opening to painful stimulus (deep sedation)]. Postoperative sedation was assessed every 30 min for 2 h and then at 1 h intervals till 6 h.

Motor block was assessed in the PACU every 30 min for 2 h and then at 1 h intervals till 6 h by using Bromage score.[7] However, younger children who could not move their legs on command were stimulated by tapping on the legs and feet. After transferring to the ward adverse effects such as postoperative nausea and vomiting, hypotension, pruritis and bradycardia were monitored and recorded up to24 h.

Summary data were calculated using the SPSS IBM software version 21 (IBM SPSS advanced statistics; Chicago), compiled in the Microsoft Excel sheet and represented as median (95% of confidence interval) or mean (SD) for all quantitative variables. The frequency of all variables was displayed in charts and tables. Unpaired student 't' test was applied for comparing quantitative data (mean) and fisher exact test was applied for qualitative data. The difference was considered significant if p value is less than 0.05 at 95% confidence interval using Mann Whitney U test.

Results

Table 1: Demographic parameters of participants

Parameter	Group 1 Mean±SD	Group 2 Mean±SD	p value
Age (years)	3.59 (±2.10)	4.16 (±2.11)	2.50
No of males/females	36/1	20/17	<0.0001
Weight (kg)	13.37±3.04	14.43±2.71	0.120
Type of surgery Circumcision Hernia repair Genitourinary surgeries (cystolithotomy, urethroplasty, etc)	5 27 5	2 19 16	

Demographic data are given in Table 1. There was no significant difference between two groups in terms of age and weight of patients. In our study male patients were comparatively higher than the female patients. As shown in Figure 1 difference in the mean heart rate amongst two groups at 1st to 9th hour postoperatively was insignificant (p value >0.05). Intergroup comparison demonstrated significant difference in the mean heart rate 12 h postoperatively between groups 1 and 2 (p value < 0.0001).

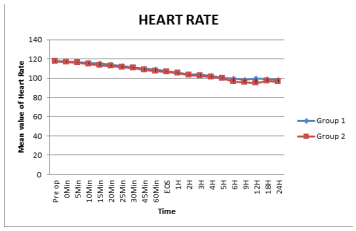

Figure 1: Heart rate in preoperative, intraoperative and postoperative period

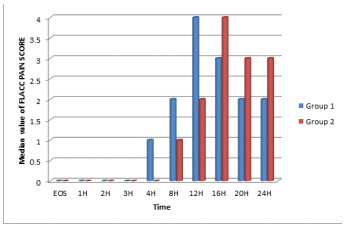

Figure 2: FLACC scores of patients in post operative period

There was a significant difference in the FLACC scores of all patients at various time intervals in post operative period [Figure 2]. During the first 8 hours after giving caudal block, all patients in both groups had adequate analgesia (FLACC score <4). After 9th hour patients in group 1 had significantly higher FLACC scores (>4) whereas, Group 2 patients had FLACC score of 4 or more after 16th hour and FLACC score of all patients diminished after receiving rescue analgesic, Inj. Paracetamol 10mg/kg intravenously. Therefore, in Figure 3 none of the patients show FLACC score more than 4. Time to first paracetamol administration i.e mean duration of analgesia was comparatively longer (p value = <0.0001) in group 2 (932.4± 54 mins) than group 1 (666.2 ± 35.8 mins) and it was statistically significant [Figure 3]. In group 1, 27 patients out of 37 show total duration of analgesia between 600-690 minute while in group 2, 32 patients out of 37 show total duration of analgesia between 871-960 minutes [Table 2].

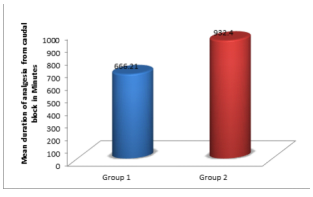

Figure 3: Mean duration of analgesia

Table 2: Number of patients requiring first dose of rescue analgesia from performing of caudal block

Time to first rescue analgesia (in min) from performing caudal block	Group 1	Group 2		
	No. of patients requiring rescue analgesic	% of patients requiring rescue analgesic	No. of patients requiring rescue analgesic	% of patients requiring rescue analgesic
600-690	27	72.97	1	2.70
691-780	10	27.03	0	0
781-870	0	0	0	0
871-960	0	0	32	86.49
>960	0	0	4	10.81
Median	670	940		
Range	600-725	645-990		
Mean±SD	666.21±35.81	932.40±53.98		

The mean duration of motor block in was similar in both groups (Group 1: 113.3±6.2 min vs Group 2: 115.5±5.4 min; p value < 0.100).Variations of respiratory rate and SPO2 values during preoperative, intraoperative and upto 24 h postoperative period were comparable between the two groups. (p value >0.05).

We observed initially at end of surgery, patients in both groups were sedated with similar sedation scores during first 90 min

postoperatively [Figure 4]. Sedation scores at 120 min were higher in Group 2. But at all the time patients had eye opening response to painful stimuli and there was no respiratory depression. In both groups patients had spontaneous eye opening between duration of 2- 3 hrs.

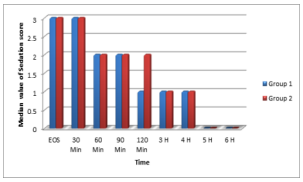

Figure 4: Sedation score in post operative period

Discussion

In this prospective randomized double-blind study age and weight were comparable between the two groups although male/female ratio between the groups was uneven. There was no failure of caudal block in any patient. There were no significant differences between the two groups regarding their MAC requirements of sevoflurane and haemodynamic parameters in the intra operative period. In the post operative period, patients in Group 1 had significantly higher heart rate values from 9th hour when compared to group 2 (figure 1), which can be possibly attributed to early occurrence of pain in Group 1 patients. Dexmedetomidine provides dose-dependent hypotension and bradycardia due to reduction in the plasma levels of norepinephrine and epinephrine. We found decrease in heart rate in both groups after caudal block which was not significant on inter group comparison. However, no episode of bradycardia was reported. Similarly Saadawy et al reported decrease in heart rate and mean arterial pressure in dexmedetomidine group within 25–35 min of caudal administration.[8]

Dexmedetomidine, a stereoisomer of medetomidine, possesses anxiolytic, sedative, sympatholytic, and analgesic properties with manageable hypotension and bradycardia without respiratory depressant effect.[9] Currently, worldwide, there is no approval for its administration to the paediatric population. Despite the lack of paediatric labelling, dexmedetomidine for paediatric use has been described for almost a decade in the literature. While there have not been any large-scale clinical trials conducted, the current body of evidence suggests that dexmedetomidine is suitable for use as an adjuvant analgesic to intravenous, spinal canal, and nerve block for peri-operative acute pain treatment.[8,9] Nevertheless, there are still some concerns regarding its safety.[10] The α2-adrenergic effects of dexmedetomidine, relative contraindications, and biphasic effect on blood pressure in both children and adults should be well understood by any provider who administers or cares for a patient receiving dexmedetomidine.

Analgesic effects of dexmedetomidine are due to its effect on three sites i.e. brain and brainstem, spinal cord and peripheral tissues. In brain it act on locus cerulus and at spinal level activation of medullospinalnoradrenogeneric descending pathway and inhibition of sympathetic outflow tract provides analgesic effects. Moreover interaction with opioid receptors facilitates its analgesic properties.[11] In this study, we observed that duration of postoperative analgesia (FLACC<4) without the need rescue analgesic was longer in Group 2 (mean duration 932.4±54 min)when compared with Group 1 (mean duration 666.2±35.8 min). The need for rescue analgesic injection in postoperative period was significantly lower in children who received caudal dexmedetomidine 2µg/kg (Group 2).The time to first paracetamol administration i.e. duration of analgesia was significantly longer in Group 2 (932.4±54 min) when compared with Group 1 (666.2±35.8 min). Fares and collegues[12] compared analgesic efficacy of caudal 1 mL/kg bupivacaine 0.25% with dexemedetomidine 1 µg/kg versus 1 mL/kg bupivacaine 0.25% alone in pediatrics major abdominal cancer surgeries and found a significant reduction in FLACC score in dexedetomidine group in first 12 hours postoperatively which is similar to analgesic duration of our study Group 1. Our findings for Group 1 are similar to that conducted by Goyal et al[13] who studied that addition of dexmedetomidine 1 µg/kg to 1 mL/kg bupivacaine 0.25% for caudal block in pediatric patients prolongs the mean duration of analgesia to 9.88 ± 0.90 in h. Duration of analgesic efficacy of Group 2 is comparable to as observed by Anand et al[14] when they administered dexmedetomidine in a dose of 2 µg/kg as an adjuvant with 0.25% ropivacaine (1ml/kg) 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 Kamal and collegues[15] administered dexmedetomidine 2µg/kg along with ropivacaine 0.25% (1 ml/kg) caudally and observed that the duration of postoperative analgesia was (median [95% CI] 750 [771.08-926.92] min) which is comparable to analgesic duration of our Group 2. El-Hennawy et al[16] administered dexmedetomidine and clonidine, both in a dose of 2 µg/kg as 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 hours (14–18)] which correlates with our findings.

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. Dexmedetomidine provides a unique form of arousable sedation caused by hyper polarization of excitable cells in the locus ceruleus, which can be easily reversed with verbal or physical stimuli and do not cause respiratory depression even at high doses. Furthermore, respiratory rate, oxygen saturation and carbon dioxide tension are generally maintained during dexmedetomidine sedation in children.

The incidence of postoperative nausea and vomiting and duration of motor block were comparable in Group 1 and Group 2. There was no incidence of other complications like hypotension, bradycardia and urinary retention amongst the two groups.

Thus, we conclude from our study that the addition of dexmedetomidine caudally with dose of 2 µg/kg as compared to 1µg/kg of dexmedetomidine as an adjuvant to caudal 0.25% ropivacaine (1ml/kg) significantly reduced the intensity of postoperative pain and prolonged the duration of postoperative analgesia in children undergoing infra-umbilical surgeries, with no potential side effects. So we recommend addition of dexmedetomidine in a dose of 2 µg/kg to caudal 0.25% ropivacaine for infraumbilical surgeries in pediatric patients.

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