Journal of Anesthesia & Clinical Research

Goswami et al., J Anesth Clin Res 2015, 6:11
DOI: 10.4172/2155-6148.1000583

Research Article

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A Comparative Study between Caudal Bupivacaine (0.25%) and Caudal Bupivacaine (0.25%) with Dexmedetomidine in Children Undergoing Elective Infra-Umbilical Surgeries

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Received date: September 27, 2015; **Accepted date:** November 23, 2015; **Published date:** November 30, 2015

Abstract

Background: 74 children, either sex, aged 2-7 years, ASA grade I, II, scheduled to undergo infra-umbilical surgeries included in a prospective, double blind, randomized, parallel group study. Aim was to compare duration of analgesia and level of sedation after single dose caudal bupivacaine versus caudal bupivacaine with dexmedetomidine.

Methods: The children were randomly allocated into Group B (n=37) and Group BD (n=37). Group B children received caudal bupivacaine (0.25%) 1 ml/Kg B/W in 1ml normal saline and Group BD children received same with dexmedetomidine 2 µg/kg B/W in 1ml normal saline after induction . Pulse rate, blood pressure, SPO_2 were monitored and recorded at 0min (after administration of caudal anesthesia) and intra-operatively at 15 minutes interval till the end of operation. Postoperative hemodynamic monitoring, FLACC pain scoring and Ramsay sedation scoring was done at 2 hour interval after extubation upto 8 hrs., then 4 hrly upto 24 hrs. Rescue analgesia was administered when pain score was 4.

Results: The study groups were comparable in terms of demographic characteristics, body weight, duration and type of surgeries. Decrease in mean intraoperative heart rate, systolic blood pressure, diastolic blood pressure, post-operative pulse rate, systolic and diastolic blood pressure in Group-BD was statistically significant.

Mean FLACC pain scores were significantly low in group BD compared to group B at 0 mins, 120 mins, 240 mins and 360 mins after extubation (p<0.001). Mean duration of analgesia in group BD 648.9 ± 130.59 mins compared to 289.7 ± 78.21 mins in group B. Mean Ramsay sedation scores were significantly high in group BD compared to group B at 0 mins,120 mins and 240 mins after extubation (p<0.001).

Conclusion: The study demonstrated that addition of dexmedetomidine to caudal bupivacaine prolongs duration of analgesia, provides better quality of sleep, prolong duration of arousal sedation and better hemodynamic stability to the children compared to caudal bupivacaine.

Keywords: Anesthesia; Caudal; Analgesia; Bupivacaine; Dexmedetomidine

Introduction

The International Association for the Study of Pain defines Pain as "An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage." [1].

Pain is a complex, subjective, perceptual phenomenon with a number of dimensions like intensity, quality, time course and impacts that are uniquely experienced by each individual. Pain experienced by children and infants often goes unrecognized even neglected because of the operational definition of pain that requires self-report [2,3].

Surgical trauma not only causes postoperative pain but also results in well-characterized human responses to stress. The stress response is mediated by hypothalomo-pituitary-adrenal and sympatho-adrenal interactions which cause increased liberation of catecholamines and catabolic hormones on one hand and decreased secretion of anabolic hormones on the other. Thus a catabolic state is produced and negative nitrogen balance results if the process continues in the postoperative period.

Children receive significantly less medication regardless of the intensity of pain because round the clock opioid analgesics increase the risk for sedation and respiratory depression [4].

Postoperative pain control is important in pediatric patients because poor pain control may result in increased morbidity and mortality [5]. Pediatric anesthesiologists must remain on the forefront of knowledgeable and safe use of pain interventions for infants and children and integrate pain management into the overall perioperative plan [6]. The management of acute postoperative pain in pediatric patients can be accomplished by using a multimodal approach. Neuraxial blocks being virtually free of measurable hemodynamic effects are particularly well tolerated by young children. So these approaches have become about routine in infra-umbilical surgeries.

The most common technique of epidural analgesia in children is caudal analgesia used commonly in lower abdominal, urological and lower limb surgeries. The ease of performing the block and the extensive safety record of its use in children are the reasons for the popularity of caudal analgesia. They can be combined with general anesthesia to reduce the requirement for volatile agents and opioids, allowing rapid, pain-free recovery with minimal postoperative vomiting and an early resumption of oral intake. Depending on the volume, dose or concentration of local anesthetic, caudal epidural blocks results in sympathetic block, sensory analgesia and motor block. Complications are rare. Single dose caudal analgesia with bupivacaine is very safe and has been effectively used in pediatric surgical procedures for provision of postoperative analgesia [7]. The major drawback is the relatively limited duration of post-operative analgesia with bupivacaine alone.

Different methods like using adjuvants have been tried to increase duration of analgesia with bupivacaine.

Clonidine, an alpha-2 adrenergic agonist, increases duration of analgesia and produces sedation without respiratory depression after systemic, intrathecal and epidural administration [8].

Dexmedetomidine, a newer member of alpha 2 adrenergic agonist groups, is highly specific and selective for alpha-2 receptor. Addition of dexmedetomidine prolongs duration of action of bupivacaine after intrathecal and epidural administration in adult patients and causes sedation without respiratory depression [9].

In this randomized, prospective, double-blind study, involving caudal analgesia in pediatric population, 0.25% bupivacaine alone was given to one group and equal volume of 0.25% bupivacaine with dexmedetomidine was given to other group for comparing duration of analgesia and sedation.

Methods

After local ethical committee approval and obtaining informed parental consent, 74 ASA status I and II patients, aged 2-7 yrs. undergoing elective infra-umbilical surgeries were prospectively enrolled in this study.

Study exclusion criteria included a history of developmental delay or mental retardation, which could make observational pain intensity assessment difficult; a known or suspected coagulopathy; a known allergy to any of the study drugs; and any signs of infection at the site of the proposed caudal block. Children thus enlisted for the study were randomly allocated into two groups using a computer generated randomization chart. Children belonging to Group B (n=37) received caudal epidural injection of 0.25% bupivacaine in the dose of 1 ml/Kg body weight with 1ml normal saline. Children in Group BD (n=37) received caudal epidural injection of 0.25% bupivacaine 1ml/Kg body weight with dexmedetomidine 2 µg/kg in 1ml normal saline.

All health-care personnel providing direct patient care the subjects, and their parents or guardians were blinded to the caudal medications administered. All medications were prepared by pharmacy staff not participating in the study except for preparing the drugs. They received and kept the computer-generated table of random numbers according to which random group assignment was performed. After obtaining subjects weight, and according to the 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.

All subjects received a conventional preoperative dose of oral midazolam (0.5 mg kg21) 20–30 min before anesthetic induction, and then underwent a standard inhalation induction with sevoflurane in oxygen followed by insertion of an IV canula and administration of a neuromuscular blocking agent to facilitate endotracheal intubation. Induction was strictly inhalation. Glycopyrolate used routinely. After endotracheal intubation, patients were placed in the lateral decubitus position, and a single-dose caudal block was performed according to the group under sterile conditions using a 23 G needle and standard loss of resistance technique.

General anesthesia was maintained with sevoflurane delivered in oxygen. The inhaled concentration of sevoflurane was adjusted to achieve hemodynamic changes, 30% of the baseline values. No other narcotics, analgesics, sedatives, or antiemetics were administered intraoperatively. At the conclusion of surgery, the patient was awakened and transported to the post-anesthetic care unit (PACU).

Standard monitoring was used during anesthesia and surgery. Heart rate and arterial pressure were recorded before operation and every 15 min until the end of surgery.

The occurrence of intraoperative hypotension requiring a fluid bolus, bradycardia requiring atropine, and the maximum maintenance end-tidal concentration of sevoflurane (%) were recorded. Perioperative blood loss was replaced meticulously using crystalloids. During the postoperative period, moist oxygen was administered for 2 hours.

The parameters assessed were:

1) The time between completion of caudal epidural administration and first post-operative rescue analgesic (Duration of analgesia).

2) Pain intensity was assessed at the end of operation, then every 2 hrly for 8 hours, then 4 hrly for next 16 hrs using FLACC Pain scale.

3) Level of sedation was assessed by Ramsay sedation scale.

4) Post-operative hemodynamic changes were noted.

5) Occurrence of any side effect like vomiting, urinary retention, and bradycardia was noted.

Categories	0	1	2
Face	smile/no particular expression	Occasional grimace / frown, withdrawn, disinterested	frequent to constant frown, clenched jaw, quivering chin
Leg	normal position or relaxed	uneasy, restless, tense	kicking/ legs drawn up
Activity	lying quietly, normal position, moves easily	Squirming, shifting back and forth, tense	arched, rigid/ jerking
Cry	no cry (awake/ asleep)	moans/ whimpers occasional complaint	Crying steadily, screams or sobs, frequent complain
Consolability	content, relaxed	reassured by occasional touching, hugging/ talking, distractible	Difficult to console

Table 1: The FLACC (The Facial Expression-Leg Movement-Activity-Cry-Consolability) pain scale [10].

Normally distributed numerical variables were analyzed using unpaired t-test. Non parametric numerical variables within the two groups were analyzed using the Man-Whitney -U test. Categorical variables analyzed by Fischer‘s exact test.

Sample size estimation done using PS power and sample size calculation software. Based on clinical experience and review of literature the duration of post-operative analgesia was taken as the primary outcome measure for the purpose of sample size calculation. It was estimated that 37 subjects required for each group in order to detect the 2hr difference in this parameter, between groups with 80%power and 5%probability of type 1 error. This calculation assumed the SD of 3hr for duration of post-operative analgesia.

All tests were two tailed. A "p" value of less than 0.05 was considered statistically significant, less than 0.001 strongly statistically significant.

Results

None of the 74 attempted caudal blocks was perceived as being a failed attempt. Table 2 and 3 shows that there was no statistically significant difference in the demographic profile of the children, duration of surgeries performed in the children and distribution of the various types of surgeries performed in the children in the study groups.

Variables		Group B	Group BD	p Value
Age (yrs)	Range (min-max)	2.3-7.0	2.00-7.00	0.962
	Mean ± SD	4.3 ± 1.63	4.3 ± 1.28	
Weight (kilogram)	Range (min-max)	10.0-22.0	10.0-22.0	0.435
	Mean ± SD	15.2 ± 3.74	14.6 ± 3.03	
Sex	M:F	32:5	31:6	1.000
Duration of surgery (in minutes)	Range (min-max)	30.0-150.0	30.0-135.0	0.446
	Mean ± SD	77.3 ± 29.45	71.6 ± 27.86	

Table 2: Demographic profile of the children.

Type of surgery	Group B	Group BD	Total
Urethroplasty	7 (18.92%)	8 (21.61%)	15
Hernia	9 (24.32%)	9 (24.32%)	18
Hypospadias	7 (18.92%)	5 (13.51%)	12
Orthopaedic	5 (13.51%)	6 (16.22%)	11
Circumcision	5 (13.51%)	5 (13.51%)	10
Orchidopexy	4 (10.81%)	4 (10.81%)	8
Total	37	37	74

Table 3: Distribution of the various types of surgeries.

The mean heart rates at 0 min, 15 min, 30 min, 45 min were not statistically different between Group-B and Group-BD (p>0.05); but statistically highly significant at 60 mins, 75 mins, 90 mins and 105 mins (p<0.001). There is significant decrease in intra-operative heart rates in group BD compared to group B at the mentioned time points.

There was no statistical difference between the intraoperative mean SBP of the two the study groups at 0 mins, 15 mins, 30 mins (p>0.05); but statistically significant at 45 mins, 60 mins, 75 mins, 90 mins, 105 mins, 120 mins. There was no statistical difference between the DBP of the two study groups at 15 mins and 30 mins (p>0.05); statistically highly significant at 45 mins, 60 mins and 75 mins (p<0.001).

The difference in the mean pulse rate between the two groups at 120 min,240 mins and 360 mins were found statistically highly significant. (p<0.001). There is significant decrease in post-operative pulse rate in group BD compared to group B at the mentioned time points.

The difference in the mean systolic blood pressure between the two groups at 120 min and 240 mins were found statistically highly significant (p<0.001) and at 360 mins difference also statistically significant (p<0.05). There is significant decrease in post-operative systolic blood pressure in group BD compared to group B at the mentioned time points.

The difference in the mean diastolic blood pressure between the two groups at 120 min and 240 mins were found statistically highly significant (p<0.001) and at 360 mins difference also statistically significant (p<0.05).

There is significant decrease in post-operative diastolic blood pressure in group BD compared to group B at the mentioned time points.

Table 4 shows the comparison of duration of analgesia or time to 1st rescue analgesic between the two study groups. The mean duration of analgesia in Group B was 289.7 mins ± 78.21. In Group BD mean time to 1st rescue analgesic was 648.9 ± 130.59.

The mean duration of pain relief calculated from the time of caudal analgesia administration to time of rescue analgesic. The difference in duration of analgesia between study groups was statistically highly significant (p<0.001). Duration of analgesia prolong in group BD.

Duration of analgesia (mins)	Group B	Group BD	p value
Range (min-max)	120-420	480-1000	<0.001
(Mean ± SD)	289.7 ± 78.21	648.9 ± 130.59	

Table 4: Duration of analgesia.

Table 5 shows the comparison of FLACC pain scores 60 at various time points between the two groups. This pain assessment tool is recommended for children between 2-7 years of age. It is measured by observing the following-minimum score is 0 which indicate that the child is pain free, analgesia is excellent. Score 4 indicates significant pain and rescue analgesia is required. The mean pain scores at 0 mins, 120 mins, 240 mins and 360 mins after extubation were significantly lower in group BD (p<0.001).

Table 6 shows the comparison between Ramsay sedation score 61 between two groups at various time points. When sedation score is 1 patient is anxious, agitated or restless and taken as end point of studying sedation. The mean sedation scores at 0 mins, 120 mins and 240 mins after extubation were significantly higher in group BD (p<0.001).

FLACC pain score	Group B (mean ± SD)	Group BD (mean ± SD)	p value
FLACC 0 at end of operation	2.5 ± 0.55	0.6 ± 0.50	<0.001
FLACC 120 min after operation	3.3 ± 0.49	1.6 ± 0.55	<0.001
FLACC 240 min after operation	3.8 ± 0.34	2.2 ± 0.53	<0.001
FLACC 360 min after operation	4.0 ± 0.00	2.8 ± 0.56	0.001

Table 5: Comparison of FLACC pain scores.

Ramsay sedation score	Group B (mean ± SD)	Group BD (mean ± SD)	p value
RSS 0 at end of operation	1.9 ± 0.16	3.7 ± 0.46	<0.001
RSS 120 min after operation	1.6 ± 0.49	2.8 ± 0.39	<0.001
RSS 240 min after operation	1.1 ± 0.34	2.3 ± 0.45	<0.001

Table 6: Ramsay sedation score.

Incidence of side effects like vomiting and urinary retention was equal between two groups. In BD group only 3 patients were given atropine for bradycardia (HR<60/mins) which was also not statistically significant compared to group B.

Discussion

Alpha 2 Adrenergic receptor agonists could prolong the duration of action of bupivacaine and improve the quality of analgesia [12,13], by causing local vasoconstriction [12] and increasing the potassium conductance in Ad and C fibers [13,14]. They may also potentiate the action of local anesthetic by entering the central nervous system either via systemic absorption or by diffusion into the cerebrospinal fluid and reach alpha 2 receptors in the superficial laminae of the spinal cord and brainstem [15], or indirectly activating spinal cholinergic neurons [16].

Caudal epidural anesthesia is one of the most common regional techniques used in the pediatric age group. It is recommended for most infraumbilical surgical procedures like herniorrhaphy, operations on the urogenital tract, anus and rectum and orthopedic procedures on the lower extremities.

The disadvantage of single-shot caudal anesthesia is the relatively limited duration of postoperative analgesia. Dexmedetomidine, although currently available for iv use only, has been successfully administered epidurally for postoperative analgesia in humans in clinical trials [13,18-20].

The present study demonstrated that addition of dexmedetomidine to caudal bupivacaine prolongs duration of analgesia, provides better quality of sleep and prolong duration of arousal sedation and better hemodynamic stability to the children compared to only caudal bupivacaine. Intraoperative diastolic, systolic blood pressure and heart rate decreases significantly after around 45 mins but not to the acceptable limit.

In a recent prospective randomized double blind study, the effects of caudal clonidine and dexmedetomidine as an adjunct to caudal bupivacaine for postoperative analgesia in pediatric patients undergoing sub-umbilical surgeries have been studied. 90 patients aged 1 to 8 years scheduled for sub-umbilical surgeries were randomly allocated into three groups of 30 patients each. Group A received 1 ml/kg of 0.25% bupivacaine with dexmedetomidine 2 μg/Kg in normal saline 1 ml. Group B received 1 ml/kg of 0.25% bupivacaine with clonidine 2 μg/Kg in normal saline 1 ml and Group C received 1 ml/kg of 0.25% bupivacaine with normal saline 1ml. All the patients in their study remained hemodynamically stable throughout the intraoperative and postoperative period. Addition of either dexmedetomidine 2 μg/kg or clonidine 2 μg/kg to 0.25% caudal bupivacaine significantly prolonged the postoperative analgesia time without increasing the incidence of side effects like nausea, vomiting, pruritis or urinary retention.

No episodes of clinically significant postoperative respiratory depression, hypotension, or bradycardia were identified.

In this study, we used the FLACC Pain Scale. Previous studies of pediatric postoperative caudal analgesia have alternatively used the Children's Hospital of Eastern Ontario Pain Scale [21], the Children and Infants Postoperative Pain Scale [22] or the Objective Pain Scale [23].

So we conclude that addition of dexmedetomidine (2 μg/kg) to caudal bupivacaine 0.25% (1 ml/kg) prolongs duration of analgesia, provides better quality of sleep and prolong duration of arousal sedation and better hemodynamic stability to the children compared to only caudal bupivacaine 0.25% (1 ml/kg).

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