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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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Abstract:
Background: *74 children, either sex, aged 2-7 years , ASA grade I, II, scheduled to undergo infraumbilical 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 2µg/kg B/W in 1ml normal saline after induction . Pulse rate, blood pressure, SPO2 were monitored and recorded at 0 min (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 analgesic 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 rates, systolic blood pressure, diastolic blood pressure, post-operative pulse rate, systolic and diastolic blood pressure in Group-BD were 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 arousable sedation and better haemodynamic stability to the children compared to caudal bupivacaine .*
Keywords: *anaesthesia; caudal; analgesia; bupivacaine; dexmedetomidine*

I. 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 paediatric patients because poor pain control may result in increased morbidity and mortality[5]. Paediatric anaesthesiologists 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 infraumbilical 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 anaesthesia 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 paediatric surgical procedures for 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 group, 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 paediatric 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.

II. Method

After local ethical committee approval and obtaining informed parental consent, 74 ASA status I and II patients, aged 2-7 yrs undergoing elective infraumbilical 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 2µg/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/ kg BW) 20– 30 min before anaesthetic induction, and then underwent a standard inhalational induction with sevoflurane and nitrous oxide in oxygen followed by insertion of an i.v. canula and administration of a atracurium to facilitate endotracheal intubation. Induction was strictly inhalation .Glycopyrolate (0.01mg /kg BW) 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 anaesthesia was maintained with sevoflurane delivered in oxygen and nitrous oxide. No other narcotic, analgesic, sedative, or antiemetic were administered intra-operatively. At the end of surgery reversal from general anaesthesia was done with injection neostigmine 0.05 mg/kg BW and injection glycopyrrolate 0.01 mg/kg BW. Patient transported to the post-anaesthetic care unit (PACU) when fully awake, moving all four limbs and adequate cough reflex present.

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

The occurrence of intra-operative 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 haemodynamic changes were noted.
5) Occurence of any side effect like vomiting,urinary retension,bradycardia was noted. When FLACC Score was 4 or more inj. Diclofenac 1mg/kg im was given as rescue analgesic to the child.

Once transferred to the in-patient care unit, the oxygen saturation, heart rate, and arterial pressure were continuously monitored in the presence of a staff nurse. The occurrence of postoperative respiratory depression (defined as oxygen saturation of ,95%), hypotension (defined as systolic arterial pressure ,70 plus twice the age in years and associated with altered peripheral perfusion), bradycardia (defined as heart rate below 60 beats min).

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

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 occational complaint	Crying steadily, screams or sobs, frequent complain
Consolability	content,relaxed	reassured by occational touching, hugging/ talking, distractable	Difficult to console

For assessment of sedation **Ramsay sedation scale[11]** was used:
1-Anxious and agitated or restless or both 2-Co-operative,oriented and calm 3-Responsive to commands only 4-Exhibiting brisk response to light glabellar tap or loud auditory stimulous 5-Exhibiting a sluggish response to light glabellar tap or loud auditory stimulous 6-Unresponsive

III. Statistical Analysis

Softwares used-:

1)Microsoft excel(Ver 10.2627.2625) [Microsoft corporation,USA,2002]
2) SPSS 16.0 [SPSS inc.ILLINOIS,USA,2008]
3) Statistica 6.0[statsoft inc.,Tulsa, Oklahama,USA,2001]
4) PS power and sample size calculation (Ver 2.1.30) Plummer and Dupont Feb‖2003.

All raw data were entered into an excel spread sheet and analyzed using appropriate statistical software. Categorical variables (eg.demographic parameters like sex, ASA, physical status) will be analyzed using Pearson's Chi square test.

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 primery 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.

IV. Results

None of the 74 attempted caudal blocks was perceived as being a failed attempt;

Table 1 and 2 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.

The mean intra-operative 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 was no statistical difference between the intra-operative 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 intra-operative 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 post-operative 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 ($p<0.001$). 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. ($p<0.001$). 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 3 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.

Table 4 shows the comparison of FLACC pain scores 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 5 shows the comparison between Ramsay sedation score between two group 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 ($p<0.001$).

Table 1-Age (in years),**Weight**(in kilogram) ,**Sex distribution,duration of surgeries** (in minutes) in 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-Types of surgery performed in study groups

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-Comparison of **Duration of analgesia / Time to First rescue analgesic (in mins)** between two study groups.

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-Comparison of **FLACC pain scores** between groups at various time points.

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 **Ramsay sedation score** between groups at various time points.

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

Incidence of side effects like vomiting and urinary retention were 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.

V. 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 fibres.[13,14] They may also potentiate the action of local anaesthetic 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 neurones.[16]

Caudal epidural anaesthesia is one of the most common regional techniques used in the paediatric age group. It is recommended for most infra-umbilical surgical procedures like herniorrhaphy,operations on the urogenital tract, anus and rectum and orthopaedic procedures on the lower extremities.

The disadvantage of single-shot caudal anaesthesia is the relatively limited duration of postoperative analgesia

Dexmedetomidine, although currently available for iv use only, has been successfully a dministered 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 arousable sedation and better haemodynamic stability to the children compared to only caudal bupivacaine.Intraoperative diastolic, systolic blood pressure and heart rate decreases

significantly after around 45 mins.

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 paediatric patients undergoing sub umbilical surgeries have been studied.[21] 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 1ml/kg of 0.25% bupivacaine with dexmedetomidine 2µg/Kg in normal saline 1 ml. Group B received 1ml/kg of 0.25% bupivacaine with clonidine 2µg/Kg in normal saline 1 ml and Group C received 1ml/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 2µg/kg or clonidine 2µg/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.

In another study that Caudal dexmedetomidine combined with bupivacaine inhibit the response to hernial sac traction in children undergoing inguinal hernia repair.[22] Sixty children aged 12-72 months undergoing unilateral inguinal hernia repair were randomly assigned to receive either bupivacaine 0.25% 1 ml/kg(Group B) or bupivacaine plus dexmedetomidine 1 µg/kg; (Group BD). The response to hernial sac traction was defined as an increase in heart rate or systolic arterial pressure by >20%, and was treated with ketamine rescue (2 mg/ kg). After the surgery, fentanyl was administered as needed with a nurse-controlled analgesia pump.Only one subject in Group BD (3.33%) needed ketamine rescue, as opposed to 13 subjects in Group B (43.33%; P<0.001). The first fentanyl injection occurred at a much later time point in Group BD (median: 860 vs 320 min in Group B; P<0.001). Total consumption of fentanyl was significantly lower in Group BD.

In this study, we used the FLACC Pain Scale. Previous studies of paediatric postoperative caudal analgesia have alternatively used the Children's Hospital of Eastern Ontario Pain Scale,[23] the Children and Infants Postoperative Pain Scale[24] or the Objective Pain Scale[25]. We used inj diclofenac 1mg/kg BW when FLACC score 4 or more .No episodes of clinically significant postoperative respiratory depression, hypotension, or bradycardia were identified in our study .

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

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