

**COMPARISON OF DEXMEDETOMIDINE AND CLONIDINE AS ADJUVANTS TO  
0.25% BUPIVACAINE IN PAEDIATRIC CAUDAL BLOCK FOR  
INFRAUMBILICALSURGERIES**

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**Abstract**

**Background:** Caudal block is a common technique for paediatric analgesia but has disadvantage of short duration of action after single injection. Various adjuvants were tried with local anaesthetics to prolong duration of post-operative analgesia in caudal block. This prospective study was designed to assess and compare the efficacy of clonidine and dexmedetomidine used as adjuvants to bupivacaine for caudal analgesia in paediatric patients

**Materials and methods:** The study included 60 pediatric patients undergoing infraumbilical surgeries who were separated based on American Society of Anesthesiologists (ASA) status I and II and belonged to the age between 6 months and 6 years. The caudal block was administered with bupivacaine 0.25% with dexmedetomidine 1 µg/kg (group D) and bupivacaine 0.25% with clonidine 1µg/kg (group C) after sedation with propofol. Hemodynamic parameters were monitored before, during, and after the surgical procedure. Postoperative analgesic duration, total dose of rescue analgesia, pain scores, and any side effects were observed.

**Results:** Addition of dexmedetomidine or clonidine to caudal bupivacaine significantly promoted analgesic time. Also, there was statistically significant prolonged duration of analgesia with dexmedetomidine compared to clonidine. No significant difference was observed in incidence of hemodynamic changes or side effects.

**Conclusion:** Addition of dexmedetomidine or clonidine to caudal bupivacaine significantly prolonged analgesia in children undergoing infraumbilical surgeries. It was also observed that the performance of dexmedetomidine was better as compared to clonidine without an increase in incidence of side-effects

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## INTRODUCTION

Pain is perhaps the most feared symptom of disease, which a man is always trying to alleviate and conquer since ages. It is defined by the international association for study of pain as an “unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage”.<sup>[1]</sup>

Popular dogma had suggested that the human child does not feel pain, and that it is dangerous to give him powerful analgesia because of the risk of addiction.<sup>[2]</sup> Under treatment of post-operative pain even in the children and newborns may trigger biochemical and physiologic stress response and cause impairments in pulmonary, cardiovascular, neuro endocrinal, gastrointestinal, immunological, and metabolic functions.<sup>[3]</sup>

Caudal epidural block is one of the most common regional techniques in paediatric anesthesia.

Caudal block is safe and reliable technique, easy to perform and has been found to be very effective in children, especially in infra-umbilical surgeries when combined with general anaesthesia. It allows rapid recovery from anaesthesia with good post-operative analgesia.<sup>[4]</sup>

The main disadvantage of caudal analgesia is duration of action after a single injection which is limited by duration of action of local anesthetics. Placement of a catheter has an inherent risk of infection. Prolongation of caudal analgesia using a single-shot technique has been achieved by the addition of various adjuvants such as opioids, ketamine, neostigmine, midazolam and  $\alpha_2$  agonists. Many of these adjuvants have side effects like respiratory depression, vomiting, pruritus etc.<sup>[5,6]</sup>

Both Clonidine and dexmedetomidine have been used to prolong analgesia through various routes viz intravenous, intrathecal, epidural, caudal and peripheral nerve blocks

Clonidine, is an  $\alpha_2$  adrenergic agonist, offers several benefits in children when added to local anaesthetics either neuraxially<sup>[7,8,9]</sup> or peripherally<sup>[10]</sup>. It increases the duration of nerve blockade without eliciting hemodynamic disorders, decreases plasma peak concentration of the local anaesthetics, and produces a slight sedation for 1 to 3 hours postoperatively(which does not preclude hospital discharge). Clonidine provides a substantial antinociceptive effect by acting on the  $\alpha_2$  receptors in the dorsal horn of spinal cord and brain stem nuclei implicated in pain.<sup>[11,12]</sup>

Dexmedetomidine has an eight fold greater affinity for alpha 2 adrenergic receptors than clonidine and much less alpha 1 effect. A major advantage of dexmedetomidine is its higher selectivity compared with clonidine alpha 2a receptors, responsible for the hypnotic and analgesic effects of such drugs.<sup>[13]</sup>

So we conducted this study to compare the duration of postoperative analgesia, hemodynamic changes and adverse effects of 1 $\mu$ g/kg dexmedetomidine and 1 $\mu$ g/kg clonidine when added to bupivacaine for caudal analgesia in children undergoing infraumbilical surgeries.

## MATERIALS & METHODS:

After obtaining informed parental consent, 60 American Society of Anesthesiologists (ASA) status I and II patients, aged 6 months-6 year undergoing 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 proposed caudal block. Patients fulfilling the inclusion criteria were selected for the study and randomly allocated to either Group D (n= 30,

received caudal 1ml/kg of 0.25% bupivacaine with 1 µg/kg dexmedetomidine constituted to 1 ml) or Group C (n=30, received caudal 1ml/kg of 0.25% bupivacaine with 1 µg/kg clonidine constituted to 1ml) by computer generated random table.

All patients and their parents were blinded to the caudal medications administered. All medications were prepared by anesthesiologists not participating in the study except for preparing the drugs. The anesthesiologist who administered anaesthesia also monitored the patient peri-operatively and was unaware of the study drug.

All patients were pre-medicated with syrup midazolam 0.8mg/kg, 30 min prior to induction. After adequate sedation child was separated from parents. SPO<sub>2</sub>, NIBP, ECG monitors were attached. After starting O<sub>2</sub> by simple mask all patients were induced with Injection propofol 2mg/kg and then intravenous infusion of 100µg/kg/min was started and maintained on spontaneous respiration. An infusion of Ringer Lactate was started and was administered according to the calculated requirements. Patient heart rate, oxygen saturation and blood pressure were recorded every 5 minutes from starting to the end of procedure. Patient was placed in the left lateral position, vitals and adequacy of respiration were checked. Caudal anesthesia which was achieved with 23 gauge hypodermic needle under all aseptic conditions and the patients were turned supine immediately after the injection. Group C (n=30) received 0.25% bupivacaine 1 ml/kg + clonidine 1 µg/kg and group D (n=30) received 0.25% bupivacaine 1 ml/kg + dexmedetomidine 1 µg/kg via caudal route with a total volume being constant at 1 ml/kg in both the study groups

The block was deemed as successful if there is absence of gross movement of limbs to painful stimulus and when increases in heart rate or systolic arterial pressure in response to skin

incision was ≤20%. No analgesia was given by any route intra-operatively. Failed caudal block cases were excluded from the study.

Towards the end of surgery propofol infusion was stopped and the duration of surgery and time of recovery from propofol was noted. Bolus intravenous propofol 1mg/kg was given as and when required during intra-operative period to maintain sedation score 1 or 2 (opening of eyes: 3□-spontaneously, 2□-to verbal command, 1□-to physical shaking, and 0□-not arousable). Intraoperatively any adverse effects such as bradycardia (Heart rate <80bpm for age < 1yr and <60bpm for ages > 1yr) were noted and treated with 20µg/kg of injection Atropine and hypotension (defined as systolic arterial pressure 70 plus twice the age in years and associated with altered peripheral perfusion) were noted and treated with fluid boluses. Once the vitals were stable and the child was awake, the child was shifted to post operative recovery room and was monitored for heart rate, non-invasive blood pressure, oxygen saturation and pain score using modified objective pain scale (OPS) was employed to assess the postoperative pain and duration of analgesia which was based on behavioral objectives that included crying, facial expression, position of legs, position of torso and generalized motor restlessness. A score of 0 was considered as excellent analgesia, while a score of 10 signifies completely ineffective analgesia. The OPS was employed every 15 minutes for first 2 hours and thereafter every 30 minutes until the requirement of first rescue analgesia, time of which was noted.

Duration of first rescue analgesia is defined as the time interval between the administration of caudal block and the first requirement of rescue analgesia postoperatively.

Children who had a pain score of more than 3 were administered 5 mg/kg of injection paracetamol IV slowly. The total amount of analgesic dose and any complications or side effects were looked for and recorded. All the

patients were observed for next 24 h in the special room and the recordings of all parameters were done.

### Statistical analysis

Statistical analysis was done using SPSS software version 11.0. All the values are expressed as mean±SD. Unpaired t test was applied to know the difference between 2 groups in quantitative data. Chi-square test was applied for proportions and qualitative data. P<0.05 was considered as statistically significant.

### RESULTS:

We enrolled 60 children (30 children in each group) in our study profile. No difference could be detected from the data of 60 children regarding the patient profile. Demographic data of patients are given in Table 1. There were no significant difference in the groups in terms of age, bodyweight, gender distribution & duration of surgery.

**Table 1:** Demographic data... (age, weight, sex, duration and type of surgery)

	Group D	Group C	p value
Age in months	30.03±15.38	37.07±16.17	0.09
Weight in kgs	10.83±3.03	10.76±2.86	0.92
Sex (M/F)	26/4	28/2	0.39
Duration of surgery	42.3±31.6	47.5±34.3	0.54
Distribution of surgical procedures			
Herniotomy	23	23	
Hypospadias repair	2	2	
Circumcision	1	0	
Orchidopexy	2	1	
Others	2	4	

### Intraoperative hemodynamic variation

**Table 2 :** Vital parameters (Intra operative Pulse rate and MAP changes)

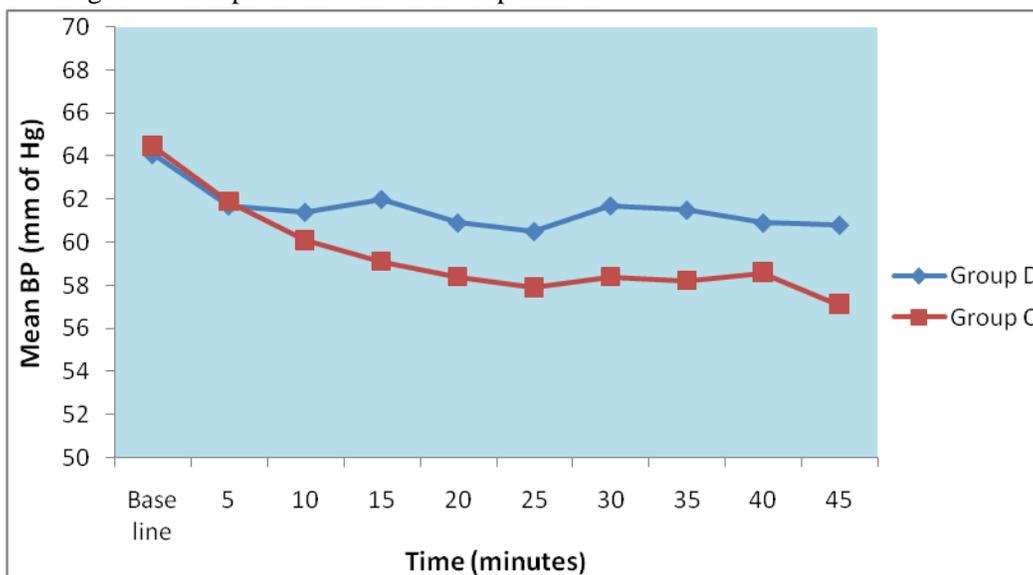
	Group D (mean ± SD)	Group C (mean ± SD)	p Value
Preop PR (per min)	(105.4±9.4)	(102.6±13.3)	0.35
Intraop PR	(107±13.2)	(104±14.2)	0.64
Postop PR	(106±10.3)	(107±9.8)	0.71
Preop MAP (mmHg)	(64.1±8.1)	(64.5±8.4)	0.84
Intraop MAP	(61.7±9.1)	(59.1±5.6)	0.15
Postop MAP	(62.5±8.6)	(60±4.5)	0.18

Table 2 conveys the comparison of various vital parameters of the patients of both the groups. Intraoperative heart rate (HR), noninvasive blood pressure (NIBP) showed no statistical significant difference between the two groups (P > 0.05). No significant hypotension or bradycardia was observed in any patient. SpO<sub>2</sub> (> 98%) was always within the clinically acceptable range in both the groups throughout the procedure (P > 0.05)

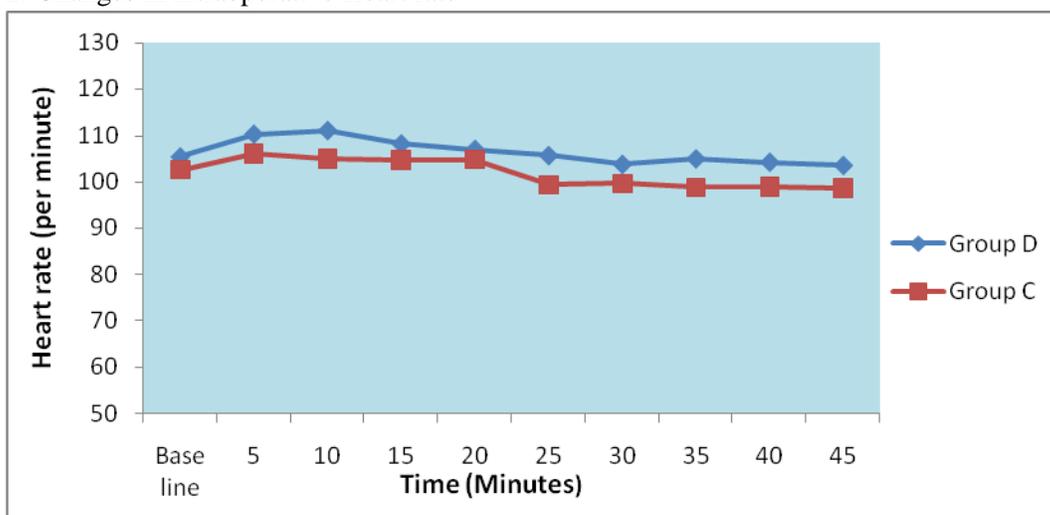
As shown in Graph 1, the mean MAP in both the groups were comparable and no significant difference between the two groups can be made out from below line diagram.

It is quite clear from the Table 3 that first analgesic requirement time was statistically prolonged in group D ( $17.6 \pm 2.9$  h) when compared to group C ( $10.1 \pm 3.2$  h) ( $P < 0.05$ ). Total analgesic consumption was statistically lesser in group D ( $60 \pm 47$  mg) when compared with group C ( $100 \pm 76$  mg) ( $P < 0.05$ ). Mean pain score in Group D was ( $3.58 \pm 0.40$ ) and in Group C was ( $3.31 \pm 0.38$ ). Mean sedation score was ( $2.86 \pm 0.52$ ) and in Group C was ( $2.72 \pm 0.49$ ).

**Graph 1:** Changes in intraoperative Mean arterial pressure.



**Graph 2:** Changes in intraoperative Heart rate



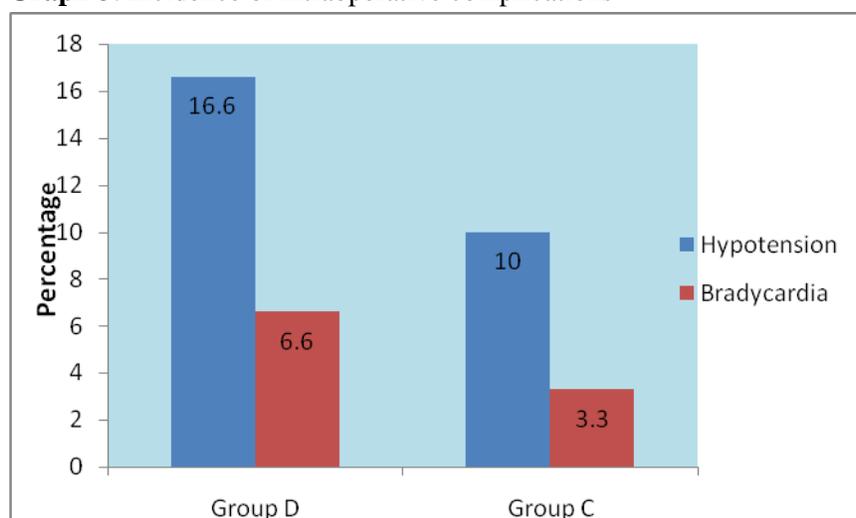
The postoperative sedation scores showed no statistically significant difference ( $P > 0.05$ ) which is clearly evident from description in Table 4. No motor impairment was seen in either group on awakening and during the next 24 h period.

**Table 3:** Drug characteristics

	Group D(mean $\pm$ SD)	Group C (mean $\pm$ SD)
Mean duration of recovery	(10.5 $\pm$ 3.83)	(9.33 $\pm$ 3.99)
Mean duration of analgesia	(1111.33 $\pm$ 74.9)	(896.5 $\pm$ 40.8)
Mean pain scores	(3.58 $\pm$ 0.40)	(3.31 $\pm$ 0.38)
Mean sedation score	(2.86 $\pm$ 0.52)	(2.72 $\pm$ 0.49)

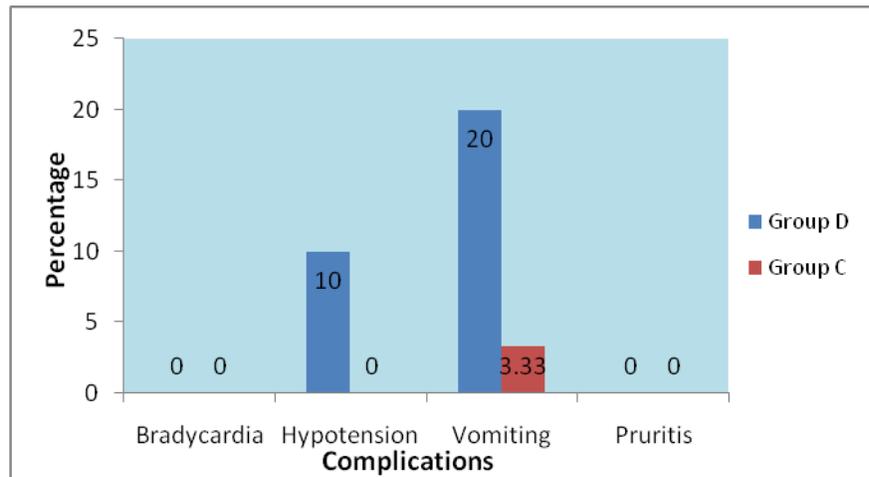
**Table 4:** Incidence of intraoperative complications

Complication	Group D (n%)	Group C (n%)	Chi square value	p- value
Hypotension	5 (16.6%)	3 (10%)	0.57	0.44
Bradycardia	2 (6.6%)	1 (3.3%)	0.35	0.55

**Graph 3:** Incidence of intraoperative complications**Table 5:** Incidence of postoperative complications

Complication	Group D (n%)	Group C (n%)	Chi square value	p- value
Bradycardia	0	0	-	-
Hypotension	3 (10%)	0	3.05	0.08
Vomiting	3 (10%)	1 (3.33)	3.75	0.06
Pruritis	0	0	-	-

The postoperative complications showed no statistically significant difference ( $P > 0.05$ ) which is clearly evident from description in Table 5.

**Graph4:** Incidence of postoperative complications**DISCUSSIONS:**

Historically it was believed that children do not feel pain and it would be harmful to give them powerful analgesics due to the risk of addiction.<sup>[2]</sup> But now alleviation of pain is felt as basic human right and currently postoperative pain management has become an integral part of pediatric anesthesia.<sup>[4,5]</sup>

The analgesic action of intrathecal or epidural clonidine was first demonstrated clinically in 1984.<sup>[14]</sup> The successful use of epidural clonidine in adults led to its evaluation in pediatric caudal block. The resulting studies have consistently shown caudal clonidine to increase the duration of postoperative analgesia.<sup>[15,16]</sup> On the other hand, dexmedetomidine has been administered epidurally for postoperative analgesia in humans in clinical trials.<sup>[17-19]</sup> Nevertheless, there are still some concerns regarding its safety.

Caudal epidural analgesia is most common regional anesthesia technique for providing anesthesia and analgesia in children undergoing infra umbilical surgeries which is safe, reliable, effective and easy to perform.<sup>[5]</sup>

The duration of action after single injection is limited by duration of action of local anesthetic used and to prolong its effect wide

range of additives have been used in combination with local anesthetics to promote analgesia.<sup>[20]</sup>

The use of additives during caudal anesthesia have increased in the last decade by 58%,<sup>[21]</sup> specially with ketamine 38% and clonidine 42%, whereas the use of opioids as additives has decreased from 36% to 18% due to the higher incidence of side-effects as nausea and vomiting, itching and respiratory depression specially in children.<sup>[22,23]</sup>

Dexmedetomidine potentiates the action of local anesthetics without increasing the incidence of side-effects. Compared to clonidine, it is a highly selective  $\alpha_2$  adrenergic receptor agonist, and this facilitates its use in larger doses for analgesia and sedation without the fear of inadvertent effects on the hemodynamics.<sup>[24]</sup>

In this study, we found that the time of adequate caudal analgesia without the need for paracetamol is significantly higher in the groups receiving the bupivacaine–dexmedetomidine mixture ( $1111.33 \pm 74.9$  minutes) than the group receiving bupivacaine–clonidine mixture ( $896.5 \pm 40.8$  minutes)

Arunaparameshwari et al <sup>[25]</sup> found that the clonidine in a dose of 1  $\mu\text{g}/\text{kg}$  added to 0.25% bupivacaine for caudal analgesia, during sub-umbilical surgeries, prolongs the duration of

analgesia of bupivacaine (10 hours) with less requirement of rescue analgesics without any side effects.

In a study conducted by Saadwy et al<sup>[19]</sup> compared 1 ml/kg of 2.5 mg/ml bupivacaine alone and along with dexmedetomidine 1µg/kg showed that there was significant prolongation of duration of analgesia in dexmedetomidine group 18.5±2.8hrs in compared to 6.2±2.8hrs in bupivacaine alone group

El-Hennawy et al<sup>[26]</sup> Single caudal dose of bupivacaine 0.25% (1 ml/ kg) combined with either dexmedetomidine 2 µg/ kg in normal saline 1 ml in group BD, clonidine 2 µg/ kg in normal saline 1 ml in group BC, or corresponding volume of normal saline in group B. They have found that the time of adequate caudal analgesia (FLACC scale score, 4) without the need for morphine is significantly higher in the groups receiving the bupivacaine-dexmedetomidine mixture [median (95% CI):16 (14–18) h] or bupivacaine– clonidine mixture [median (95% CI): 12 (3–21) h] than the group receiving plain bupivacaine [median (95% CI): 5 (4–6) h]. They concluded that addition of dexmedetomidine or clonidine to caudal bupivacaine significantly promoted analgesia in children undergoing lower abdominal surgeries with no significant advantage of dexmedetomidine over clonidine and without an increase in incidence of side effects.

Neogi et al<sup>[27]</sup> compared ropivacaine 0.25% 1ml/kg alone and dexmedetomidine 1µg/kg or clonidine 1µg/kg with ropivacaine 0.25% 1ml/kg caudally. The mean duration of analgesia was 6.32±0.46 hours in the ropivacaine group, 13.17±0.68 hours in the clonidine group and 15.26±0.86 hours in the dexmedetomidine group. They concluded that addition of both clonidine and dexmedetomidine to ropivacaine administered caudally significantly increases the duration of analgesia

Manjunath et al<sup>[28]</sup> conducted study on 90 children age 3-6yrs, ASA 1 and 2 , to study the

adjuvant effect of fentanyl 1µg/kg or clonidine 2µg/kg to ropivacaine 0.2 % 1ml/kg for pediatric caudal analgesia for lower abdominal surgeries for assessment of postoperative duration of rescue analgesia. They used Hanallah pain scale scores to assess pain. They concluded that fentanyl or clonidine when added to ropivacaine prolongs the duration and quality of analgesia when compared to ropivacaine alone group and clonidine is better adjuvant due to more prolonged analgesia and lesser side effects.

In our study when mean pain scores (assessed by objective pain scale modified Hanallah pain scale) between the 2 groups were compared in postoperative period, scores were comparable in groups till 660 min but later the mean pain scores were higher in group C in compared to group D from 660 min to the time of rescue analgesia ( when score >3) , which was statistically significant

In our study 3(10%) patients in group D had hypotension but no case had hypotension in group C and it was statistically not significant. Postoperative vomiting was seen among 6 (20%) patients in group D and 1 (3.33%) patient in group C which was statistically significant as p value was <0.05. In studies conducted by Saadwy et al<sup>[19]</sup>, El shamma et al<sup>[29]</sup> had incidence of postoperative vomiting but it was statistically not significant.

## CONCLUSION

Caudal dexmedetomidine (1µg/kg) with 0.25% bupivacaine for pediatric infraumbilical surgeries achieved significant post-operative pain relief compared to caudal clonidine (1µg/kg) with 0.25% bupivacaine without any significant difference in hemodynamic parameters. Hemodynamic variations and side effects were comparable in both the groups. In post-operative period, requirement of rescue analgesic doses in the form of syrup paracetamol 15 mg/kg in 24 hours in dexmedetomidine group was less as compared to clonidine group.

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