COMPARATIVE CLINICAL EVALUATION OF CAUDAL BUPIVACAINE VERSUS BUPIVACAINE PLUS TRAMADOL FOR PEDIATRIC INFRAUMBILICAL SURGERIES: A STUDY ON POST-OPERATIVE ANALGESIA

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ABSTRACT

Objective: Effective post-operative pain management is crucial in pediatric patients undergoing infraumbilical surgeries. Various regional anesthesia techniques, including caudal block, have been used to provide post-operative analgesia in children. The addition of tramadol, a synthetic opioid analgesic, to bupivacaine in caudal anesthesia has shown potential benefits. This study aims to compare the clinical efficacy of single-shot caudal bupivacaine alone versus bupivacaine plus tramadol for post-operative analgesia in pediatric infra-umbilical surgeries.

Methods: A prospective, randomized, double-blinded clinical study was conducted at our institute. The present study will be carried out in 60 pediatric patients of the American Society of Anesthesiologists Grades I and II between the age of 1 and 8 years, undergoing infraumbilical surgeries. These children were randomly divided into 2 groups. Group B (n=30) received caudal block with 0.25% bupivacaine (1 mL/kg) and Group BT (n=30) received caudal block with 0.25% bupivacaine (1 mL/kg) with tramadol (1 mg/kg). The variables studied were hemodynamic changes, duration of analgesia, and incidence of side effects. Pain assessment was done at 1, 2, 3, 4, 8, 12, and 24 h post-operatively using modified objective pain scale.

Results: It was observed that the mean duration of analgesia in Group BT (9.05±2.21) h was significantly longer (p=0.0001) than Group B (3.78±0.94) h. Hemodynamic parameters remained comparable during intraoperative and post-operative periods. There was no incidence of nausea, vomiting, bradycardia, hypotension, pruritus, or decrease in respiratory rate in the two groups.

Conclusion: In our study, we concluded that a single-shot caudal block with 0.25% bupivacaine (1 mL/kg) plus tramadol (1 mg/kg) resulted in longer duration of analgesia when compared to 0.25% bupivacaine (1 mL/kg) alone with no incidence of any side effects.

Keywords: Caudal, Bupivacaine, Tramadol, Children, Infraumbilical surgeries.

INTRODUCTION

All forms of pain have not been well managed in children. This may be the result of insufficient information, poor assessment, questions regarding the safety and effectiveness of analgesics, and concerns about the possibility of opioid-induced respiratory depression. It can be challenging to tell the difference between children's agitation and sobbing that are brought on by hunger or fear [1].

According to Langlade *et al.*, who adopted the philosophy of "managing pain before it occurs," post-operative pain management must be considered in the anesthetic planning even before induction of anesthesia [2].

Numerous regional anesthetic techniques have grown in popularity for post-operative analgesia over the years because, in addition to effectively reducing post-operative pain, they also lessen the need for general anesthesia during surgery without causing noticeable side effects and maintain a pain-free intra and post-operative period. For both intraoperative and post-operative analgesia during a variety of infra-umbilical procedures on children, the caudal block has proven beneficial [3].

Drugs for local anesthesia can be used in a range of concentrations. Following a single-shot caudal epidural, local anesthetics alone were not shown to increase the mean duration of post-operative pain relief; hence, other caudal additives such as clonidine, midazolam, ketamine, fentanyl, and tramadol were used [4].

Tramadol, a synthetic opioid analgesic with a moderate potency whose effects vary depending on the type of opioid-specific receptors, was employed as an additive in our investigation. Tramadol can be administered as an adjuvant for the treatment of pain or combined with local anesthetics in a variety of ways to increase their analgesic power without raising the likelihood of side effects [5].

Statistical analysis

All parameters are compared between the two groups and results of continuous variables are given either mean±SD or proportion as percentage. The difference between the two groups was assessed by student's t-test for numerical variables and chi-square test for categorical variables. For all the tests, a "p" value of <0.05 was considered statistically significant and "p" value >0.05 was considered statistically insignificant.

METHODS

A prospective, randomized double-blinded clinical study was conducted at Jhalawar Medical College and SRG Hospital, Jhalawar, Rajasthan, from March 2021 to December 2021. After ethical committee approval and written informed consent from patients and/or attendants. The present study will be carried out on 60 pediatric patients of the American Society of Anesthesiologists (ASA) Grades I and II between the ages of 1 and 8 years, undergoing infraumbilical surgeries in the department of anesthesia in our hospital.

Materials required
1. 23G needle (hypodermic)
2. 5 cc syringe (for whoosh test)
3. Sterile swabs, bowl, sponge-holding forceps, sterile hole towel, and spirit.
4. Drugs - bupivacaine 0.5% vial and tramadol 50 mg/mL ampoule.
5. Anesthesia workstation with sevoflurane vaporizer, Jackson-Rees circuit.
6. Patent IV line with the infusion of crystalloid.
7. Sterile water for dilution
8. Emergency equipment included:
   - Working laryngoscope, with assorted blades
   - Endotracheal tubes of appropriate sizes
   - Appropriate airways with masks
   - AMBU bag of pediatric size
   - Suction apparatus.
9. Emergency drugs - drugs necessary for the administration of general anesthesia and resuscitation were kept ready, e.g., adrenaline, atropine, dobutamine, dopamine, mephentermine, hydrocortisone, deriphyllin, etc.

Pre-anesthetic assessment
The children were seen on the day before surgery and a general, systemic examination including the airway and spine were examined. Parameters such as heart rate, blood pressure, and respiratory rate were measured. Blood examinations, bleeding time and clotting time, chest X-ray if required, and HIV and HBsAg were done in all patients. Informed consent was obtained from the parents and relatives.

Study group
60 patients will be divided into 2 groups. Each group will consist of 30 patients (n=30).
- GROUP B: Caudal block with bupivacaine 0.25% (1 mL/kg).
- GROUP BT: Caudal block with bupivacaine 0.25% (1 mL/kg) plus tramadol (1 mg/kg).

Group B received 0.25% bupivacaine. Group BT received 0.25% bupivacaine plus tramadol 1 mg/kg. Tramadol was available as a 2 mL ampoule containing injection of tramadol 50 mg/mL. Each 10 mL of the prepared solution contained 0.25% bupivacaine or 0.25% bupivacaine with 10 mg tramadol. The volume of the drug to be injected was calculated according to Armitage recommends 1 mL/kg for a lumbosacral block.

Inclusion criteria
- The age group of 1–8 years
- ASA Grades I and II
- Pediatric patients coming for infraumbilical surgeries.

Exclusion criteria
- ASA Grades III and IV
- Parent refusal
- Infected wounds at the sacrum
- Coagulopathy or anticoagulation
- Congenital sacral anomalies
- Meningitis patients
- History of allergy to local anesthetics.

Pre-operative fasting
Solid foods were restricted for 6 h, breastmilk for 4 h, and clear fluids for 2 h before surgery.

Pre-medication
All children were pre-medicated with glycopyrrolate (0.004 mg/kg), ondansetron (0.15 mg/kg), and midazolam (0.02 mg/kg) after securing intravenous access.

Procedure
Patients were induced with oxygen, nitrous oxide (50:50), and sevoflurane (in increasing concentration) using Jackson-Rees modification of Ayre's "T" piece and an intravenous line was secured. Injection glycopyrrolate (0.004 mg/kg) was given intravenously after securing IV access. An infusion of ringer lactate was started and fluid was administered according to the calculated requirements.

Patient was gently placed in the Sim's position (left lateral), and vitals were recorded including the adequacy of spontaneous breathing. Under strict aseptic conditions, sacral hiatus was identified by running the thumb up from coccyx toward the sacrum. After identifying the sacral hiatus, a 21G 1 ½ hypodermic needle with its bevel facing anteriorly was inserted at an angle of 60–70° to the skin till the sacrococcygeal membrane was pierced when a distinct "pop" was felt. The needle is now depressed to an angle of 20° and forwarded up to 2–3 mm to make sure that the entire bevel is inside the space. Confirmation of the needlepoint being in the epidural space was done with the "Swoosh" test and the lack of resistance encountered by injection of 2–3 mL of saline. Aspiration was done to exclude dural puncture or vessel puncture and the drug was injected, as 1 mL/kg of 0.25% bupivacaine with or without tramadol 1 mg/kg at 1 mL/3s. After injection was complete, the needle was removed and the child was placed in the supine position. Intraoperative analgesia was assessed by hemodynamic stability, as indicated by the absence of an increase in heart rate or systolic arterial pressure >15% compared with baseline values obtained just before surgical incision. No analgesia was given by any route pre-operatively or intraoperatively. Anesthesia was maintained with oxygen, nitrous oxide, and sevoflurane (0.2–3%) with patient on spontaneous ventilation throughout the surgery. Vital parameters monitored as HR, BP, SpO2, and respiration any movements due to pain. After completion of surgery, the anesthesia sevoflurane was stopped and patient was allowed to recover. All the vital parameters and timing of injections were noted and before shifting the patient to recovery room, laxity of the anal sphincter was noted in all the patients as a pointer of working caudal.

RESULTS

Mean distribution of age, weight, and gender between the two groups was comparable.

Distribution of surgeries between the groups was comparable with no significant difference between the two.

The comparison of mean heart rate between Group B and Group BT (Tables 1-8) showed no significant difference pre-operatively and during the intraoperative period (p>0.05). However, in the post-operative period, the heart rate was significantly higher in the bupivacaine group (Group B) compared to Group BT in the first 8 h (p<0.05). Beyond 8 h post-operatively, there was no significant association between the two groups in terms of heart rate (p>0.05).

While comparing pre-operative and intraoperative mean systolic blood pressure values in both the groups, it was found that the difference was clinically insignificant. In post-operative period, mean SBP was found to be increased in Group B as compared to Group BT during the first 8 h but the difference between two groups was found to be insignificant (p>0.05). Furthermore, there was statistically insignificant (p>0.05) association between two groups in 8 and 24 h.

While comparing the mean distribution of diastolic blood pressure in both the groups during pre and intraoperative period, difference in both the groups was statistically insignificant (p>0.05) (Figs. 1-5).

During post-operative period, mean DBP was found to be increased in Group B as compared to Group BT during the first 8 h but difference between two groups remained insignificant (p>0.05). Furthermore, there was statistically insignificant (p>0.05) association between two groups in 8 and 24 h.

While analyzing the distribution of respiratory rate and SpO_2 among two groups, it was observed that both parameters remained comparable between the two groups and were statistically insignificant (p>0.05).

Table 1: Distribution of age and weight between the groups

Parameter	Group B (Mean)	Group BT (Mean)	p-value
Age	5.1±2.18	5.2±2	0.8538
Weight	13.27±3.82	13.03±2.73	0.7805

Table 2: Distribution of surgeries between the groups

Type of surgery	Group B	%	Group BT	%
Circumcision	8	26.67	6	20
Herniotomy	19	63.33	20	66.67
Others	3	10.00	4	13.33
Total	30	100.00	30	100.00
p-value			0.9651	

Table 3: Comparison of post-operative heart rate

Post-operative heart rate distribution (beats/min)	Group B		Group BT		p-value
	Mean	SD	Mean	SD	
1 h	109.77	7.21	99.77	5.51	0.0001
2 h	112.1	5.88	100.47	3.30	0.0001
3 h	112.63	5.59	100.43	2.96	0.0001
4 h	113.36	4.68	100.53	3.06	0.0001
8 h	113.63	4.94	101.33	2.57	0.0001
12 h	102.1	4.35	103.13	4.54	0.3733
24 h	101.27	2.32	101	2.74	0.6819

Table 4: Comparison of post-operative systolic blood pressure (mmHg)

Post-operative Systolic Blood Pressure Distribution (mmHg)	Group B		Group BT		p-value
	Mean	SD	Mean	SD	
1 h	97.87	6.12	97.23	3.27	0.6153
2 h	98.4	4.67	97.8	3.25	0.5658
3 h	99.57	5.62	97.5	4.57	0.1230
4 h	98.7	5.08	97.63	5.21	0.4239
8 h	97.7	5.55	97.3	4.47	0.7596
12 h	96.97	5.93	97.2	4.92	0.4239
24 h	98.8	5.87	97.97	4.05	0.5263

Table 5: Comparison of post-operative diastolic blood pressure (mmHg)

Post-operative diastolic blood pressure distribution (mmHg)	Group B		Group BT		p-value
	Mean	SD	Mean	SD	
1 h	54.53	4.91	53.7	2.60	0.4166
2 h	56.1	4.45	55.3	4.13	0.4734
3 h	58.1	4.21	57.07	4.07	0.3393
4 h	58.67	4.22	57.03	4.49	0.1503
8 h	57.63	2.89	55.93	4.30	0.0748
12 h	55.17	5.01	55.87	4.24	0.5614
24 h	55.07	5.23	57.2	3.83	0.0771

Modified objective pain score

While analyzing time pediatric pain score distribution by modified objective pain scoring among the two groups, it was observed that the mean pain incidence at various time intervals in both the groups was statistically significant at 3rd, 4th, and 8th h post-operatively. The mean pediatric pain scoring in Group B in 3rd h was 3.7±1.08 and in Group BT, it was 0.76±1.13 which was found to be highly significant (p=0.0001,

Table 6: Distribution of modified objective pain score

Modified objective pain score distribution	Group B		Group BT		p-value
	Mean	SD	Mean	SD	
1 h	0	0	0	0	-
2 h	0	0	0	0	-
3 h	3.7	1.08	0.76	1.13	0.0001
4 h	3.53	1.30	2.36	0.66	0.0001
8 h	4.13	1.54	2.26	0.58	0.0001
12 h	3.1	1.55	2.5	0.94	0.0750
24 h	3.03	0.85	3.26	0.90	0.3131

Table 7: Duration of analgesia

Duration of analgesia	n	Mean	SD	p-value
Bupivacaine	30	3.78	0.94	0.0001
Bupivacaine+tramadol	30	9.05	2.21	

Table 8: Distribution of sedation scores between two groups

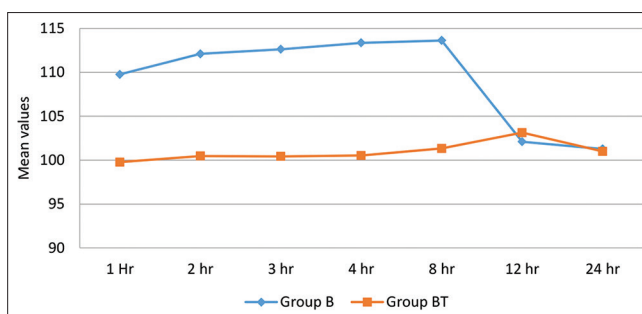| Post-operative sedation scores	Group B		Group BT		p-value
	Mean	SD	Mean	SD	
1 h	1	0	1	0	-
2 h	1	0	1	0	-
3 h	1	0	1	0	-
4 h	1	0	1	0	-
8 h	1	0	1	0	-
12 h	1	0	1	0	-
24 h	1	0	1	0	-

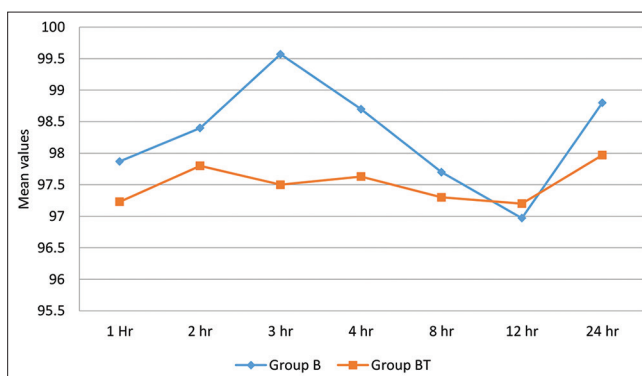**Fig. 1: Comparison of post-operative heart rate (bpm)**

Fig. 2: Comparison of post-operative systolic blood pressure (mmHg)

unpaired t-test). In 4th h, the mean pediatric pain scoring in Group B was 3.53±1.30 and in Group BT, it was 2.36±0.66 and the difference was highly significant (p=0.0001, unpaired t test). In 8th h, mean pain
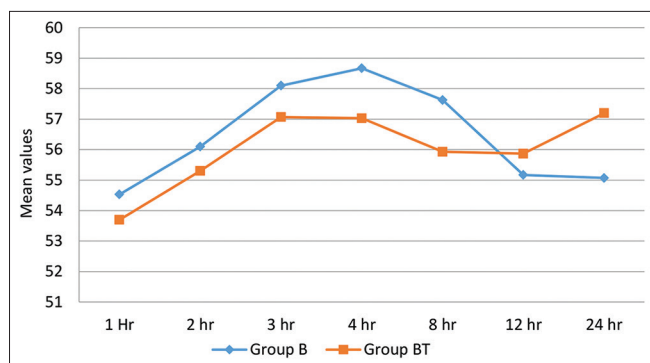
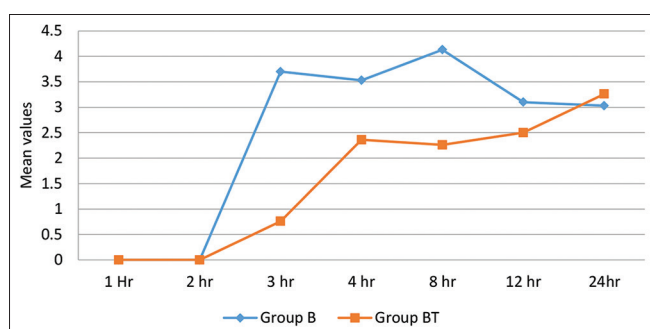**Fig. 3: Comparison of post-operative diastolic blood pressure (mmHg)**

Fig. 4: Distribution of modified objective pain score

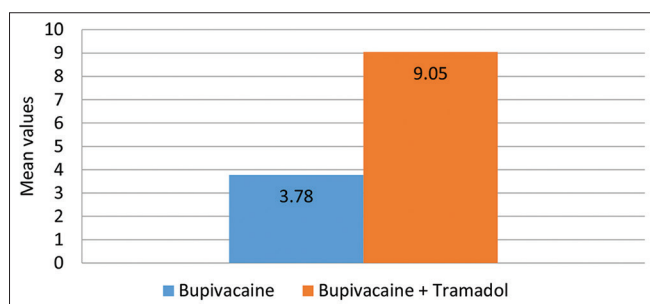**Fig. 5: Duration of analgesia**

scoring in Group B was 4.13±1.54 and in Group BT, it was 2.26±0.58 which was found to be again highly significant (p=0.0001, unpaired t test). In 12th and 24th h, the difference between two groups was found to be insignificant (p=0.075 and p=0.3131 at 12th and 24th h, respectively).

The mean duration of analgesia in the B group (3.78±0.94) h, the mean duration of analgesia in the BT group (9.05±2.21) h, and the difference between two groups were highly significant statistically p=0.0001.

Post-operative sedation scores
Distribution of sedation among two groups was observed that during post-operative period, mean sedation score remained comparable between the two groups and was statistically insignificant (p>0.05).

Furthermore, there were no incidences of complications such as nausea, vomiting, pruritus, respiratory depression, urinary retention, blood vessel puncture, dural puncture, hypotension, and bradycardia in either of the groups.

DISCUSSION

Over the last few decades, pediatric regional anesthesia has become an integral part of routine practice. The advancements in guiding techniques and their use in anesthesia practice have opened several avenues for regional anesthesia. The efficiency and safety of these techniques facilitate early ambulation with improved pain management and reduced hospital stay. Bupivacaine is most commonly used local anesthetic for caudal anesthesia in pediatric patients but it has its own side effects including motor weakness, urinary retention, central nervous system (CNS) toxicity, and CVS toxicity. Local anesthetics bind to specific sites in voltage-gated Na^+ channels. They block Na^+ current, thereby reducing the excitability of neuronal, cardiac, or CNS tissue. Local anesthetics also bind beta-adrenergic receptors and inhibit epinephrine-stimulated cAMP formation, which can explain the refractoriness of bupivacaine CV toxicity to standard resuscitation guidelines. In the CNS, local anesthetics may cause increased excitability, followed by its depression. Hence, adjuvants are added to increase the duration and decrease the side effects by decreasing the dose [7]. Neuraxial administration of opioids is based on the knowledge that opioid receptors (mu) are present in the substantia gelatinosa of the spinal cord and produce selective segmental analgesia. Unlike local anesthetics, opioids affect sensory neurons without affecting motor or sympathetic function. When combined with local anesthetic, there is a synergistic effect with an increase in the duration and quality of the regional anesthesia, allowing the use of a more dilute solution of local anesthetic. Neuraxial opioids can therefore decrease the potential for local anesthetic toxicity and side effects of motor and sympathetic blockade. The side effects caused with neuraxially administered narcotics are due to the presence of the drug either in CSF or systemic circulation. The four classic side effects of neuraxial opioids are itching, retention of urine, vomiting, and respiratory depression. Opioid-induced side effects can be antagonized without reversing analgesia by administering a low-dose infusion of naloxone 0.25–1 micro g/kg/h.

A study performed by Gune *et al.* [8] among children undergoing hypospadias repair showed that caudal tramadol (2 mg/kg) provides better and longer-lasting post-operative analgesia (>24 h) than IV tramadol 2 mg/kg. Senel *et al.* [9] studied children undergoing herniorrhaphy and concluded that caudal administration of bupivacaine (0.25%, 1 mL/kg) with the addition of tramadol (1.5 mg/kg) resulted in superior analgesia with a longer period without demand for additional analgesics compared with caudal bupivacaine (0.25%, 1 mL/kg) and tramadol (1.5 mg/kg) alone without an increase of side effects.

Hence, we conducted a prospective, double-blind, randomized study to compare and evaluate the duration of post-operative analgesia, hemodynamic parameters, and side effects if any, in children aged 1–8 years undergoing infraumbilical surgery at Jhalawar Medical college, Jhalawar (main OT).

Our findings coincide with the study conducted by Prakash *et al.* (2006) [10], Khalid *et al.* (2007) [11], Khan and Memon (2008) [12], Doda and Mukherjee (2009) [13], Laiq *et al.* (2009) [14], and Shrestha and Bhattarai (2010) [15] where they have compared bupivacaine and bupivacaine with tramadol at different doses administered caudally in pediatric patients undergoing infraumbilical surgeries and found that during intraoperative and post-operative period vital parameters remained comparable in both of the groups (p>0.05).

Our results are also consistent with the study conducted by Prakash *et al.* (2006) [10] where they studied bupivacaine alone and three doses of tramadol with bupivacaine total of four groups (0.75 mL/kg of 0.25% bupivacaine alone Group B and with tramadol 1 mg/kg Group BT1, tramadol 1.5 mg/kg Group BT 1.5, and tramadol 2 mg/kg Group BT2) in 2–8 years old undergoing inguinal herniotomy. The mean time to administration of first rescue analgesia was 4 h in Group B, 8 h in Group BT1, 11 h in Group BT1.5, and 12 h in Group BT2. The duration of analgesia in Group B was significantly shorter than that in the other three groups (all p<0.001). Sedation scores at 1 and 4 h after surgery were comparable in the four groups. None of the patients had motor

block on emergence from anesthesia. Incidence of emesis was not statistically difference between the groups; p=0.498. Facial flushing or pruritus was not in line with our study; Khalid *et al.* (2007) [16] conducted study with children 1–12 years of age, undergoing inguinoscrotal surgeries. Group BT was given 0.25%, 0.8 mL/kg bupivacaine and tramadol 2 mg/kg while the other Group B was given 0.25%, 0.8 mL/kg bupivacaine caudally. Addition of tramadol with bupivacaine resulted in significant p<0.05 increase in post-operative analgesic period (16.06±4.04 h). Sedation scores were similar in both the groups. No other side effects such as respiratory depression, pruritus, and urinary retention were found in both the groups except for nausea and vomiting.

Another study conducted by Doda and Mukherjee (2009) [13] in 2–5 years old, undergoing subumbilical surgeries were randomly divided in two groups, and received 0.25% bupivacaine 0.5 mL/kg and 0.25% bupivacaine 0.5 mL/kg with tramadol 2 mg/kg as single-shot caudal block. It was observed that the mean duration post-operative analgesia was significantly long (9.1 h) in bupivacaine plus tramadol group as compared to bupivacaine alone (6.3 h) (p<0.01). There were no significant hemodynamic changes, motor weakness, and respiratory depression and no major difference in sedation score between the two groups.

Our findings coincided with study conducted by Laiq N *et al* (2009) [14]; they had taken mean age of the children as 4.2±2.35 and 5.5±1.51 years in Groups B and BT, respectively, undergoing elective hypospadias surgery. Group B received 0.5 mL/kg of 0.25% bupivacaine and Group BT received 0.5 mL/kg of 0.25% bupivacaine with 1 mg/kg of tramadol caudally. The mean duration of analgesia was significantly prolonged and the requirement for rescue analgesics was significantly less in the bupivacaine-tramadol group (p<0.0001) post-operatively. Sedation score and minor complications were comparable (p>0.05) in the two groups.

Similar to our study, another study conducted by Pavithra *et al.* (2018) [17] as single-shot caudal epidural using 1 mL/kg of 0.25% bupivacaine alone Group 1 and 2 μg/kg fentanyl Group 2 or with 2 mg/kg tramadol Group 3 in 1–12 years old undergoing elective infraumbilical surgeries. Onset of pain is seen between 8 and 12 h in Group 3 as against 4–8 h in the other groups. Vomiting was 32% in Group 3, 28% in Group 2, and 0% in Group 1 also higher sedation score in Group 3 for 1 h post-operatively.

A recent study conducted by Angasa *et al.* (2020**)** [18] in children aged 1–14-year old undergoing elective infraumbilical surgery received caudal block with bupivacaine 0.25% 1 mL/kg and bupivacaine 0.25% 1 mL/kg with tramadol 1 mg/kg. The mean pain score was lower in (BT) group with a statistically significant difference at 4th, 8th, and 12th h post-operatively with p=0.018, 0.002, and 0.041, respectively. The study did not mention any post-operative complications.

In our study, nausea and vomiting were not present in any of the patients but reported in a study conducted by Khalid *et al.*, [16] and Pavithra *et al.* [17] may be due to the usage of increased dose of tramadol 2 mg/kg instead of 1 mg/kg as in our study.

CONCLUSION

Our study demonstrates that a single-shot caudal block with 0.25% bupivacaine (1 mL/kg) plus tramadol (1 mg/kg) resulted in longer duration of analgesia when compared to 0.25% bupivacaine (1 mL/kg) alone with no incidence of any side effects.

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