

Comparison of caudal tramadol versus caudal fentanyl with bupivacaine for prolongation of postoperative analgesia in pediatric patients

ABSTRACT

Background and Aims: Caudal block is a common technique for pediatric analgesia for infraumbilical surgeries. Because of the short duration of analgesia with bupivacaine alone various additive have been used to prolong the action of bupivacaine. The present study was aimed to evaluate the analgesic effect of tramadol or fentanyl added to bupivacaine for infraumbilical surgeries in pediatric patients.

Materials and Methods: We conducted a prospective, randomized, single-blind controlled trial. After written informed consent from parents, 100 patients belonging to American Society of Anesthesiologist physical status I-II, in the age group of 1-12 years, of either sex undergoing infraumbilical surgery under general anesthesia were divided into two groups. Group BT received 1 ml/kg of 0.25% bupivacaine with tramadol 2 mg/kg in normal saline and Group BF received 1 ml/kg of 0.25% bupivacaine with fentanyl 2 µg/kg in normal saline with maximum volume of 12 ml in both groups. All patients were assessed intraoperatively for hemodynamic changes, the requirement of sevoflurane concentration, as well as postoperatively for pain by using FLACC (F = Face, L = Leg, A = Activity, C = Cry, C = Consolability), pain score and for sedation by using four point sedation score.

Results: The mean duration of analgesia was 10–18 h in Group BT while in Group BF it was 7-11 h. The postoperatively period up to 1½ h, Group BF had higher sedation score up to two as compared to that below one on Group BT.

Conclusion: Caudal tramadol significantly prolongs the duration of analgesia as compared to caudal fentanyl without any side effects.

Key words: Bupivacaine; caudal block, fentanyl, postoperative analgesia, tramadol

Introduction

Postoperative analgesia through the caudal epidural route with bupivacaine in children is firmly established in infraumbilical surgery.^[1,2] The mean duration of surgical analgesia provided by bupivacaine is limited.^[3] Different drugs such as tramadol, fentanyl, clonidine, and

midazolam with bupivacaine prolong the postoperative analgesia.

Tramadol is a centrally acting analgesic effect via opioid receptors.^[4]

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The main site of action of epidurally administered fentanyl is the substantia gelatinosa on the dorsal horn of spinal cord.^[5]

We evaluated the duration of postoperative analgesia, intraoperative hemodynamic changes, the requirement of inhalational agent and any side effect while using caudal block bupivacaine with tramadol versus fentanyl in pediatric patients undergoing infraumbilical surgery.

Materials and Methods

After obtaining Local Ethical Committee approval, written and informed consent were obtained from parents. This prospective, randomized, controlled, single-blind study were conducted in the pediatric surgical operation theater in our institute between August 2014 and December 2014, and total 100 children of either sex with American Society of Anesthesiologist (ASA) physical status I and II, aged 1-12 years, weighing 5-30 kg were scheduled for elective infraumbilical surgeries under general anesthesia. Patients are having a local infection at the caudal site, neurological disorder, the history of allergic reaction to local anesthetics, sacral/vertebral abnormalities, and bleeding diathesis were excluded from the study. An intravenous access was secured, and glycopyrrolate injection (0.004 mg/kg) and ondansetron injection (0.15 mg/kg) were administered. Standard monitoring including an electrocardiogram (ECG), noninvasive blood pressure (NIBP) measurement, pulse oximetry, capnography, and temperature were applied. All patients were induced with either inhalational agent sevoflurane (1-6%) with 50% nitrous oxide in oxygen or intravenous thiopental in a dose of 5-6 mg/kg. In the left lateral position, caudal block was performed using 22-gauge epidural needle under complete aseptic precaution. After confirmation and negative aspiration for blood and cerebrospinal fluid, the study drugs were introduced into the caudal space slowly with continuous ECG monitoring. The patients included were randomized before induction of anesthesia using computer generated randomization numbers into two equal groups: Group BT received 1 ml/kg of 0.25% bupivacaine with 2 mg/kg of tramadol in normal saline and Group BF received 1 ml/kg of 0.25% bupivacaine with 2 µg/kg of fentanyl in normal saline with maximum volume of 12 ml in both the groups. The anesthesiologist performing the caudal block was blinded to the identity of the drug used.

The patients were repositioned supine. To facilitate insertion of an l-gel or endotracheal tube, intravenous succinylcholine 2 mg/kg was given. Intraoperatively, no analgesic was supplemented. Anesthesia was maintained with assisted ventilation using sevoflurane initially with 2% and then

after decreasing up to 0.6% with hemodynamic stability or controlled ventilation using injection atracurium (0.5 mg/kg) with 50% nitrous oxide in oxygen and sevoflurane decreases up to 0.6% with hemodynamic stability. Glucose/saline solution was infused as per requirement, and perioperative blood loss was replaced as per requirement.

During surgery, adequate analgesia was assessed by hemodynamic stability, as indicated an increase in heart rate and systolic blood pressure of no more than 15% compared with baseline values obtained just before the surgical incision with decreased requirement of sevoflurane concentration, at approximately 0.6%. An increase in heart rate and systolic blood pressure within 20 min of skin incision indicated failure of caudal anesthesia.

At the end of surgery, the residual neuromuscular block was antagonized with glycopyrrolate injection 0.008 mg/kg and neostigmine injection 0.05 mg/kg intravenously.

Intraoperatively required concentration of sevoflurane was recorded at every 15 min. Heart rate, NIBP, SpO₂, EtCO₂, and temperature were recorded at every 15 min interval till the end of surgery and every hourly interval postoperatively till rescue analgesic was given.

Duration of surgery, duration of anesthesia, and perioperative complications such as brady/tachycardia, hypo/hypertension, vomiting, and urinary retention were recorded.

In the recovery room, hemodynamic parameters, sedation, and pain score were recorded at hourly interval till rescue analgesic was given. Postoperative sedation was assessed by using four point sedation score (0 - spontaneous eye opening, 1 - eye open on speech, 2 - eye open on shake, 3 - unarousable), and pain was evaluated by using FLACC (F = Face, L = Leg, A = Activity, C = Cry, C = Consolability), score (maximum score of 10) at 1 h interval for first 3 h and thereafter every 2 h interval till score >4, and rescue analgesic was given. The use of FLACC is a valid and reliable tool for assessing procedural pain in children aged 5-16 years.^[6-8]

In this study, the sample size was calculated using formula $n = 4pq/E^2$, which is based on Hardy-Weinberg principle. In this formula, p is the prevalence of sub-umbilical pediatric surgery at our institute. One hundred patients were allocated randomly to two equal groups (50 patients/group). Collected data were presented as a mean ± standard deviation, numbers, and percentages as appropriate. Categorical variables were analyzed using Chi-square with yate's correction and Fisher's exact test (two-tailed) as appropriate. Continuous variables were tested

using an unpaired Student's *t*-test. Statistical calculations were carried out using Microsoft Office Excel 2010 and GraphPad Prism 6.05 (GraphPad Software, Inc., La Jolla, CA, USA) (QuickCalc) Software. *P* < 0.05 was considered statistically significant.

Results

No statistically significant difference was observed in both the groups regarding age, sex, weight, ASA grade, duration of surgery, and device used to secure an airway [Table 1]. Most of the children in both groups are between 1 and 6 years old [Table 2]. The majority of children in both groups underwent hypospadias and hernia repair surgeries [Table 3].

Compared with a baseline value of the respiratory rate after caudal block, respiratory rate decreased significantly in Group BT compared to Group BF, when I-gel is used without nondepolarizing muscle relaxant [Table 4].

Baseline heart rate, systolic blood pressure, and diastolic blood pressure recorded before the induction of general anesthesia were similar in both groups. Compared with the baseline value after caudal block, heart rate decreased significantly in Group BT compared to Group BF. No patients in either group had a drop in heart rate to <80 beats/min [Table 5]. After 15 min of caudal blocks, systolic blood pressure decreased below 100 mmHg in Group BF while in Group BT systolic blood pressure remained above 100 mmHg [Table 6]. Diastolic blood pressure did not decrease significantly [Table 7].

Mean hourly pain score in the recovery room in both the groups without requiring additional analgesic were similar for 4 h. Thereafter, the mean score in Group BF was significantly higher than that in Group BT [Figure 1]. The duration of analgesia was 7-11 h for Group BF and 10-18 h for Group BT.

Sedation score was between one and two (opening eye on shake) in Group BF for first 1½ h. In Group BT, sedation score was below one. All children were opening eye on the speech from the immediate postoperative period in Group BT [Figure 2].

Immediately after caudal block in both groups, sevoflurane 2% concentration was set. 15 min after caudal block, 38 children in Group BT, and 26 children in Group BF were hemodynamically stable with sevoflurane concentration of 1% [Figures 3 and 4].

Neuraxial opioid prolongs motor blockage of local anesthetics and can delay recovery of bladder function. In

Table 1: Demographic data

Patient characteristics	Group BT (n = 50)	Group BF (n = 50)	P
Age (year)	4.87±3.46	3.85±3.01	0.1190
Sex (male/female)	42/8	36/14	0.2274
Body weight (kg)	15.66±7.98	13.10±6.14	0.0753
ASA ^s grade I/II	30/20	25/25	0.4215
Duration of surgery (h)	1.32±0.65	1.28±0.67	0.7625
I-gel/ET tube insertion	32/18	29/21	0.6818

Data presented as mean ± SD or number; **P* < 0.05 is considered significant; ^sASA- American Society of Anesthesiologist; SD- Standard deviation; ET- Endotracheal

Table 2: Demographic data (age: subgroup analysis)

Age (year)	Group BT (n = 50) (%)	Group BF (n = 50) (%)	P
1-6	38 (76)	42 (84)	0.4539
7-12	12 (24)	8 (16)	

Data presented as number (%); **P* < 0.05 is considered significant

Table 3 Types of surgery

Surgical procedures	Group BT (n = 50) (%)	Group BF (n = 50) (%)	P
Hypospadias	19 (38)	16 (32)	0.9772
Inguinal herniotomy	14 (28)	16 (32)	
PSARP ^s	7 (14)	9 (18)	
Orchidopexy	3 (6)	1 (2)	
Others	7 (14)	8 (16)	

Data presented as number (%); **P* < 0.05 is considered significant; ^sPSARP- Posterior sagittal anorecto plasty

Table 4: Comparison of respiratory rate per minute

Duration (Time)	Group BT (n = 50)	Group BF (n = 50)	P
Basal	23.04±2.69	24±4.52	0.1999
5 min after caudal	22.04±2.61	23.6±3.89	0.0199*
15 min	20.76±2.04	22.16±3.24	0.0112*
30 min	19.96±1.81	21.28±2.39	0.0024*
45 min	19.48±1.37	22.24±2.21	0.0414*
60 min	19.08±1.21	19.84±2.07	0.0273*

Data presented as mean ± SD or number; **P* < 0.05 is considered significant; SD- Standard deviation

Table 5: Comparison of pulse rate per minute

Duration (Time)	Group BT (n = 50)	Group BF (n = 50)	P
Basal	135.12±22.29	143±19.5	0.0629
5 min after caudal	127.60±19.50	135.78±19.01	0.0362*
15 min	119.88±20.54	130.48±19.74	0.0099*
30 min	115.04±19.25	123.16±17.12	0.0281*
45 min	112.68±18.40	121.10±15.81	0.0159*
60 min	110.92±19.31	117.58±22.95	0.119

Data presented as mean ± SD or number; **P* < 0.05 is considered significant; SD- Standard deviation

our study, 70-75% patients were catheterized intraoperatively. Remaining patients did not have a problem to void urine postoperatively. Postoperative nausea and vomiting were

Table 6: Comparison of systolic blood pressure (mmHg)

Duration(Time)	Group BT (n = 50)	Group BF (n = 50)	P
Basal	109.14±12.73	105.26±11.29	0.1101
5 min after caudal	104.16±12.71	101.72±10.82	0.3038
15 min	102.18±12.69	94.54±10.71	0.0016*
30 min	101.1±13.8	94.00±12.53	0.0083*
45 min	101.37±13.94	93.90±12.64	0.0060*
60 min	101.78±15.18	94.96±11.64	0.0133*

Data presented as mean ± SD or number; *P < 0.05 is considered significant; SD- Standard deviation

Table 7: Comparison of diastolic blood pressure (mmHg)

Duration (Time)	Group BT (n = 50)	Group BF (n = 50)	P
Basal	65.35±10.11	62.94±9.47	0.2216
5 min after caudal	63.78±10.02	60.58±9.88	0.1111
15 min	60.71±9.9	58.82±10.23	0.3502
30 min	58.73±10.51	56.52±10.64	0.2986
45 min	59.69±11.16	55.90±11.79	0.1020
60 min	61.35±10.91	58.72±10.65	0.2255

Data presented as mean ± SD or number; *P < 0.05 is considered significant; SD- Standard deviation

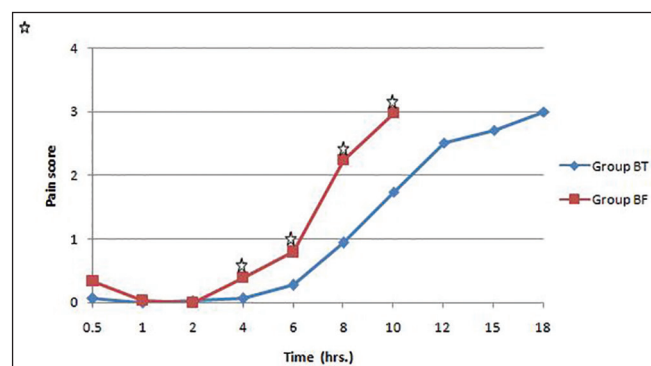


Figure 1: Postoperative pain score (F = Face, L = Leg, A = Activity, C = Cry, C = Consolability score) during first 24 h in both groups. The difference was statistically significant at 4, 6, 8, and 10 h after surgery (*shows P < 0.05). Data presented as mean

observed in four patients in Group BT. Another side effect such as respiratory depression and pruritus were not noticed in any case.

Discussion

Pain after surgery is inevitable, and the relief of postoperative pain has been consistently and systematically inadequate. A caudal block is one of the common regional anesthetic techniques used in pediatric age group undergoing infraumbilical surgery.^[6] It is generally considered a simple, safe procedure with more reliability, and predictability of the cephalic spread of local anesthetic solution in children than in adults. It produces minimal hemodynamic changes and provides some pain-free period intraoperatively and postoperatively in infraumbilical surgeries in children.^[1,2,9]

Analgesic effect of caudal bupivacaine terminates early, and supplementary analgesics are required in the postoperative period. Various adjuvant drugs such as ketamine, midazolam, tramadol, fentanyl, clonidine, dexmedetomidine have been

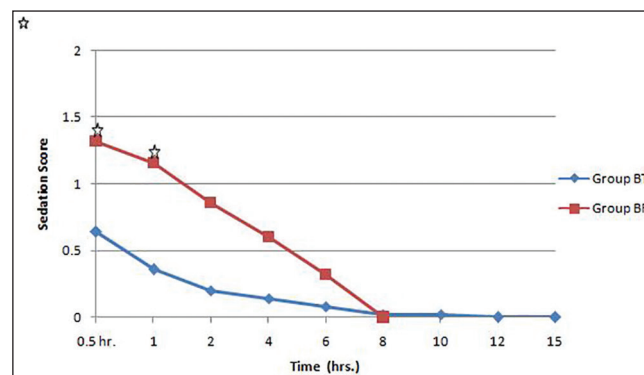


Figure 2: Postoperative sedation score (four-point sedation score) during first 24 h in both groups. Group BF had higher sedation score up to two in immediate postoperative period (*shows P < 0.05). Data presented as mean

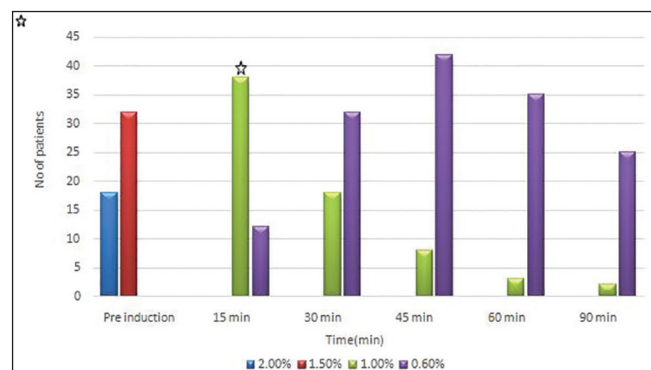


Figure 3: Concentration of sevoflurane required in a number of patients during the intraoperative period in Group BT (*shows 38 patients required 1% sevoflurane concentration). Data presented as number of patients

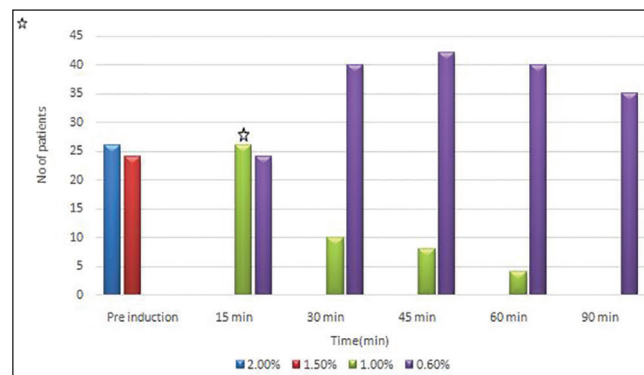


Figure 4: Concentration of sevoflurane required in a number of patients during the intraoperative period in Group BF (*shows 26 patients required 1% sevoflurane concentration). Data presented as number of patients

used to prolong the duration of analgesia for the caudal block.^[1,10]

In our study, single shot caudal epidural using 1 ml/kg of 0.25% bupivacaine with 2 mg/kg tramadol or 2 µg/kg fentanyl with a maximum volume of 12 ml were given.

Tramadol is a racemic mixture of two enantiomers. The (+) enantiomer has moderate affinity for the opioid µ receptor, which is greater than that of the (–) enantiomer. In addition, the (+) enantiomer inhibits serotonin reuptake, and the (–) enantiomer is a norepinephrine reuptake inhibitor. These complementary properties result in a synergistic antinociceptive interaction between the two. The resulting opioid has a striking lack of respiratory depressant effect despite having analgesic potency approximately equal to that of pethidine.^[3]

Fentanyl is a synthetic opioid agonist. It exerts its analgesic action by binding to mu receptor, as well as to kappa and delta receptors within the spinal cord, producing spinal analgesia. It easily crosses the lumbar dura and penetrates quickly the lipid phase of the underlying tissue of the cord with minimal migration of opioids in rostral direction, hence, avoiding central nervous system depression of respiratory and cardiovascular system.^[1,11]

Caudal bupivacaine with tramadol 1 mg/kg provides prolonged, and good quality postoperative analgesia compared to plain bupivacaine in children.^[10-13]

Caudal tramadol 2 mg/kg with 0.5 mg/kg of 0.25% bupivacaine provided longer duration of postoperative analgesia up to 16 or 18 h without having significant side effects but with higher sedation score for 1 h postoperatively.^[4]

Similarly in our study, the duration of postoperative analgesia was more than 10 h up to 18 h without significant side effects in caudal bupivacaine 0.25% 1 ml/kg with tramadol 2 mg/kg.

Greater epidural use of tramadol 2 mg/kg may be preferred to morphine 0.1 mg/kg for postoperative analgesia in children undergoing urological surgery without any significant side effects.^[14]

Caudal tramadol 2 mg/kg combined with bupivacaine 0.25% 0.75 ml/kg provided longer duration of postoperative analgesia and reduced requirement for rescue analgesic compared with tramadol 1 mg/kg or 1.5 mg/kg in children undergoing inguinal herniotomy.^[15]

El Hamamsy *et al.* observed analgesia for up to 4.5 and 5 h with caudal fentanyl 2 µg/kg and tramadol 2 mg/kg, respectively. The mean duration of surgery was 140 min. They also observed that if the period of time between performing the caudal injection and recovery of the child from anesthesia was <2 h, the incidence of immediate pain (requiring rescue analgesia) was high (30%), demonstrating a slow onset of action of caudal tramadol. However, with a longer duration surgery, caudal tramadol produced good quality analgesia for an average of 10.7 h. The slow onset of action of caudal tramadol may imply that there is little advantage in injecting tramadol into the extradural space. Bupivacaine tramadol may prove more useful in young children and infants than other opioids because of its lack of respiratory depressant effects. A bupivacaine-fentanyl mixture as a single caudal epidural injection does not change the onset, quality and duration of analgesia, and sedation score.^[3]

We observed analgesia for up to 11 h and 18 h with caudal fentanyl 2 µg/kg and tramadol 2 mg/kg, respectively. The time for onset of analgesia in both groups was respectively same.

Prosser *et al.* observed no significant effects of tramadol on prolongation of analgesic effects of bupivacaine when administered caudally after hypospadias surgery.^[16]

Cook and Doyle concluded that the addition of caudal fentanyl to local anesthetics offered no advantage over the administration of local anesthetics alone for short surgical procedures in children.^[17]

Doctor *et al.* mentioned that addition of fentanyl 1 µg/kg to ropivacaine or bupivacaine administered through the caudal epidural route imparts no added advantage to bupivacaine except a less intense motor block in children undergoing surgery below the umbilicus.^[18]

Kawaraguchi *et al.* concluded that the addition of fentanyl 1 µg/kg to ropivacaine 0.2% for caudal analgesia provides no further analgesic advantages to ropivacaine.^[19]

Shukla *et al.* observed a transient decrease of oxygen saturation to 91% in five cases and vomiting in eight patients out of 45 who received fentanyl 1 µg/kg with ropivacaine caudally.^[5]

Patel mentioned in his case series that fentanyl does not prolong the duration of analgesia but significantly increases the incidence of nausea and vomiting.^[2]

El Hamamsy *et al.* observed that caudal fentanyl 2 µg/kg produced useful analgesia for up to 4.5 h. However,

the addition of fentanyl to local anesthetics increased significantly the incidence of vomiting and desaturation compared with other groups who did not receive fentanyl.^[3]

In our study, we observed that caudal fentanyl 2 µg/kg prolong the duration of analgesia with mild sedation in an immediate postoperative period without any side effects.

Khalid mentioned postoperative analgesia up to 16 ± 4 h with increased incidence of vomiting with tramadol 2 mg/kg.^[12]

Demiraran *et al.* reported statistically higher sedation scores in the morphine group compared with the tramadol group. The incidence of nausea and vomiting was 25% in the tramadol group.^[14]

Prakash *et al.* concluded that the most frequently reported side effect of epidural tramadol is nausea. The longer time to first void in patients receiving tramadol 2 mg/kg though statistically significant appears clinically acceptable. None of the patients required bladder catheterization.^[15]

In a study done by Prosser *et al.*, 35-40% patient required a urinary catheter in bupivacaine and tramadol groups. According to them first indication for additional analgesia was related to the acute attack of bladder spasm.^[16]

In our study, nausea and vomiting were observed in four patients of Group BT, and respiratory depression and pruritus were not observed in any patients of both the groups. About 70-75% patients in both groups were catheterized intraoperatively. Remaining patients did not have a problem to void urine postoperatively.

The addition of caudal epidural analgesia to general anesthesia inhibits the stress responses from the lower part of the body during surgery and reduces the neurohormonal responses. It was demonstrated that small doses of a mixture of bupivacaine 0.25% alone or with fentanyl 1 µg/kg when administered through the caudal epidural does not have any beneficial effect on pain scores and catecholamine levels.^[20,21]

In our study intraoperatively, there was a decrease in the heart rate and systolic blood pressure and decreases the requirement of end tidal sevoflurane concentration in both the groups.

Conclusion

Caudal bupivacaine 0.25% with tramadol 2 mg/kg provided longer duration of postoperative analgesia and reduced

requirement for rescue analgesic with lesser sedation in immediate postoperative period compared to caudal bupivacaine 0.25% with fentanyl 2 µg/kg.

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Conflicts of interest

There are no conflicts of interest.

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