

A Comparative Study Of Ketamine And Tramadol As Additives To Plain Bupivacaine In Caudal Anaesthesia In Children

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Citation

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Abstract

Background: Studies examining the benefits of additives to bupivacaine in caudal anaesthesia have produced mixed results. Although the mechanism of action of these analgesics remains unclear, ketamine and tramadol have been used successfully in caudal block for prolonged postoperative pain relief. We compared the onset, quality and duration of analgesia produced by bupivacaine, either alone or combined with tramadol and ketamine.

Material & Methods: This study was conducted in 100 pediatric patients of ASA Grade I and II, aged between 1 to 7 years undergoing infra-umbilical surgery, during the study period. Cases were selected on the basis of simple random sampling method and were randomly allocated into three groups as follows:

Group B: (n=34) who receives 0.75 ml/kg of 0.25% Bupivacaine caudally

Group BK: (n=33) who receives combination of Ketamine 0.5 mg/kg + 0.75 ml/kg of 0.25% Bupivacaine caudally

Group BT: (n=33) who receives combination of Tramadol 2 mg/kg + 0.75ml/kg of 0.25% Bupivacaine caudally

Results: The mean duration of action after addition of Ketamine and Tramadol to Bupivacaine by the caudal epidural route was 9.3 h (559.39±27.15 minutes) and 7.9 h (478.48 ± 54.15 minutes) respectively as compared to caudal Bupivacaine 4.0 h (240.59 ± 15.36 minutes). There were no significant differences between the groups in cardiac parameters, recovery characteristics and incidence of side effects.

Conclusion: We conclude that Caudal Ketamine 0.5 mg/kg & Caudal Tramadol 2 mg/kg appear as satisfactory adjuncts to caudal Bupivacaine, which produced satisfactory intraoperative analgesia and also satisfactory postoperative analgesia without the use of any epidural catheter.

INTRODUCTION

Although General Anesthesia continues to be used for pediatric surgical procedures, regional anesthesia as an analgesic adjunct for pain control, both intra and postoperatively, has become increasingly popular for pediatric patients of all ages, including premature infants. ² Caudal epidural analgesia is the most widely employed technique for the management of pain within the distribution of T10-S5 dermatomes, covering the lower abdomen, perineum and lower extremities. ² This simple technique allows rapid recovery from anesthesia together with

effective postoperative analgesia. However, the mean duration of surgical analgesia provided by local anesthetics is limited and thus single shot caudal anesthesia is suitable only for surgery expected to last less than 90 minutes. Various drugs have been added to local anesthetic solutions to prolong the duration of caudal anesthesia provided by a single injection. ⁶ Opioids are added frequently to local anesthetics in children, but its beneficial effects are debated. Side effects such as nausea, vomiting, and respiratory depression are not uncommon. Tramadol is a synthetic opioid with a striking lack of respiratory depressant effect despite an analgesic potency equal to that of Pethidine ^{10,11}.

It has been shown to provide effective, long lasting analgesia after extradural administration. ¹² Extradural Ketamine produces analgesia by a spinal mechanism. This NMDA receptor antagonist is devoid of opioids side effects but may produce behavioral side effects. In children, addition of Ketamine to local anesthetics prolongs the duration of postoperative analgesia after inguinal hernia repair and orchidopexy. ^{13,14,15} Therefore, this randomized, prospective study is designed to study the effects of addition of Ketamine and Tramadol on duration of caudal block with Bupivacaine in children and its safety & usefulness in pediatric anesthesia.

MATERIALS AND METHODS

This study was conducted in 100 pediatric patients of ASA Grade I and II, aged between 1 to 7 years undergoing infra-umbilical surgery, during the study period.

Figure 1

Table 3: Mean age, weight and duration of surgical Procedure undergone.

OBSERVATION	SCORE
Asleep	3
Awake but drowsy	2
Fully Awake	1

The local ethical committee approved the study and written informed consent was obtained from a parent for each child in the study

Figure 2

Table 4: Showing the various types of surgical procedures in each group

Type of surgery	Group B	Group BK	Group BT
Congenital Inguinal Hernia	14	14	15
Undescended Testis	1	3	3
Hypospadias	6	11	6
Phimosis	4	-	4
Umbilical Hernia	5	2	2
Epispadias	4	-	3
Chordee	-	3	-
Total	34	33	33

Cases were selected on the basis of simple random sampling method and were randomly allocated into three groups as follows:

Group B: (n=34) who receives 0.75 ml/kg of 0.25% Bupivacaine caudally

Group BK: (n=33) who receives combination of Ketamine 0.5 mg/kg + 0.75 ml/kg of 0.25% Bupivacaine caudally

Group BT: (n=33) who receives combination of Tramadol 2 mg/kg + 0.75ml/kg of 0.25% Bupivacaine caudally.

All patients were assessed on the day prior to surgery. Detailed history from the parents was taken. Complete clinical examination of cardiovascular, respiratory, central and peripheral nervous systems was done. Following patients were excluded from the study: Children with Infection at the site of injection, Bleeding disorders, Congenital anatomic anomalies of spinal cord or vertebral anomalies or any other obvious congenital disease and allergic for any anesthetic drug were excluded from the study. Routine laboratory investigations such as blood and urine analysis were obtained. Pre-operatively patients were kept nil by mouth for 4-6 hours. Parents were explained about the procedure and informed consent was taken

Technique of Anaesthesia: On the day of surgery, patients were shifted to the operation theatre. The following equipments needed intraoperatively and for the performance of the block procedure were kept ready: Caudal block for all the patients was administered after induction of general anaesthesia (GA) and before the beginning of surgery. Premedication with Midazolam 0.03 mg/kg and Glycopyrrolate 40microgm/kg 10 minutes prior to induction was administered intravenously. Patient was shifted to the operation table. After securing an appropriate size intravenous cannula in the left upper limb, intravenous drip was started with Ringer Lactate at a calculated rate according to the body weight. monitors was attached and baseline blood Pressure, pulse rate, oxygen saturation were recorded. Anesthesia was induced with pentothal sodium and succinyl choline and the patient was intubated with an appropriate sized portex endotracheal tube. After induction, Oxygen ;nitrous,50;50 and Halothane was used for maintenance with the help of jackson rees circuit and vecuronium was used as the relaxant throughout the surgery. Under GA the study drugs were administered via caudal epidural route. Then the patient was turned supine , oxygen, nitrous ,and Halothane was used for maintenance with the help of J R circuit and relaxation was maintained with vecuronium throughout the surgery. . After about 15 - 20 minutes onset of the block was assessed using the homodynamic response to skin incision.

Parameters observed are: Intra-operative parameters: -

- Onset of analgesia was assessed with Pulse rate, Systolic arterial pressure 8 .
- Ineffective analgesia is defined as a rise in pulse rate and systolic arterial pressure of more than 15% from the baseline 8,³⁴
- Pulse rate and Systolic arterial pressure was noted soon after induction, after caudal block and every 15 minutes thereafter throughout the surgery.
- Oxygen saturation (SpO2) level was monitored throughout the surgery.
- Duration of block intra-operatively, was assessed with hemodynamic parameters. Post-operative parameters:-

The following parameters were observed at every 15 minutes in the first hour and there afterwards at 1, 2, 3, 4, 6, 8, 12

and 24 h after surgery.

- Pain score - using modified OPS 14,15 as described by Hannallah et al ⁵⁷
- Sedation - using a 3-point objective score based on eye opening 8,14,15

Figure 3

Table 5: 3-point Objective Sedation Score based on Eye-opening

OBSERVATION	SCORE
Asleep	3
Awake but drowsy	2
Fully Awake	1

- Pulse rate, Systolic arterial pressure and respiratory rate
- Time of first micturition - defined as the time from administration of caudal block to spontaneous voiding of urine
- Duration of motor blockade – defined as the time from administration of caudal block to first spontaneous movement of limbs
- Side effects like nausea, vomiting, pruritis
- Any other effect.

Duration of post operative analgesia was defined as the time between the injection of the drug caudally to the first administration of postoperative analgesia. Oral Paracetamol 10mg/kg was used as rescue analgesic for these patients with a total pain score of ≥ 4 and on complaints of pain. The nurse in the post-operative ward was however instructed to administer the rescue analgesic if the child was very restless or had excessive cry before the next period of follow up.

STATISTICAL ANALYSIS

The data collected was tabulated according to various epidemiological and statistical parameters. Statistical analysis of the data is done using: -

- Arithmetic mean
- Standard deviation

Analysis of variance (ANOVA) for inter group comparisons among the 3 groups using the Bonferroni Multiple Comparisons Test

Unpaired 't' test for parametric data comparison between two groups and Chi-square test for non parametric data comparison between two groups

P<0.05 is considered statistically significant

Continuous variables are expressed as mean (SD)

OBSERVATIONS

The three groups are similar in characteristics like mean age, weight, duration of surgery (table 3) and the type of surgery (table 4) they underwent. Most patients underwent herniotomy, urogenital surgeries like orchidopexy and hypospadias repair or lower lib surgeries.

Figure 4

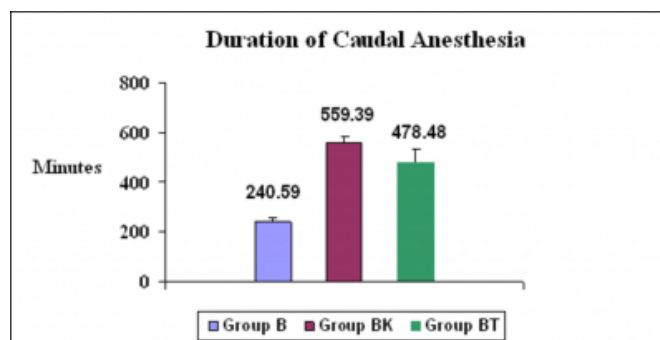
Table 6: Duration of caudal analgesia in the 3 groups

	Group B (n=34)	Group BK (n=33)	Group BT (n=33)	
Duration of caudal Analgesia (minutes)	240.59 ± 15.36	559.39 ± 27.15	478.48 ± 54.15	P<0.001

P < 0.001 denotes extreme significance.

The mean time to first analgesia was 240.59 ± 15.36 minutes in Bupivacaine (B) group, 559.39 ± 27.15 minutes in Bupivacaine-Ketamine (BK) group, 478.48 ± 54.15 minutes in Bupivacaine-Tramadol (BT) group. This difference is statistically very significant (P<0.001) when groups BK and BT were compared with the control group B. There was significant statistical difference (p<0.001) between groups BK and BT in the time to first analgesia.

Figure 5



In all the three groups intraoperative parameters like pulse rate and systolic arterial pressure was maintained throughout the surgery and did not differ significantly from the preoperative baseline value. Also there were no significant differences in the mean values of pulse rate and systolic arterial pressure between the groups. (Table 7) Oxygen saturation was maintained through out the procedure within normal limits. (SpO2 > 97%)

Recovery Characteristics The mean eye opening time was 18.12 minutes for group B, 24 minutes for group BK and 25 minutes for group BT after cessation of anaesthesia. There was no significant difference between the groups. The time to micturition (group B 206.47 minutes, group BK 216.67 minutes and group BT 203.64 minutes) and spontaneous leg movements (group B 22.94 minutes, group BK 26.55 minutes and group BT 30.27 minutes) were similar in the three groups. Five children in each group all undergoing hypospadias repair required indwelling urinary catheter for some days after surgery. There was no significant difference in this incidence between groups. There was no significant difference between the mean sedation scores in the groups for up to 4h after the operation. (Table 8)

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Figure 6

Table 7: Mean hemodynamic changes

Intra operative parameters	Group B (n=34)	Group BK (n=33)	Group BT (n=33)	Remark
PR				
Baseline	90.76 ± 2.06	91.48 ± 2.18	89.82 ± 2.14	P > 0.05
15 min	94.41 ± 1.79	95.88 ± 1.56	91.67 ± 2.16	
30 min	94.41 ± 1.79	95.88 ± 1.63	91.67 ± 2.16	
45 min	92.79 ± 1.77	94.76 ± 1.82	91.67 ± 2.16	
60 min	92.79 ± 1.77	94.43 ± 2.09	91.71 ± 2.25	
75 min	94.41 ± 1.85	93 ± 1.07	91.33 ± 1.99	
90 min	96.25 ± 1.48	92.57 ± 0.98	90.73 ± 1.95	
Systolic Arterial Pressure				
Baseline	85.88 ± 2.95	85.58 ± 2.82	84.67 ± 5.13	P > 0.05
15 min	85.88 ± 2.95	86.12 ± 2.74	84.67 ± 5.13	
30 min	88.35 ± 3.17	86.76 ± 2.49	87 ± 5	
45 min	88.35 ± 3.17	87.52 ± 2.55	87 ± 5	
60 min	88.06 ± 2.58	86.38 ± 3.14	84.39 ± 5.17	
75 min	88.06 ± 2.58	86.25 ± 3.11	85.46 ± 4.75	
90 min	92.12 ± 2.51	86 ± 3.27	87.27 ± 3.82	

P > 0.05, not significant

Figure 7

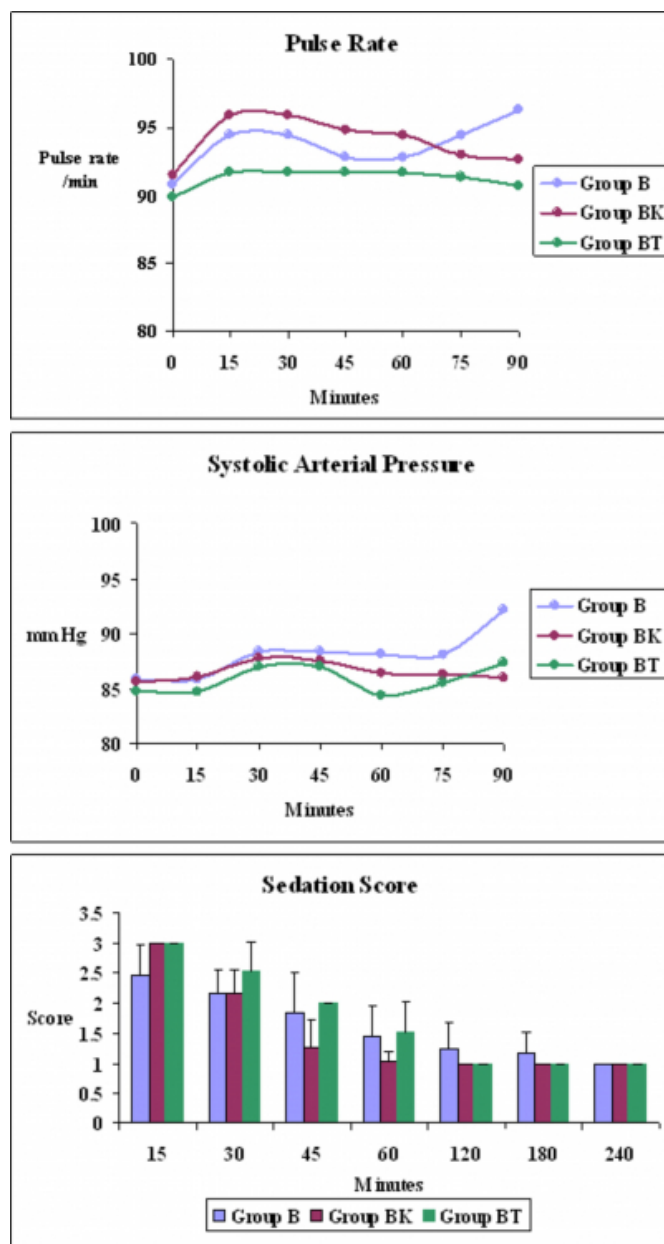
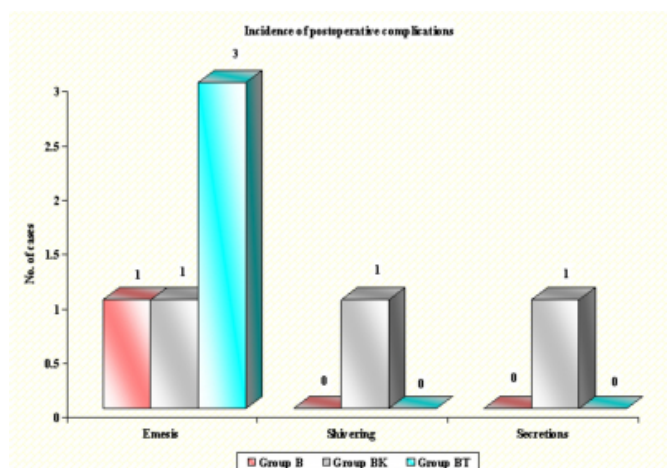


Figure 8



RESULTS

One hundred children between 1-7 years of age undergoing infraumbilical surgery were randomly allocated into three groups: the B Group received Caudal Bupivacaine 0.25% 0.75 ml/Kg; the BK Group received Caudal Bupivacaine 0.25% 0.75 ml/Kg + Ketamine 0.5 mg/Kg; the BT Group received Caudal Bupivacaine 0.25% 0.75 ml/Kg + Tramadol 2 mg/Kg under general anesthesia. Intraoperatively Pulse rate (PR), Systolic Arterial Pressure (SAP), and SpO₂ were measured. Postoperative measurements included duration of caudal block, Eye opening time, duration of motor Blockade, time to first micturition and hemodynamic monitoring & respiratory monitoring till administration of first dose of analgesic. Analgesia was assessed using a modified Objective Pain Score (OPS) and any side effects were noted.

The mean duration of action after addition of Ketamine and Tramadol to Bupivacaine by the caudal epidural route was 9.3 h (559.39±27.15 minutes) and 7.9 h (478.48 ± 54.15 minutes) respectively as compared to caudal Bupivacaine 4.0 h (240.59 ± 15.36 minutes). There were no significant differences between the groups in cardiac parameters, recovery characteristics and incidence of side effects.

DISCUSSION

The present study of 100 children aged between 1 to 7 years undergoing infra-umbilical surgery belonging to ASA I & II and randomly allocated into 3 groups was conducted in order to study the effects of addition of Ketamine and Tramadol on duration of caudal Bupivacaine in children. In this study by addition of Ketamine 0.5 mg/kg (group BK) and Tramadol 2 mg/kg (group BT) to caudal Bupivacaine it was found that there was good postoperative analgesia of 9.3 h and 7.9 h

respectively. This is in comparison to the Bupivacaine control group (group B) in which we got a mean duration of postoperative analgesia of 4 h without any significant increase of side effects or variations in cardiopulmonary parameters and with good recovery. In group BK of this study when Ketamine 0.5 mg/kg was added to Bupivacaine, the mean duration of action achieved was 9.3 h (559.39 minutes). Ketamine is known to exert its action by binding to NMDA, opioid, nor-epinephrine and serotonin receptors at the spinal cord level ¹. A number of studies have demonstrated its efficacy when administered through the caudal epidural route in children. Cook et al ² demonstrated that the addition of Ketamine 0.5 mg/kg to Bupivacaine provided a 12.5 h median duration of postoperative analgesia. In determining the postoperative analgesic efficacy of S(+) Ketamine in children, Martindale et al ³ found that caudal Ketamine 0.5 mg/kg produced a 10 h median time to first analgesia. In this study when 2 mg/kg of Tramadol was added to Bupivacaine in group BT, the mean duration of action in this study was 7.9 h (478.48 minutes). Tramadol is a racemic mixture of two enantiomers: (+)-Tramadol and (-)-Tramadol ⁶. The (+)-enantiomer has a moderate affinity for the opioid m-receptor

and also inhibits serotonin uptake, while the (-)-enantiomer is a potent norepinephrine inhibitor. These complementary properties result in an opioid with an analgesic potency approximately equal to that of meperidine, but without any respiratory depressant effect ⁷.

The mean duration of action of caudal tramadol as additive to Bupivacaine in this study appeared somewhat shorter than that found in other studies. This difference in the methodology like demographic characteristics of patient, systemic drugs administered and method of assessment of pain & recovery characters probably accounted for the difference in the duration of postoperative analgesia obtained by the studies. In this study it is shown that caudal Tramadol provides effective post operative analgesia in children. As regards iv route of administration and the analgesic profile of Tramadol by the caudal route no pharmacokinetic studies in children are available. Hence the comparative study of the pharmacokinetic profile regarding analgesic requirements of iv and caudal Tramadol with respect to dosage, duration is necessary for exact determination of dosage of caudal Tramadol. Prosser et al ⁷ has mentioned the same. Baseline hemodynamic parameters were comparable in the groups. There was no increase in

pulse rate or blood pressure after induction, administration and throughout the intraoperative period. In the post operatively pulse rate, blood pressure or respiratory rate increased after 4 h in group B, 9.3 h in group BK and 7.9 h in group BT. This is because the effect of drugs administered caudally had worn out which is in concurrence with other studies.^{3,4,5,6,7,8} There was no major difference in SpO₂ observed intraoperatively as the analgesia obtained was satisfactory and there was no change in rate or depth of respiration.

The time to first micturition and spontaneous leg movements were similar in the three groups. Five children in each group all undergoing hypospadias repair required indwelling urinary catheter for some days after surgery. There was no significant difference in this incidence between groups. While motor blockade did occur in all groups, it was not a major problem and has been shown to be no worse than when Bupivacaine alone is used.^{2,3,7,15,16}

Opioids are known to cause side effects like respiratory depression, urinary retention, pruritus, nausea & vomiting.¹ But Tramadol is an opioid without any respiratory depression effect. In this study it was noted that caudal Tramadol was not associated with respiratory depressant side effect. The nausea and vomiting was present more with Tramadol due to the presence of opioid receptor in the vicinity of the chemoreceptor trigger zone.⁸ Although the incidence of complications like nausea and vomiting in group BT, increased secretions & post-op shivering of group BK was higher compared to the other groups, the differences were not statistically significant. The addition of Ketamine 0.5 mg/kg & Tramadol 2 mg/kg to Bupivacaine improved significantly the duration of analgesia compared with that of Bupivacaine solution alone, without increase in the incidence of side effects. Also there were no significant changes in the sedation score and cardiopulmonary parameters. The current study indicates sufficient intra and postoperative analgesic effectiveness of caudal Ketamine and Tramadol. Caudally administered Ketamine and Tramadol were more effective in terms of duration of analgesia.

CONCLUSION

Caudal Ketamine 0.5 mg/kg & Caudal Tramadol 2 mg/kg appear as satisfactory adjuncts to caudal Bupivacaine, which produced satisfactory intraoperative analgesia and also satisfactory postoperative analgesia without the use of any epidural catheter. This appears to be simple, safe and a

reliable technique. Caudal Ketamine 0.5 mg/kg as an adjunct to caudal Bupivacaine produced the maximum duration of post operative analgesia [9.3 h (559.39 +/- 27.15 minutes)] as compared to Caudal Tramadol 2 mg/kg as an adjunct to caudal Bupivacaine [7.9 h (478.48 +/- 54.15 minutes)] or plain Caudal Bupivacaine [4.0 h (240.59 +/- 15.36 minutes)]. In all the three groups intraoperative parameters like pulse rate and systolic arterial pressure was maintained throughout the surgery and did not differ significantly from the preoperative baseline value. Also there were no significant differences in the mean values of pulse rate and systolic arterial pressure between the groups. The mean eye opening time, the time to micturition, and spontaneous leg movements were similar in the three groups. There was no significant difference between the mean sedation scores in the groups for up to 4h after the operation.

There were no significant complications in the post operative period in either of the three groups.

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