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Original Research Article

Comparison of Three Doses of Tramadol as Adjuvant to Bupivacaine for Caudal Analgesia in Paediatric Hypospadias Repair Surgery

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Abstract:

Introduction: Bupivacaine is a commonly used long acting, local anaesthetic agent for Caudal epidural block in paediatric population for providing post-operative analgesia. However use of bupivacaine as a single shot administration provides post-operative analgesia for a shorter duration. This study aimed to compare different dose of tramadol, as an adjunct to bupivacaine caudal epidural block in children undergoing elective hypospadiasis repair surgery.

Material and Methods: This hospital based, randomized, double blind, controlled clinical study included 80 male pediatric patients between 2 years to 8 years of age, with ASA I or II undergoing elective hypospadias repair surgery (Urethroplasty). Patients were randomized to 4 groups (N=20) - Group B (1ml/kg 0.25% bupivacaine), Group BT1 (bupivacaine with 1mg/kg tramadol), Group BT2 (bupivacaine with 1.5mg/kg tramadol) and Group BT3 (bupivacaine with 2mg/kg tramadol) by caudal block. Duration of analgesia was defined as the time from administration of block till the time, the Objective pain score (OPS) reached 4 or the child complained of pain.

Results: The duration of analgesia was significantly longer in group BT3 (705.8 min) as compared to Group BT2 (632.65 min), BT1 (474.05 min) and B group (236.10 min). Additional analgesic requirement in 24 hours showed dose dependent reduction with tramadol. No significant difference was seen in motor blockage or sedation score among the study groups. Post operative OPS score was significantly lower with increasing dose of tramadol. No significant difference was seen in incidence of vomiting or hemodynamic parameters.

Conclusion: Tramadol showed dose dependent prolongation of duration of analgesia in pediatric hypospadiasis surgery, without any increase in incidence of adverse effects.

Keywords: Caudal Analgesia, Bupivacaine, Tramadol, Hypospadiasis.

Introduction

Post-operative analgesia is a critical component of successful perioperative management. Caudal block has established its use in infraumblical paediatric surgeries, including inguinoscrotal procedures [1-3]. Bupivacaine is a commonly used long acting, local anaesthetic agent for Caudal epidural block in paediatric population for providing post-operative analgesia. However use of bupivacaine as a single shot administration provides post-operative analgesia for a shorter duration [1,4]. Continuous infusion requires placement of catheter in epidural space, which however leads to increased risk of infections and delayed mobilization adding to the post-operative morbidity [5]. This leads to requirement of further analgesia during the postoperative period in many children undergoing inguinoscrotal surgery with caudal analgesia require [6].

Prolongation of anaesthesia can be achieved by adding various adjuvants including opoids, midazolam [7], clonidine [8], ketamine [5] and others [9-11]. Caudal opioids administration offers analgesic advantage, however they also increases risk of adverse events including severe complications like respiratory depression.[3,4] Tramadol is a synthetic opioid with a good analgesic efficacy, providing long-lasting analgesia after epidural administration. Tramadol is 4-phenyl piperidine analogue of codeine with a weak μ opioid agonist that provides the advantage of no or minimal risk of severe respiratory depression. [3,12,13] Studies have shown that the addition of tramadol to bupivacaine for caudal epidural block

in children significantly prolongs the duration of postoperative analgesia. [3,5,14-16] The dose of tramadol used for caudal epidural block in these studies ranged between 1 and 2 mg/k. The goal of an anasthesist is to provide required analgesia at minimum possible dose of drugs so as to reduce the incidence of undesired adverse event.

Thus, it is imperative to find the optimal dose of tramadol to be used as adjuvant to bupivacaine. Hence present study was conducted with the aim to compare different dose of tramadol, as adjunct to bupivacaine caudal epidural block, in terms of duration of caudal analgesia and adverse effects in children undergoing elective hypospadiasis repair surgery.

Material and methods:

This hospital based, randomized, double blind, controlled clinical study was conducted in the Department of Anesthesiology, Urology, Plastic surgery and paediatric surgery operation theatre at one of the largest tertiary care centre of western India. The study included 80 male pediatric patients between 2 years to 8 years of age, with ASA I or II undergoing elective hypospadias repair surgery (Urethroplasty). Patients with known neurological deficits, neurological diseases, bleeding disorders, and with obvious skeletal deformities, sensitivity/ allergy to bupivacaine and/or tramadol were excluded from the study.

Patients were randomized to 4 group using block randomization with variable block size to ensure equal number of patients in each group (N=20). Sealed opaque envelops were used for allocation concealment.

The drugs for respective groups were prepared by an independent anesthetist not part of research study. The parents and the anesthetist administering the drugs were blinded for the drug administered. The group allocation was to be disclosed in case of any untoward effect, which however did not occur in this study.

Sample size was calculated at alpha error 0.05 and study power 80% to verify an expected difference in duration of analgesia of 1 ± 1 hour between two different dose of tramadol [4]. Sample size was calculated to be a minimum of 16 subjects in each group, which was further round to 20 subjects in each group.

The patients were randomized into following groups - **Group B** patients received 1ml/kg 0.25% bupivacaine alone, **Group BT1** patients received 1 ml/kg 0.25% bupivacaine with 1mg/kg tramadol, **Group BT2** patients received 1ml/kg 0.25% bupivacaine with 1.5mg/kg tramadol and **Group BT3** patients received 1ml/kg 0.25% bupivacaine with 2mg/kg tramadol by caudal block.

The parents were instructed to keep the child NBM for 6 hrs before surgery. Oral midazolam 0.5 mg/kg (made upto 5ml in a palatable honey base) was given 45 minutes prior to the procedure. The patients were given with Inj. Glycopyrrolate 0.005 mg/kg intravenously at the time of induction. All patients received propofol as induction agent (3 mg/kg). Anaesthesia was maintained with propofol infusion (0.5%) prepared by double diluting its 1% solution with 5% Dextrose, infused at the rate of 12mg/kg/hr for the first 20 minutes and 9mg/kg/hr thereafter till the completion of surgery. After induction the patients were positioned in the left/right lateral position with spine flexed and the sacral hiatus identified.

Under aseptic conditions a 23G disposable hypodermic needle was used for spinal puncture. The drug prepared by a person blinded to the study for the particular group was administered. The puncture site was sealed by tincture benzoin seal. The surgery was allowed to commence after conforming the adequacy of block by pin prick. Throughout the procedure, oxygen was administered by mask. Routine monitoring of each patient included ECG, NIBP, SpO2 and temperature. Isolyte-P was infused for maintenance and replacement of preoperative deficit as calculated by the 4:2:1 rule. The patient were transferred and observed in the Post anaesthesia care unit (PACU) for 1 hour and thereafter in the post-operative ward for upto 24 hrs by an anesthetist blinded to the study group.

The duration of analgesia was defined as the time from administration of block till the time, the Objective pain score (OPS) reached 4 or the child complained of pain. The OPS score used five criteria – systolic blood pressure, crying, movement, agitation and complain of pain [17]. Rescue analgesia in the form of syrup paracetamol 15mg/kg every 4 hours was provided to a child who's OPS score reached 4 or more.

Total requirement over 24 hours was recorded. Motor blockade was assessed by the Modified Bromage Scoring system. A four point sedation score ranging from 1 to 4 was used to assess level of sedation.

Ethical aspect: Ethical clearance was obtained from Institutional Ethics committee prior to initiation of study. Written informed consent was obtained from parents / legally acceptable guardian or relative prior to inclusion in the study.

Statistical analysis: Categorical variables were summarized as mean and standard deviation and analyzed using ANOVA test. Ordinal variables were summarized as median and interquartile range and analyzed using Kruskal wallis test. Categorical variables were expressed as frequency and percentage and were analyzed using Chi square

test. A p value <0.05 was taken as statistically significant. All statistical analysis was done using 'Epi info version 7.2.1.0' statistical software.

Results

Table 1: General characteristics among study groups

	Group B (N=20)	Group BT1 (N=20)	Group BT2 (N=20)	Group BT3 (N=20)	P value
Age (years)	4.93 ± 1.65	5.11± 1.86	5.31± 1.74	5.15±1.70	0.922
Weight(Kgs)	14.30±4.27	14.70±4.60	14.48±4.41	14.50±4.11	0.992
Duration of surgery (minutes)	41.60±8.41	41.25±11.34	43.00± 10.43	38.45 ± 9.68	0.541

A total of 80 patients were included in the study. The four groups were comparable with respect to their age, weight and duration of surgery (Table 1).

Table 2: Comparison of analgesic and anaesthetic characteristics among the groups

	Group B	Group BT1	Group BT2	Group BT3	P value
Duration of analgesia (minutes)	236.10±32.91	474.05±42.24	632.65±50.60	705.80±49.85	**< 0.001**
Degree of motor block after 1 hour	4.55± 0.51	4.70± 0.47	4.65± 0.49	4.85± 0.37	0.233
Oral intake Time (minutes)	297.40±43.08	293.15± 4.15	296.45±39.01	281.00 ±32.88	0.547

The duration of analgesia was significantly shorter in B group ($p < 0.001$). On post hoc analysis, mean duration of analgesia was significantly longer in group BT3 (705.8 min) as compared to Group BT2 (632.65 min) and BT1 (474.05 min) with $p < 0.001$. No significant differences was seen between degree of motor blockade and time to oral intake among the study groups ($p>0.05$). All children fully recovered from the motor blockade in the first post-operative hour. (Table 2). No significant difference was seen in motor blockage or sedation score among the study groups.

Table 3: Comparison of mean OPS at various interval

PO time	Group B	Group BT1	Group BT2	Group BT3	P value
1 hr	0.10± 0.31	0.10 ± 0.31	0.05 ± 0.22	0.00± 0.00	0.520
4 hrs.	2.55 ± 1.00	0.50± 0.51	0.45± 0.60	0.35± 0.67	**<0.001**
6 hrs.	3.40 ± 1.10	2.70± 0.66	2.20 ± 0.77	1.55± 0.51	**<0.001**
12 hrs.	4.30 ± 1.42	4.85± 1.18	4.50 ± 0.89	3.50± 1.05	**0.003**
24 hrs.	4.45 ± 1.15	4.65± 0.81	4.40± 0.75	4.10 ± 0.85	0.292

Post op OPS score was significantly lower with increasing dose of tramadol from 4 hours to 12 hours (Table 3).

Table 4: additional analgesic requirement among study groups

	Group B	Group BT1	Group BT2	Group BT3	P value
1 dose	**0**	**0**	**0**	**15**	**<0.001**
2 dose	**0**	**16**	**17**	**5**	
3 dose	**12**	**4**	**3**	**0**	
4 dose	**8**	**0**	**0**	**0**	
Median (IQR) analgesic dose	3 (3,4)	2 (2,2)	2 (2,2)	1 (1,2)	**<0.001**

The median analgesic dose requirement was 3 dose in Group B, which showed dose dependent reduction with 2 dose in Group BT 1 & BT2 and only 1 dose in Group BT3 ($p<0.001$). Most patients in Group B required 3 or 4 dose, while in Group BT1 & BT2 most required 2 or 3 dose and in BT 3 group given 2mg/kg tramadol, most required only 1 or 2 dose of additional analgesic in 24 hours (Table 4).

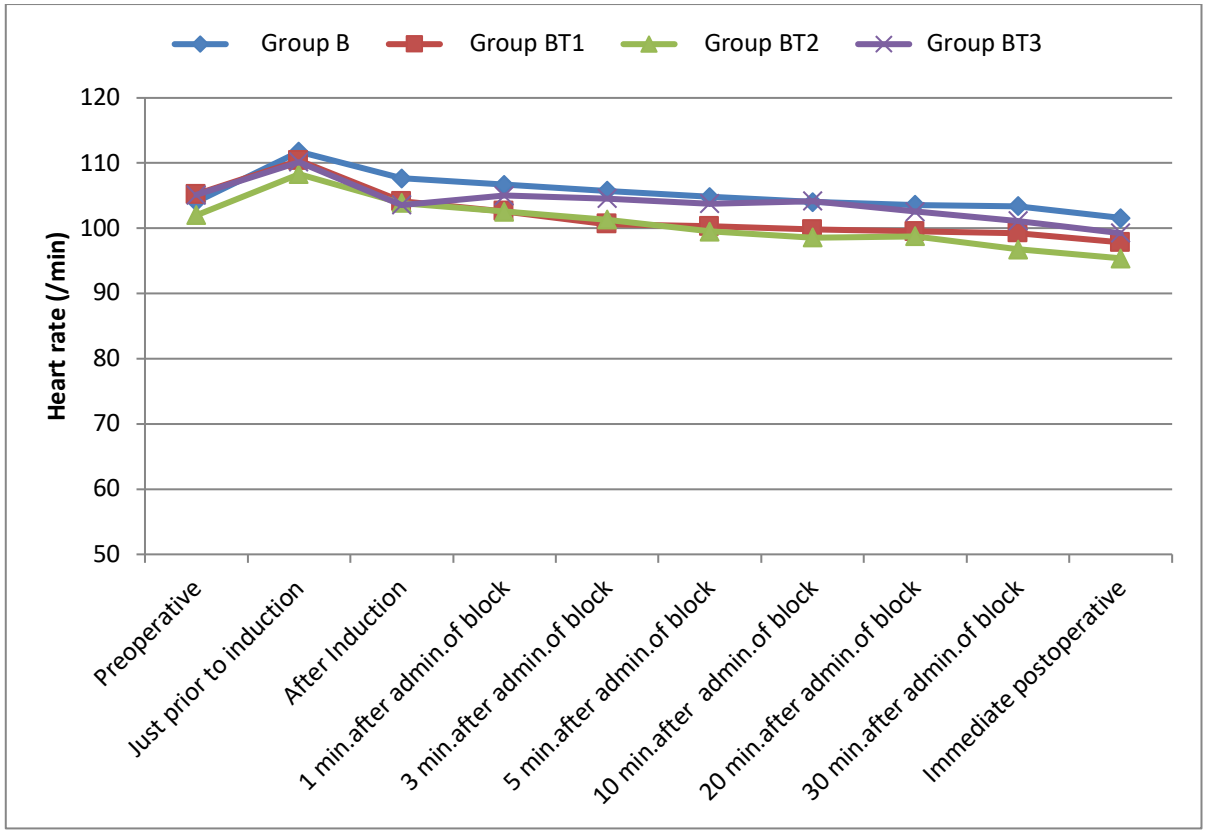

Figure 1: Trend of Heart rate among study groups

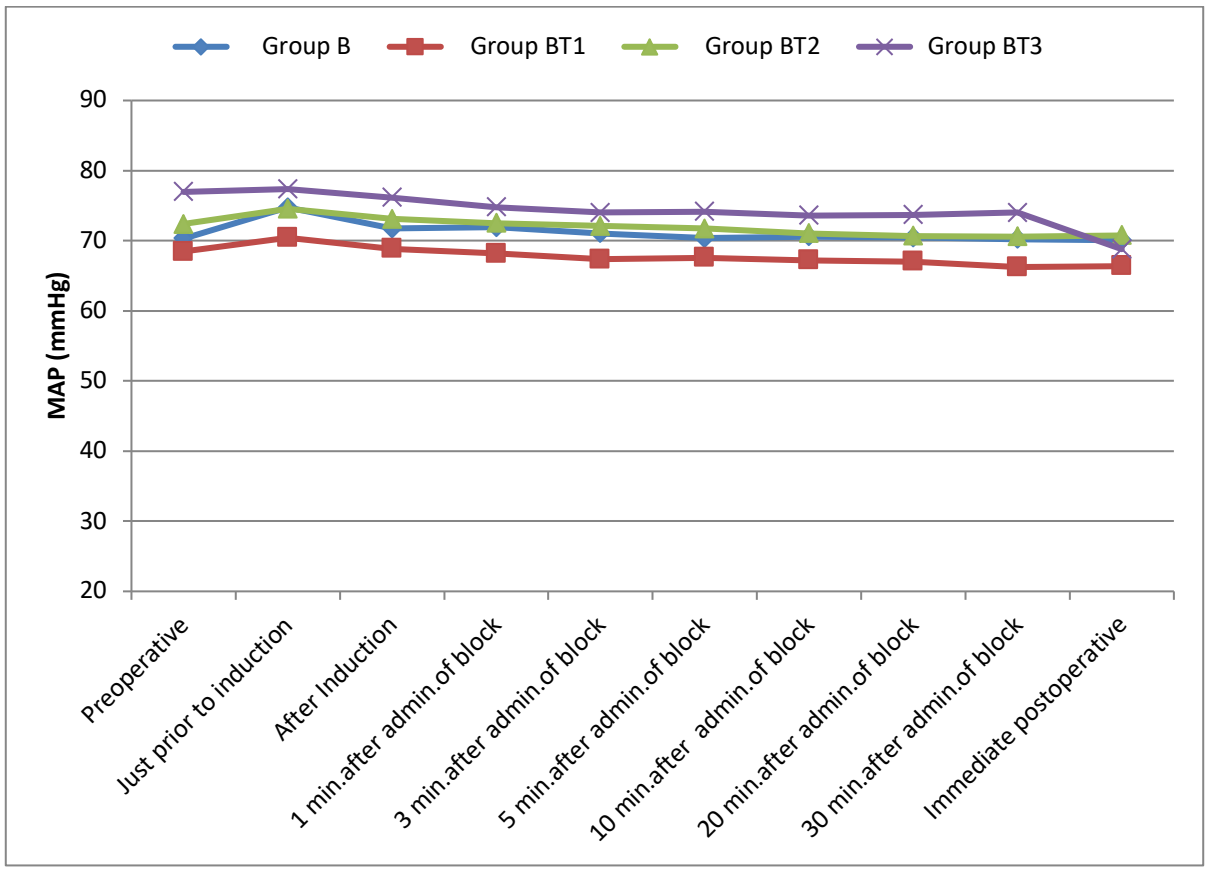

Figure 2: Trend of MAP among study groups

No significant difference was seen in heart rate and Mean arterial pressure at any time during the study period (figure 1 and 2). Post op vomiting was seen in only one (5%) patient in Group B and 2 (10%) patient each in group BT1 and BT1.5 and 3 (15%) patient in Group BT2 of the patient in group (p=1.000).

Discussion

Postoperative analgesia provided through the caudal route in children undergoing uro-genital surgeries is used widely these days. Present study aimed to evaluate dose dependent analgesic effect of tramadol as adjuvant to bupivacaine in pediatric hypospadias surgery. Duration of postoperative analgesia was significantly longer in all three groups with tramadol as compared to bupivacaine alone ($p<0.001$). Studies have demonstrated similar results with patients receiving bupivacaine and tramadol showing significantly longer duration of analgesia than bupivacaine alone in pediatric infraumblical sugeries [18-20]. Batra et al [15] also concluded that caudal tramadol (1 mg/kg) is a useful adjuvant to caudal bupivacaine for postoperative analgesia.

Another similar study by Choudhary et al concluded low dose tramadol (1 mg/kg) to be an effective adjuvant to bupivacaine [1]. Nasreen et al [21] reported a lower pain score in the bupivacaine–tramadol group during the first 24 hours compared to bupivacaine alone, in children undergoing hypospadiasis surgery. Tramadol (2 mg/kg) has shown to be similar to caudal morphine (0.03 mg kg1) in providing pain relief in children undergoing herniorrhaphy. [14]

An increase in duration of postoperative analgesia and reduction in requirement of rescue analgesics was noted with increasing dose of tramadol from 1 mg/kg to 2mg/kg as adjuvant to bupivacaine. Prakash et al [4] in a similar study reported that the duration of analgesia was significantly shorter with bupivacaine alone as compared to other three groups with tramadol adjuvant ($P<0.001$). Time to first rescue analgesia reported in this study was 4 ± 1 hour in Group B, 8 ± 0.9 hours in Group BT1, 11 ±1 hours in Group BT 1.5 and 12 ± 0.9 hours in Group BT2. The difference in mean time to first analgesia between groups BT1, BT1.5 and BT2 was also significant ($P<0.001$).

In present study, most patients in Group B required 3 or 4 dose, while in Group BT1 & BT2 most required 2 or 3 dose and in BT 3 group given 2mg/kg tramadol, most required only 1 or 2 dose of additional analgesic in 24 hours. Prakash et al [4] similarly reported that 15 in Group B required between 3 and 4 doses of postoperative analgesic compared with 5, 3 and 0 patients in groups BT1, BT1.5 and BT2, respectively. Animal studies showed tramadol to have opioids like action at spinal level and depresses spinal nociceptive receptors hence reduced analgesic requirements by caudal route compared to intravenous tramadol [22]. Gunes et al [22] concluded that caudal tramadol (2 mg/kg) provided longer postoperative analgesia than i.v. tramadol in same dose (2 mg kg). Murthy et al [23] concluded that tramadol injection in the epidural space acts only as a depot for immediate and delayed systemic release. This slow absorption of tramadol from the epidural space into the systemic circulation could be responsible for the prolonged duration of action of caudal tramadol [4].There was no difference in degree of motor blockade and none of the patients had motor block on emergence from anaesthesia, as has been reported by past studies [4].

This increase in duration of analgesia was not associated with any addition sedation as evident by sedation scores at different time intervals. Past studies have reported similar sedation even with addition of tramadol [1,21]. Prakash et al [4] also reported that sedation scores at 1 and 4 hours after surgery were comparable in all four groups. In present the incidence of post-operative vomiting was also not significantly different among the study groups.

Past studies have reported no increase in incidence of emesis on addition of tramadol [1,3,18,19]. Prakash et al [4] also reported similar incidence with different dose of tramadol. In present study no significant difference was seen in hemodynamic parameters between the study groups. Studies have reported no change in hemodynamic stability when tramadol is used as an adjuvant [24].

Conclusion

Tramadol is an effective adjuvant to bupivacaine to prolong duration of analgesia in pediatric hypospadiasis surgery.

Higher dose of tramadol (2 mg/kg) provides even longer duration of caudal epidural analgesia with bupivacaine in children, and the requirement for postoperative analgesia in 24 hours is less than with tramadol 1 or 1.5 mg/kg. This advantage of prolonged analgesia is without any increase in adverse effects or effect on hemodynamics.

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