ISSN: 0975-833X

*Available online at http://www.journalcra.com*

*International Journal of Current Research*
*Vol. 8, Issue, 06, pp.32630-32635, June, 2016*

**INTERNATIONAL JOURNAL OF CURRENT RESEARCH**

## RESEARCH ARTICLE

# COMPARISON OF CAUDAL TRAMADOL-BUPIVACAINE AND FENTANYL-BUPIVACAINE FOR POST-OPERATIVE ANALGESIA IN PEDIATRIC HYPOSPADIAS SURGERY

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**ARTICLE INFO**

***Article History:***
Received 04th March, 2016
Received in revised form
07th April, 2016
Accepted 28th May, 2016
Published online 15th June, 2016

***Key words:***

Bupivacaine,
Fentanyl,
Pediatric caudal-epidural analgesia,
Post-operative analgesia,
Tramadol.

**ABSTRACT**

**Background:** Caudal epidural analgesia with bupivacaine is very popular in pediatric anesthesia for providing intra and post-operative analgesia. Several adjuvants have been used to prolong the action of bupivacaine.

**Objective:** To compare the efficacy of Tramadol and Fentanyl in terms of quality and duration of analgesia they produce when added with bupivacaine by single shot caudal-epidural technique in children.

**Study design:** Randomized Controlled Trial.

**Method:** Sixty children, aged three to seven years, undergoing hypospadias surgery were prospectively randomized into two groups:

1.Caudal analgesia with 1 ml/kg of 0.25% bupivacaine with Tramadol 1mg/kg in Group A.

2.Caudal analgesia with 1 ml/kg of 0.25% bupivacaine with Fentanyl1 µg/kg as Group B.

Post-operatively pain was assessed by Modified Objective Pain Score (MOPS).

**Result:** The mean duration of analgesia was significantly longer in Group A(756.24±67.83) than the mean analgesic duration of Group B (464±31.79).The pain score assessed using Modified Objective Pain Score (MOPS).The children of group A has required less analgesic dose than the group B. Hemodynamics and level of sedation were similar in two groups. Post- operatively analgesia was supplemented with inj. Febrinil 8 mg/kg by intravenous route. Any adverse effects like respiratory depression, nausea, vomiting were recorded in all patients.

**Conclusion:** For caudal block, Tramadol 1 mg/kg or Fentanyl 1 µg/kg significantly prolong the duration of analgesia and reduces the intra and post-operative analgesic requirements with preserved hemodynamic stability and lack of sedation, thus allowing single shot caudal anesthesia to be recommended for surgery lasting more than 150 minutes. So they may be the drug of choice to prolong duration of caudal anesthesia without respiratory depression.



**Citation: Dr. Deepti N. Anandani, Dr. Shahin S. Pathan and Dr. Jaydeep B. Vaniya, 2016.** "Comparison of caudal Tramadol-bupivacaine and Fentanyl-bupivacaine for post-operative analgesia in pediatric Hypospadias surgery", *International Journal of Current Research*, 8, (06), 32630-32635.

## INTRODUCTION

Post-operative pain is the most distressing symptom experienced by most of the patient. Pain is defined by the International Association for study of pain as an "Unpleasant sensory and emotional experience associated with actual or potential tissue damage" (International association for study of pain subcommittee on taxonomy pain terms, 1979). Pain induces metabolic, hormonal and cardio-respiratory response that affects the outcome of surgery (Desborough, 2000). Metabolic stress can be prevented if analgesia given thirty minutes prior to incision which stay well in post- operative period and save the patients from neuroendocrine stress responses (Sekair *et al*., 2004). The children cannot express their feeling of pain they were being frequently ignored and given secondary importance (Rana, 1987). The society of pediatric anesthesia on its 15th annual meeting clearly defined the alleviation of pain as a "Basic Human Rights" irrespective of age, medical condition, treatment, primary service response for the patient care or medical institution (Frank, 2002). General Anesthesia continues to be used for pediatric surgical procedures, regional anesthesia as an analgesic adjuvant for pain control both intra and post-operatively has become increasingly popular for pediatric patient of all age groups (Sethna and Berde, 2003). Caudal epidural analgesia is most widely employed technique for the management of pain within the distribution of $T_{10}$-$S_5$ dermatomes, covering the lower

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abdomen, perineum and lower extremities (Sethna and Berde, 2003). This simple technique allow rapid recovery from anesthesia together with effective post-operative analgesia. However, mean duration of surgical analgesia provided by local anesthetics is limited by various drugs added to local anesthetic solution to prolong the duration of caudal anesthesia provided by single injection (Beer and Thomas, 2003). Different drugs like morphine, tramadol, fentanyl, ketamine, clonidine, and midazolam were added to caudal space to prolong the post-operative analgesia irrespective of their side-effects. In longer surgical procedures, insertion of extradural catheter may be required to achieve sustained analgesia. It is time consuming, expensive and various problems such as vascular damage, leak or difficulty in insertion may occur (Muartl *et al*., 1987). Fentanyl is a powerful synthetic opiate analgesic similar to but more potent than morphine. It is typically used to treat patients with severe pain or to manage pain after surgery. It is also sometimes used to treat people with chronic pain who are physically tolerant to opiates. Fentanyl, a lipophilic opioid, is added frequently to local anesthetics in children. Side effects such as nausea, vomiting or respiratory depression are not uncommon (Scott *et al*., 1995). Tramadol is a centrally acting analgesic drug which has been used in children older than 1 year of age in European countries since 1977 (Cook and Doyle, 1996). Tramadol acts at opioid receptor and also appear to modify transmission of pain impulse by inhibition of monoamine re-uptake. Tramadol is a racemic mixture of two enantiomers. The (+) enantiomer has moderate affinity for the opioid $\mu$ receptor, greater than that of (-) enantiomer. In addition, the (+) enantiomer inhibits serotonin reuptake and (-) enantiomer is a nor-epinephrine reuptake inhibitor. These complimentary properties result in a synergistic anti-nociceptive interaction between the two enantiomers. It is an opioid with a striking lack of respiratory depression effect despite of an analgesic potency approximately equal to that of pethidine (Raffa *et al*., 1993). Tramadol has been shown to provide effective long-lasting analgesia after epidural administration inboth adults and children. Objectives of present study was to compare the quality and duration of analgesia after single shot caudal block using bupivacaine with tramadol and bupivacaine with fentanyl and thereby try to find out which can be effective adjuvant to bupivacaine for providing intra and post-operative analgesia in children undergoing hypospadias surgeries.

## MATERIALS AND METHODS

It was a randomized controlled trial. This study was done in department of pediatric surgery, V.S General. hospital, Ahmedabad in Feb 2014 to January 2015. Informed parental consent were taken. We studied sixty healthy boys, ASA grade *I II,* aged 3-7 years, who required surgical repair of hypospadias. Those children receiving medication likely to have interactions with opioids or cause sedation and those in whom caudal analgesia was contraindicated were excluded. No pre-medication was used. Patients induced with inj. glycopyrrolate 4-8µg/kg, inj. thiopentone 5 mg/kg and succinylcholine 2 mg/kg. ET intubation was done with appropriate size ETT, position confirmed and secured the ET. Caudal block was given in right lateral position using 23G needle under aseptic condition. Glucose /saline solution was infused intravenously at the rate of 10 ml/kg/hr. syringe containing equal volume of either 0.25 % bupivacaine 1 ml/kg plus injection tramadol 1 mg/kg or 0.25% bupivacaine plus injection fentanyl 1 µg/kg were prepared. Group A: patients received injection bupivacaine 0.25 %, 1 ml/kg with injection Tramadol 1 mg/kg.

Group B: Patients received injection bupivacaine 0.25%, 1 ml/kg with injection Fentanyl 1 µg/kg into caudal epidural space. Surgery was conducted with $o_2$+ $n_2o$ +sevoflurane +atracurium 0.5 mg/kg on IPPV. No analgesics were used intra-operatively. Intra-operative heart-rate (HR), pulse-oximetry saturation ($spo_2$), Mean arterial pressure (MAP) and end-tidal $co_2$ (Et $co_2$) were monitored. Anesthesia maintained till the dressing was applied. Duration of operation was noted i. e. time from skin preparation to application of dressing. Residual neuromuscular block was antagonized with neostigmine 0.05 mg/kg given together with glycopyrolate and patient was extubated before transfer to the recovery room. Sedation was assessed at 30 minutes, 1 hour, 2 hour, 4hour and 6 hour using an objective score based on eye opening post-operative.

Eye opening spontaneously =0
Eye opening in response to verbal command=1
Eye opening in response to physical stimulation=2
Unresponsive=3

Pain was assessed by Modified Objective Pain Score (MOPS). MOPS is an observational pain scoring system which has been validated for use by parents (Wilson and Doyle, 1996). Score describes five points: crying, agitation, movement, posture, localization of pain. Each observation scores from 0-2 to get a total of 0-10. The score would appear to have some limitations in preverbal children. So it was a better pain assessment tool in this study where minimum age group of children was 3 years. When MOPS reached 4 or more, rescue analgesia was given in the form of injection Febrinil 8 mg/kg through intravenous route. Duration of analgesia was described as time between caudal injection to first dose of analgesia demanded. The existence of motor block was assessed by determining the time of caudal injection to the time when child started moving his legs.

**Statistical analysis**

All results were expressed as mean±SD (standard deviation). Student t-test was used for continuous variables and chi square test for categorical variables with significant level set at $p < 0.05$. Age, weight, ASA physical status was comparable in Group A and Group B (Table -1).

**Table 1. Demographic Data of Both Groups [mean±SD]**

| Variables | Group A | Group B | P value |
|---|---|---|---|
| Age (year) | 4.8±1.70 | 4.6±1.75 | 0.652 |
| Body WT(kg) | 14±3.2 | 15±2.8 | 0.197 |
| ASA class 1/2 | 28±2 | 26±4 | 0.014 |

Time from caudal block to surgical incision, duration of operation, time to extubate and duration of GA in minutes are as given in (Table-2)

**Table 2. Average time interval between caudal anesthesia and duration of operation**

| | Variables (min) | Group A | Group B | P value |
|---|---|---|---|---|
| 1 | Time from caudal block to surgical incision | 20±14 | 22±13 | 0.568 |
| 2 | Duration of operation | 142±10 | 140±8 | 0.389 |
| 3 | Time to extubate | 11±2 | 10±4 | 0.218 |
| 4 | Duration of GA | 152±7 | 150±8 | 0.303 |

**Table 3. Heart rate changes during study period**

| HEART RATE CHANGES DURING STUDY PERIOD (Rate/min) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| GROUP | BASELINE | AFTER GA | 10 min AFTER CA | 30 min AFTER CA | 60 min AFTER CA | 90 min AFTER CA | 120 min AFTER CA | 150 min AFTER CA |
| GROUP A | 130.24±9.36 | 125.44±8.64 | 115.24±10.46 | 90.35±11.07 07 | 88.32±12.26 | 86.22±12.22 | 83.41±11.27 | 80.26±11.62 |
| GROUP B | 132.64±10.21 | 130.77±11.23 | 126.42±12.67 | 101.21±10.32 | 95.36±9.26 | 93.21±10.31 | 90.41±8.23 | 87.41±11.51 |
| P VALUE | 0.342 | 0.038 | 0.0001 | 8.50E-05 | 0.012 | 0.0168 | 0.0057 | 0.0168 |

**Table 4. Systolic pressure changes during study period**

| SYSTOLIC PRESSURE CHANGES DURING STUDY PERIOD (mm/Hg) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| GROUP | BASELINE | AFTER CA | 10 min AFTER CA | 30 min AFTER CA | 60 min AFTER CA | 90 min AFTER CA | 120 min AFTER CA | 150 min AFTER CA |
| GROUP A | 108.21±9.61 | 102.26±8.61 | 104.71±10.21 | 102.46±9.23 | 100.84±11.21 | 96.23±12.17 | 94.21±11.21 | 98.41±12.72 |
| GROUP B | 105.23±12.23 | 101.41±10.21 | 101.30±12.72 | 101.77±11.33 | 104.96±13.26 | 101.46±9.23 | 98.21±10.41 | 98.21±9.36 |
| p VALUE | 0.0293 | 0.726 | 0.254 | 0.794 | 0.193 | 0.061 | 0.152 | 0.904 |

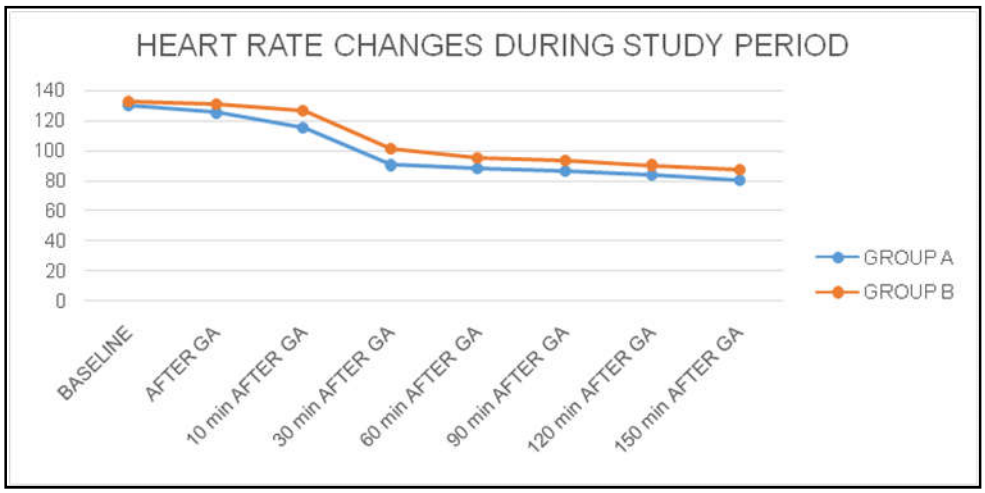


**Figure 1.**

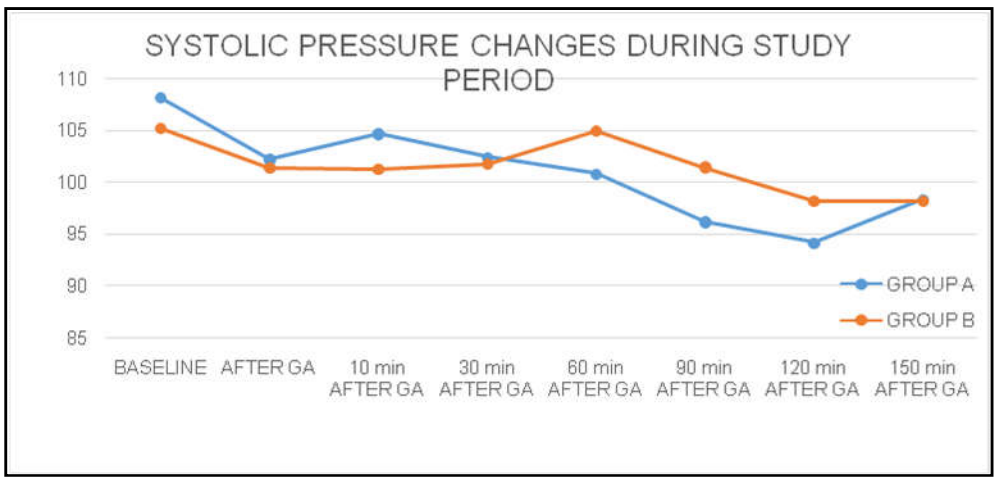


**Figure 2.**

**Table 5. Duration of caudal analgesia and first dose of analgesic**

| Variables | Group A | Group B | p Value |
|---|---|---|---|
| Mean analgesic duration (min) | 756.24±67.83 | 464.±31.79 | <0.00001 |
| No. Of time analgesic needed in first 24hour | 1.2±0.61 | 2.41±0.36 | <0.00001 |

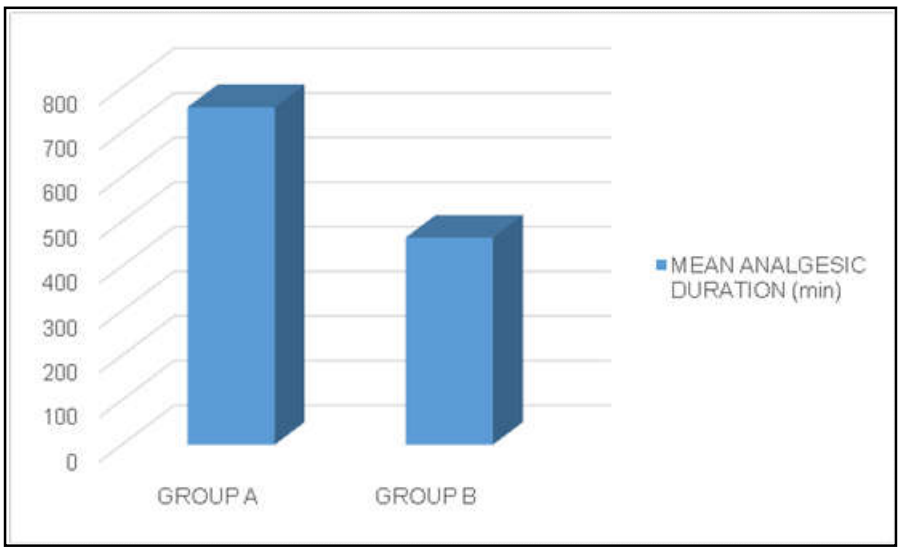


**Figure 3. Mean analgesic duration (in mins)**

**Table 6. Incidence of adverse effects in groups**

| | Group A | Group B | p Value |
|---|---|---|---|
| Vomiting | 3 | 2 | O.67 |
| Pruritis | 2 | 4 | 0.36 |

In (Table-3) heart rate changes during study period in both groups show significant difference of heart rate by comparing both groups.

(Table-4) showing mean±SD of systolic pressure changes during study period show no significant difference of pressure changes by comparing both groups.

Mean duration of post-operative analgesia was significantly longer in Group-A (756.24±67.83) minutes as compared to Group-B (464±31.79) minutes. No. of time analgesic needed was Mean duration of post-operative analgesia was significantly longer in Group-A (756.24±67.83) minutes as compared to more Group-B (2.41±0.36) as compared to Group–A (1.2±0.61) (Table-5). The time for emergence from anesthesia to awakening is similar in both groups. There was no major difference in sedation score after first post-operative period.

Only three patients in Group A and two patients in Group B had developed vomiting and four patients in Group B along with two in Group A had developed pruritus. No other complications like respiratory depression, hypotension, bradycardia observed in any patient.

## DISCUSSION

Caudal-epidural block provides reliable and good quality of analgesia which is particularly useful for anoperineal, peno-scrotal and abdominal surgical procedure in children (Raffa *et al*., 1993). Fentanyl is added commonly to local anesthetic in the extradural space to improve analgesia in the post-operative period (Lejus *et al*., 1994). However, few studies have addressed the benefit of fentanyl for single shot procedures. The addition of fentanyl produced only a slight change in the quality and duration of analgesia after administration of 2% lidocaine with epinephrine for a short surgical procedure or after administration of 0.125% bupivacaine. Therefore, it was concluded that addition of fentanyl to local anesthetic offer no advantage over administration of local anesthetic alone for short surgical procedure in children (Cook and Doyle, 1996; Jonex *et al*., 1990). Another study (Constant *et al*., 1998) concluded that addition of fentanyl to local anesthetic prolong the duration of surgical analgesia of caudal block along single shot caudal anesthesia to be recommended for surgery lasting 90-150 minutes. In this study, fentanyl 1 µg/kg when injected into the caudal-extradural space produced useful analgesia for 464±31.79 minutes (Table 5, Fig. 3) without any significant side-effects. The emetic and pruritic side-effects are well-known for fentanyl. It affected only two and four patients respectively which is not significant (Table 6). Tramadol is a centrally acting opioid analgesic, used to treat moderate to severe pain .It is more specific action at mu opioid receptor and noradrenergic serotonergic system (Raffa *et al*., 1993). Also in this study, tramadol 1 mg/kg when injected into caudal extradural space produced analgesia for 756.24±67.83 minutes (Table 5, Fig. 3). And the mean duration of surgery was 150

minutes. In other studies, caudal tramadol produced useful analgesia without a significant incidence of side-effect (Table 6) (Constant *et al*., 1998). The slow onset time of caudal tramadol may imply that there is a little advantage in injecting tramadol into the extradural space and that intravenous administration may be equally efficacious as an adjuvant to bupivacaine, tramadol may prove more useful in young children and infants than the other opiates because of its lack of respiratory depressant effect (Constant *et al*., 1998). If operative surgery was longer then caudal tramadol had been produced good quality of analgesia for an average of 10.7 hours (Russel *et al*., 1998). The present study of 60 patients aged 3-7 years undergoing hypospadias surgery belonging to ASA *I & II* and divide into two groups, were conducted in order to study the effects of additional fentanyl and tramadol on caudal bupivacaine in patients. We add tramadol 1 mg/kg in group-A and fentanyl in 1 µg/kg in group-B. It was found that good post-operative analgesia in group-A than group-B. In this study, when 1 mg/kg tramadol added to bupivacaine in group-A. The mean duration of post-operative analgesia was (756.25±67.83 minutes). When compared to group B which was (464±31.79 minutes). Our results are consistent with previously published result (Khalid *et al*., 2007; Khans and Memon Iqbal, 2008). Parekh and colleagues studied caudal tramadol plus bupivacaine. They have used different doses of 1 mg, 1.5 mg and 2 mg/kg plus 0.5ml/kg of 0.25% bupivacaine. Observed that 2 mg/kg tramadol used as an adjuvant prolonged the post-operative analgesic period (Prakash *et al*., 2006). Senel and colleagues studied the efficiency of tramadol with bupivacaine in children undergoing inguinal herniorraphy. They observed patient who received bupivacaine 0.25 ml/kg body weight and tramadol 1.5 mg/kghad longer time to administration of first analgesia (13±2 hours) (Senel *et al*., 2001). Opioids are known to cause side-effects like respiratory depression, urinary retention, pruritus, nausea, vomiting. But tramadol is an opioid without any respiratory depressant effect. In this study it was noted that caudal tramadol and fentanyl was not associated with respiratory depression side effect. Nausea and vomiting was present with tramadol due to pressure of opioid receptors in the vicinity of the chemo receptor trigger zone (Gundaz *et al*., 2006). Although incidence of complications like nausea and vomiting occur in patients, few patients have shown pruritus in fentanyl groups.

But there was significant increase in duration of analgesia by addition of fentanyl 1 µg/kg and tramadol 1 mg/kg in bupivacaine. There were no significant changes in sedation score and cardio-pulmonary parameters. The current study gives information of intra and post-operative analgesic effectiveness of caudal fentanyl and tramadol. Both drugs are more effective in terms of duration of analgesia. Base line pulse rate or blood pressure after induction, administration and throughout the intra-operative period (Table 3, 4 & Fig. 1,2). This is because the effect of drugs administered caudally had worn out which is in concurrence with other studies (Sethna and Berde, 2003; Beer and Thomas, 2003). There was no major difference in $SpO_2$ observed intraoperatively as the analgesia obtained was satisfactory and there was no change in rate or depth of respiration. In this study it is shown that caudal tramadol provides effective post-operative analgesia than fentanyl. As regards intravenous route of administration and the analgesic profile of tramadol by the caudal route. No pharmacokinetic studies in children available. Hence the comparative study of the pharmacokinetics profile regarding analgesic requirements of intravenous and caudal tramadol with respect to dosage, duration is necessary for exact determination of dosage caudal tramadol. Prosser *et al*. (Russel *et al*., 1998) at has mention the same.

**Conclusion**

Caudal epidural tramadol 1 mg/kg and fentanyl 1 µg/kg appear a good adjuvant with bupivacaine for hypospadias surgery without using any epidural cathetor.it is simple, safe and reliable technique. Caudal tramadol produce the maximum duration of post-operative analgesia than the fentanyl. Intra-operative parameters like pulse rate, and systolic arterial pressure was maintained throughout surgery. There was no sedation effect and no significant complication in the post-operative period in both groups. So both groups may prove more useful in young children than the other opioids because of its lack of respiratory depressant effects. So these drugs were safe for children.

**Conflict of interest:** None

**Source of support:** Nil

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