Original article

Comparison of Caudal Tramadol with different doses of Midazolam add-on for Postoperative analgesia in Children Undergoing Inguinoscrotal Operations

S Koirala, BK Bhattarai, TR Rahman, BP Sah
Department of Anesthesiology and Critical Care, BP Koirala Institute of Health Sciences

Abstract

Background: Safe and effective postoperative analgesic modalities have remained a subject of contemporary clinical research, particularly in children. The present study aimed at comparing the effectiveness of pain relief in children undergoing inguinoscrotal surgery with caudal tramadol alone and in combination with different doses of midazolam.

Methods: Ninety children of either sex, aged one year to fifteen years, undergoing inguinoscrotal surgical procedures under general anaesthesia were recruited in a randomized double blinded fashion to receive one of the three study medications through caudal route. Group T (n= 30) received injection tramadol 2mg/kg in a volume of 0.5ml/kg up to a maximum volume of 20ml, while group TM (n= 30) and TM/2 (n= 30) received additional midazolam 50mcg/kg and 25mcg/kg respectively. The study medications were administered immediately after induction of anaesthesia. Postoperative analgesia was measured using a modified Hannallah 10 points Paediatric Objective Pain Scale described by Hannallah and colleagues. Pain score of ≤ 4 was considered effective analgesia. Duration of analgesia was defined as the time between caudal injection to the first need of analgesia.

Results: The duration of analgesia in group TM (1145±281.41 min) and TM/2 (1012.67±260.68 min) was significantly longer than that in group T (690.83±215.7 min) ($p<0.005$). The sedation score was the highest in group TM and the least in group T. Nausea vomiting was the commonest side effect in all the three groups without any significant differences in the incidences between the groups.

Conclusion: Addition of midazolam to tramadol for caudal administration in children undergoing inguinoscrotal operations produces significantly longer duration of postoperative analgesia than produced by epidural administration of tramadol alone.

Keywords: Caudal analgesia, inguino-scrotal operation, paediatric analgesia, postoperative pain

Introduction

Despite significant progress in the field, search of effective modalities for postoperative pain relief still remains a subject of contemporary clinical research, particularly in paediatric anaesthesia practice. Inability of small children to report pain and difficulty in assessing pain make this topic a subject of ongoing interest. Better understanding of the deleterious consequence of poorly managed pain has been further urging the researchers to discover more effective pain modalities. Caudal opioids combined with or without local anaesthetics and/or other adjuvants have been found to be effective analgesics in children undergoing inguinoscrotal procedures.[1,2] Morphine, a commonly used opioid used caudally provides

Address for correspondence
Dr. Siddhartha Koirala
Department of Anesthesiology and Critical Care
BP Koirala Institute of Health Sciences, Dharan
Email: drsiddharthakoirala@gmail.com

excellent analgesia for 24 hours.[3] However, its use is limited because of its unpleasant side effects and potential risk of respiratory depression.[4] Moreover, lack of easy availability limits the use of this modality, particularly in a community setting of a developing country, like ours. Tramadol is easily available and has been shown to produce reasonable duration of analgesia in children when used caudally. Further, midazolam has been shown to significantly prolong the duration of analgesia in children when added to caudal local anaesthetic.[5] Keeping these facts in mind, the present study aimed at comparing the post operative analgesic effect of caudal tramadol with combination of caudal tramadol and different doses of midazolam in children undergoing inguinoscrotal surgeries.

Methods

After approval from the Institute ethics committee, this double blinded randomized clinical study was carried out in 90 paediatric and adolescent patients aged 1-15 years undergoing inguinoscrotal surgeries. Written informed consent was obtained from the parents of each patient. Exclusion criteria included: history of coagulopathy, ongoing analgesic intake, injection site infection, neurological or spinal disease and American Society of Anaesthesiologist Physical Status III or more. All the patients were premedicated with promethazine (1mg/kg) night before and 2 hours prior to surgery. Clinical and intraoperative monitoring included non-invasive blood pressure (NIBP), pulse oximetry, Electro-cardiography and capnography. Induction of anaesthesia was achieved intravenously or by inhalation method depending upon the age. Propofol (2-2.5 mg/kg) was used for intravenous induction and halothane in oxygen for inhalation induction. Injection vecuronium bromide (0.5mg/kg) was used intravenously for facilitating laryngoscopy and tracheal intubation as well as muscle relaxation. The airway was secured with appropriate size endotracheal tube or a laryngeal mask airway. Anaesthesia was maintained with halothane in oxygen given through Jackson-Rees modification of Ayre's T piece. Injection pethidine (0.5mg/kg) was used for intraoperative pain relief. Using computer generated random sequence, patients were allocated in equal numbers to receive caudally either tramadol (2mg/kg, 0.5ml/kg, max 20ml)-group T, or tramadol (2mg/kg, 0.5ml/kg, max 20ml) + midazolam (50 mcg/kg) – group TM, or tramadol (2mg/kg, 0.5ml/kg, max 20ml) + midazolam (25 mcg/kg) – group TM/2. The combinations of the drug were prepared by one of the investigators not involved in anaesthetic care of the patient. The volume of the drug was attained by diluting the drug with normal saline. Caudal administration of the study drug was done after induction of anesthesia. Caudal epidural was performed in the lateral decubitus or prone position with strict aseptic precaution by one of the investigators experienced in performing pediatric caudal blocks. The caudal epidural was performed by using a 22 gauge needle and the drugs were administered through a 10ml syringe in all the patients.

In the recovery area; heart rate, NIBP, pulse oximetry, pain score were recorded at ½ hour interval and the patients were followed up in the ward for post operative pain relief four hourly for 24 hours. The analgesic effect of the caudal drugs was evaluated using 10 points pediatric

objective pain scale described by Hannallah et al.[6] Duration of analgesia was defined as the time from caudal injection to the first need for systemic analgesic. Pain score of ≤ 4 was considered adequate analgesia. This observation was made by one of the investigators blinded to the treatment groups. The analgesic used when the pain score >4 was IV ketorolac (0.7mg/kg). Sedation was recorded using five point scale. Fully awake and oriented- 1, drowsy- 2, eyes closed but arousal to command- 3, eyes closed but arousal to mild physical stimulation (earlobe tug)- 4, eyes closed but not arousal to mild physical stimulation (earlobe tug)- 5. All data were entered in excel 2000 and analysis was done using SPSS to find out statistical significance of difference among and within the groups. Students-t test was used for continuous data and mean comparison test was used according to the variables studied.

Result

Patient and operative characteristics are given in Table 1. All the groups were similar in terms of patient and operative characteristics.

Table 1: Comparison of patient characteristics between three groups. Values are expressed as mean ± standard deviation unless otherwise stated.

	Group T (n= 30)	Group TM (n= 30)	Group TM/2 (n= 30)	P Value
Sex M/F	30/0	29/1	30/0	
Age (yrs)	5.90±3.36	5.67±2.99	5.27±2.64	0.713
Weight (kgs)	16.70±7.25	17.77±7.31	17.27±7.38	0.853
Height (cms)	105.67±20.04	103.92±17.35	103.83±15.81	0.904
Duration of Anesthesia (min)	57.67±24.27	48.50±13.91	50.17±16.13	0.138
Duration of Surgery (min)	47.17±23.26	38.50±12.94	40.90±14.64	0.148

The types of surgical procedures performed are given in Table 2. Herniotomy was the commonest procedure performed.

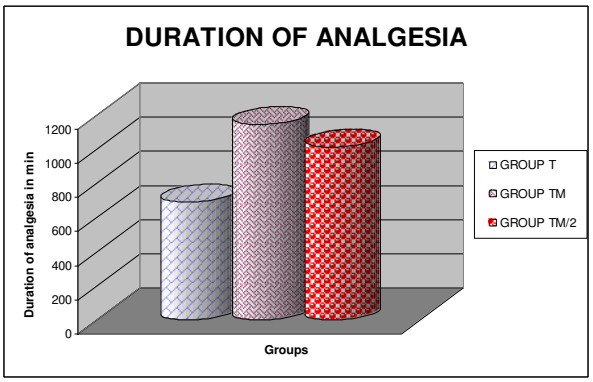
Table 2: Distribution of Surgical procedures performed

Surgeries	T (n= 30)	TM (n= 30)	TM/2 (n= 30)
Herniotomy	26	29	28
Circumcision	2	1	2
Hypospadias repair	2		

Postoperative Pain

The total duration of analgesia was 690.83±215.7 min in group T, 1145±281.41 min in group TM and 1012.67±260.68 min in group TM/2. The duration of analgesia was significantly longer in the combination group as compared to tramadol alone ($p<0.05$). Though group TM had longer duration of analgesia as compared to group TM/2, there was no statistically significant difference between the two groups ($p= 0.064$).

Fig 1. Comparison of duration of Analgesia among the groups



Postoperative Sedation

The postoperative sedation was highest among group TM. When the three groups were compared, the comparisons were statistically significant at 0 hours and 2 hours (Table 3). The median and the interquartile range along with the P values of the three groups are given in the table below.

Table 3. Comparison of post-operative sedation as median (Interquartile range)

Time (Median-IR)	T	TM	TM/2	P Values
0hr	3 (2-3)	3 (3-3)	3 (3-3)	0.019
2hr	2 (2-2)	3 (2-3)	3 (2-3)	0.001
4hr	2 (1-2)	2 (2-2)	2 (1-2)	0.07
6hr	1 (1-1)	1 (1-1)	1 (1-1)	0.4
8hr	-	1 (1-1)	1 (1-1)	1.00

Postoperative Complication

Nausea and vomiting were the commonest undesirable effect with highest incidence in group T (16.6%) compared to group TM (3.3%) and group TM/2 (6.6%). However, the difference was not statistically significant among the groups. One patient in group T developed itching. None of the patients developed other undesirable side effects like respiratory depression, urinary retention and motor block.

Discussion

Genitourinary and lower abdominal surgeries are often associated with moderate to severe postoperative pain in children. Recognition of this problem has made it desirable to find safe and effective ways of postoperative analgesia. Now a days, the use of caudal narcotics has become widespread to provide effective and long lasting analgesia, but is associated with major side effects, in particular the potential of delayed respiratory depression. Newer opioids have been developed and used including tramadol, a synthetic opioid analgesic in clinical practice. The (+) enantiomer has a moderate affinity for the opioid mu receptor, greater than that of (-) enantiomer. In addition, the (+) enantiomer inhibits serotonin uptake and the (-) enantiomer is a potential noradrenalin inhibitor, which results in a synergistic antinociceptive interaction between the two enantiomers. The result is an opioid with a striking lack of respiratory depressant effect despite an analgesic potency approximately equal to that of pethidine.[19] The present study has shown that addition of midazolam for caudal analgesia in children provides effective and prolonged pain relief following inguinoscrotal surgeries. In the present study, tramadol when used alone caudally provided analgesia for 11.5 ± 3.6 h. This duration is very close to the duration of 10.7 h reported by Prosser and colleagues.[7] Delikan et al[5] also reported 9.4 h of effective analgesia with tramadol given epidurally. Fu and colleagues[8] have also reported 12 h

analgesia with tramadol 75 mg. In both the latter studies, the duration of analgesia was similar to tramadol arm of our study. However, other investigators have reported longer duration of postoperative analgesia than ours. Baraka and others[9] reported effective analgesia lasting for 24 h by using single dose of tramadol epidurally. Batra et al[10] reported effective postoperative analgesia for 16-20 h in children following caudal tramadol with lower total consumption of postoperative analgesic than with caudal bupivacaine.

Our study has shown significant prolongation of duration of analgesia with addition of midazolam to tramadol for caudal administration. Addition of 25µgm of midazolam to tramadol prolonged duration of analgesia by more than 5 hours while addition of 50µgm of midazolam prolonged analgesia by almost 7 and half hour. We did not come across any study that compared analgesia with caudal tramadol and combination of tramadol and midazolam. However, other studies have consistently demonstrated prolonged analgesia ranging from 11h to more than 21h following caudal administration of midazolam added to bupivacaine.[11-14] Ozkan et al[15] also demonstrated that caudal tramadol was superior to bupivacaine in analgesic efficacy and in reducing the need for additional analgesia during the postoperative period in pediatric patients. In recent studies where Tramadol was used as an additive for regional anaesthesia, the authors found that tramadol increased the duration of analgesia and also free from any incidence of respiratory depression, nausea, vomiting and urinary retention.[16-18] Since there is great variation in the study design as well as the dose of midazolam used in these studies, it is not possible to compare their findings with our findings. Our study has, however, clearly shown that addition of 25 µgm/kg of midazolam produced almost equal analgesic duration when compared with 50 µgm/kg midazolam combined to tramadol.

In our study, the sedation score remained more than 1 (1= fully awake and oriented) in all the three groups up to 2 h postoperatively. Among the three groups, the group receiving 50 µgm/kg of midazolam combined with tramadol showed higher (deeper) sedation score. This finding is not unexpected since we used higher doses of midazolam in this group. Sedation potential of tramadol has been reported to be less than that of morphine[19] and limited to light level.[20] It may be argued that sedation is a disadvantage in the postoperative period. In the contrary, light sedation may actually be desirable in small children for smooth emergence from general anaesthesia, provided airway and ventilation are not compromised.

Post operative nausea and vomiting (PONV) is known undesirable effect of any opioids including tramadol. Tramadol was used in all the 3 groups in our study and we observed an overall incidence of 4.5%. In the group receiving tramadol alone, the incidence was higher than the ones receiving combination of tramadol and midazolam. Incidence of PONV following caudal tramadol are varying and generally dose dependent and have been reported to be up to 50%.[5] This incidence is relatively low and can be attributed to the use of promethazine as premedication and propofol as induction agent.

In conclusion, our study has shown that addition of 50µgm/kg or 25µgm/kg of midazolam to 2 mg/kg tramadol for caudal administration in children produces significantly longer duration of postoperative analgesia than produced by caudal administration of tramadol alone. With the exception of sedation, undesirable effects of the combination were minor and few. Tramadol midazolam mixture can be recommended for caudal blocks in children undergoing inguino-scrotal operations. Addition of 25 µgm/kg of midazolam to 2mg/kg of tramadol provides comparable prolongation of analgesia with less sedation than addition of 50µgm/kg of midazolam.

Limitation of the study

- Use of two different scales for measuring pain.
- We had to use promethazine as premedicant which is likely to mask side effects like PONV and enhance sedation.

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