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Original Article

Efficacy of tramadol as an adjuvant to bupivacaine for caudal analgesia in children: a randomised controlled trial

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Abstract

Background: The goal of postoperative analgesia is to minimise pain with least possible side effects and in our setting be as cost effective as possible. In children, caudal anaesthesia is typically combined with general anaesthesia for intraoperative and postoperative analgesia. Adjuvants can be added to local anaesthetics for prolonging the duration of analgesia. This study was done to find out the duration of analgesia of caudal Bupivacaine in combination with Tramadol.

Methods: This prospective, randomised, double-blind, comparative study was done by taking a total of 60 patients, aged between 2 to 7 years undergoing elective lower abdominal, urological and lower extremity surgeries. The patients were randomized to group A (*n*=30) receiving 1 ml/kg of 0.25% bupivacaine and group B (*n*=30) receiving 1 ml/kg of 0.25% bupivacaine plus 1mg/kg of tramadol caudally. Duration of analgesia, hemodynamic responses and adverse effects were noted and analysed.

Results: Thirty patients in both groups were comparable with regard to demographic data and hemodynamic response and were statistically non-significant (*P*>0.05). It was observed that the mean duration of analgesia was significantly longer in group B (467.5±164.5 min versus 240.5±69.4 min, *P*<0.001). One patient in each group had postoperative vomiting.

Conclusion: Tramadol 1mg/kg as an adjuvant to bupivacaine 0.25% for caudal analgesia in children is effective in increasing the duration of analgesia without an increase of adverse effects.

Keywords: bupivacaine; caudal analgesia; tramadol

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Introduction

The society of Paediatric Anaesthesia, on its 15th annual meeting at Louisiana clearly defined the alleviation of pain as a "basic human right",[1] irrespective of age, medical condition, treatment or medical institution. The goal of postoperative analgesia is to reduce or eliminate pain with least possible side effects and in our set up as cost effective as possible.

Various regional anaesthetic procedures have gained popularity for postoperative analgesia because in addition to provide analgesia, they also reduce the need of general anaesthetic intra-operatively without significant adverse effects and maintain a smooth intraoperative as well as postoperative period. In children, caudal anaesthesia is typically combined with general anaesthesia for intraoperative supplementation and postoperative analgesia. It is commonly used for surgical procedures below the diaphragm like urogenital, rectal, inguinal, and lower extremity.[2]

Caudal anaesthesia is a type of regional anaesthesia in which local anesthetic is injected into epidural space. It is most popular regional anaesthesia with a predictable level of blockade used in pediatric surgeries. The main drawback of caudal analgesia is the short duration of action with a local anaesthetic agent in a single injection. To overcome this problem, various drugs can be added to local anaesthetics as an adjuvant to prolong the duration of analgesia.

Tramadol is one of those various adjuvants and is a centrally acting synthetic opioid analgesic equipotent to pethidine with a striking lack of respiratory depressant effect. It acts at opioid receptors and it also enhances the function of the descending inhibitory pathways by inhibition of neuronal reuptake of monoamines.

Tramadol is a racemic mixture of two enantiomers having complementary properties which result in a synergistic antinociceptive interaction. In addition, biotransformation of Tramadol in the liver results in many metabolites of which O-desmethyl tramadol is the major metabolite exerting modest analgesic effect.[3]

We commonly practice intravenous Tramadol for analgesia but the practice of administering Tramadol epidurally is not commonly practised in our set up. Similarly, there are a lot of studies done by administering Tramadol epidurally as an adjuvant to Bupivacaine in different parts of the world but there is the lack of sufficient adequately powered studies from our set up. From those studies, it has been shown that epidural Tramadol prolongs the duration of analgesia. So this study was conducted to find out the duration of analgesia of Bupivacaine in combination with Tramadol caudally so that we can routinely use this drug for the benefit of the patients.

Methods

This was a randomised, prospective, double-blind, comparative and parallel group trial done in a tertiary care hospital in Kathmandu. This study was conducted to determine the duration of analgesia of caudal Tramadol as an adjuvant to Bupivacaine as a primary outcome and compare the hemodynamic response and assess the adverse effects of study drugs as secondary outcomes.

Following Institutional Review Board approval and before enrolling the patients into the study, their parents were informed about the study and the procedures to be performed and both written and verbal consents were taken from those parents whose child met the inclusion criteria. The ASA physical status I and II of both sexes of aged two to seven years scheduled for elective lower abdominal, urological and lower extremity surgeries were included in the study. The exclusion criteria included parents' refusal, neurological deficit, mental retardation, coagulopathy, allergy to study drugs, infection at the injection site and obvious spinal or skeletal deformity.

The sample size was calculated based on the study done by Meena Doda et al[4] taking the alpha error as 1.96, beta error as 1.28 and mean difference of 2.8 hours with 90% power at 95% confidence interval. The sample size taken was 30 in each group.

One day prior to the surgery, pre-anaesthetic evaluation of the patients was done with detailed history, physical examination and relevant laboratory investigations. Patients were kept nil per orally for at least six hours before the time of surgery but they were allowed to have milk till four hours before and water till two hours before the time of surgery.

In operation room, standard monitors were attached which included an electrocardiogram, non-invasive blood pressure, pulse oximeter and temperature. Induction was done either with intravenous anaesthetic (propofol or sodium thiopentone) after appropriate-sized intravenous cannulation or gaseous induction with halothane. The pulse rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, electrocardiogram, arterial oxygen saturation and temperature were monitored.

Patients enrolled into the study were randomised into two groups by lottery withdrawn by a trained staff from a sequentially numbered container. After a trained staff generated the random allocation sequence, an anesthesiologist enrolled participants and assigned them to interventions who was not involved in observing the outcome variables. The baseline hemodynamic parameters were noted before performing the caudal block. A trained staff was asked to prepare the drugs, so that neither the investigator nor the subjects were aware of the study group.

Group A received 0.25% Bupivacaine. Group B received 0.25% Bupivacaine plus Tramadol 1 mg/kg. Tramadol

was available as 2 ml ampoule containing injection Tramadol 50 mg/ml. Each 10ml of the prepared solution contained 0.25% Bupivacaine or 0.25% Bupivacaine with 10mg Tramadol. The volume of the drug to be injected was calculated according to Armitage recommends 1 ml/kg for a lumbosacral block. The anesthesiologist and the staffs involved in measuring hemodynamic parameters, measuring the duration of analgesia, noting the adverse effects of study drugs and the patient remained unaware of the group allocations. Duration of analgesia (time of caudal administration of drugs to the first dose of rescue analgesia) was noted. The degree of analgesia was assessed using FLACC (Face Legs Activity Cry Consolability) scale. The assessment was done every 30 minutes for 2 hours, then hourly till the patient received the first dose of rescue analgesia. At the same time, the adverse effects of the study drugs (nausea, vomiting, and arrhythmia) were also noted.

Interpreting the FLACC score: 0 = relaxed and comfortable; 1 to 3 = mild discomfort; 4 to 6 = moderate pain; 7 to 10 = severe pain or discomfort or both.

Patients with a score of 4 or more than 4 received rescue analgesic. Inj. Pethidine 0.5 mg/kg intravascularly was injected as rescue analgesic.

Collected data were analysed by means of statistical software SPSS 20 and appropriate tests. Chi-square test was used for categories like sex and incidence of adverse effects. Student's t-test was used for continuous parametric data like age, weight, heart rate, blood pressure and duration of analgesia. The p-value of less than 0.05 was taken as statistically significant.

Results

Sixty patients were included in the study. The details of the patient flow through the study has been shown in the following figure.

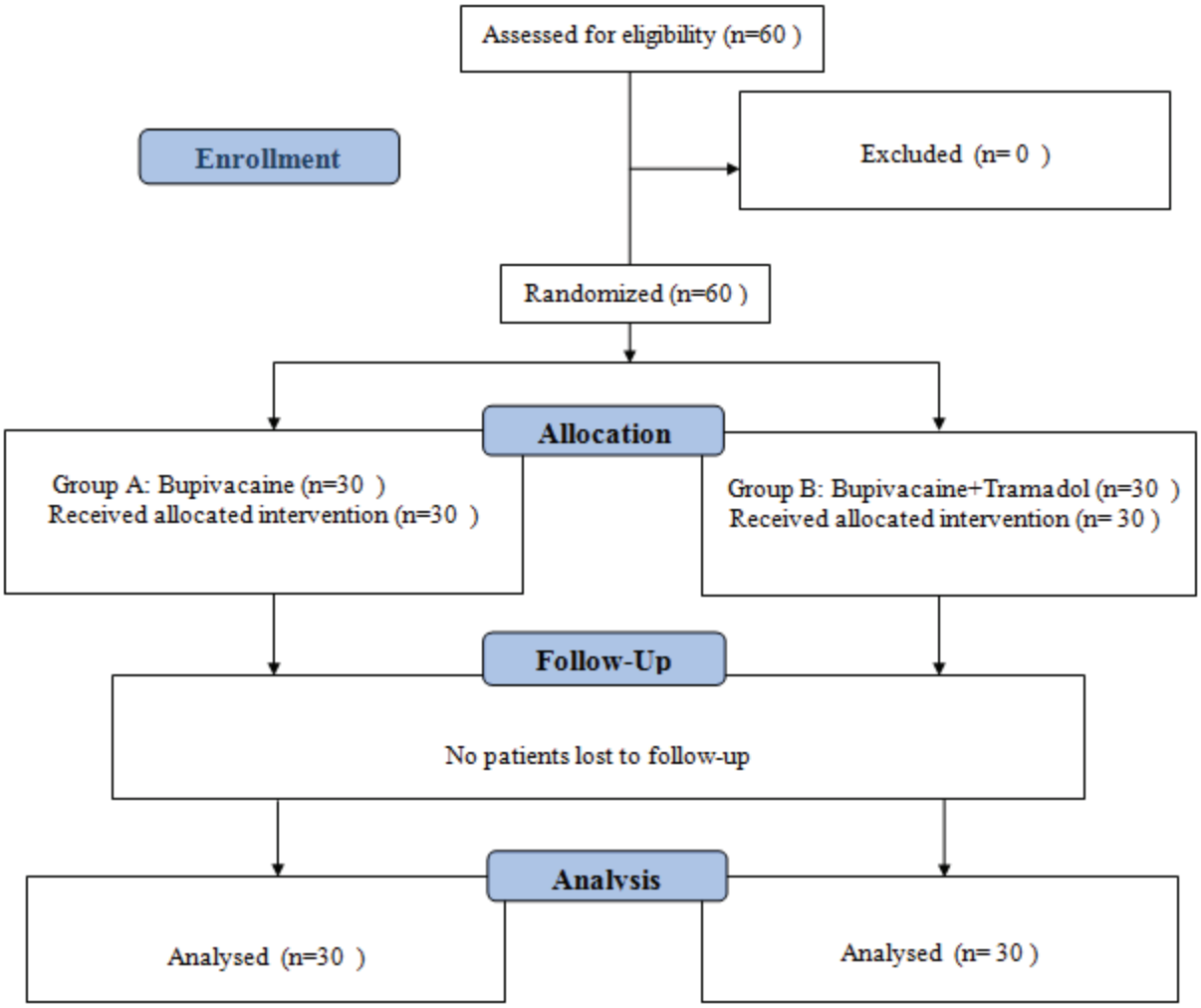

Figure 1: CONSORT 2010 Flow Diagram

The age, sex, weight and ASA physical status were comparable between the two groups.

Table 1: Demographic Data

Variables	Group A (n=30)	Group B (n=30)	P value
Age (months)	45.07±19.9	52.87±22.8	0.164
Sex (M/F)	23/7	19/11	0.260
Weight (kg)	13.73±4.1	15.08±4.5	0.235

Heart rate and mean arterial pressure at different intervals of time were comparable between two groups.

Table 2: Heart rate at different intervals of time

Heart rate (beats per minute)	Group A	Group B	P value
Baseline	109.9±14.6	109.0±14.9	0.807
Just after administration of study drug	109.9±14.6	109.8±14.9	0.972
3 min after administration of study drug	109.3±14.3	108.6±14.7	0.846
5 min after administration of study drug	110.4±12.8	108.4±15.6	0.596
10 min after administration of study drug	109.8±13.2	109.5±13.6	0.916

Table 3: Mean arterial pressure at different intervals of time

Mean arterial pressure (mm of Hg)	Group A	Group B	P value
Baseline	61.6±7.8	65.4±7.6	0.062
Just after administration of study drug	59.4±7.7	63.8±9.7	0.060
3 min after administration of study drug	59.6±7.5	64.1±9.7	0.052
5 min after administration of study drug	59.9±8.3	64.3±8.7	0.051
10 min after administration of study drug	61.2±7.3	64.3±7.8	0.118

The mean duration of analgesia in group A was (240.5±69.4) minutes whereas in group B it was (467.5±164.5) minutes with the P<0.001. The incidence of vomiting was equal in both the groups (3.3% in each group). No other adverse effects like arrhythmia, hypotension, bradycardia, seizure, respiratory depression or urinary retention were seen.

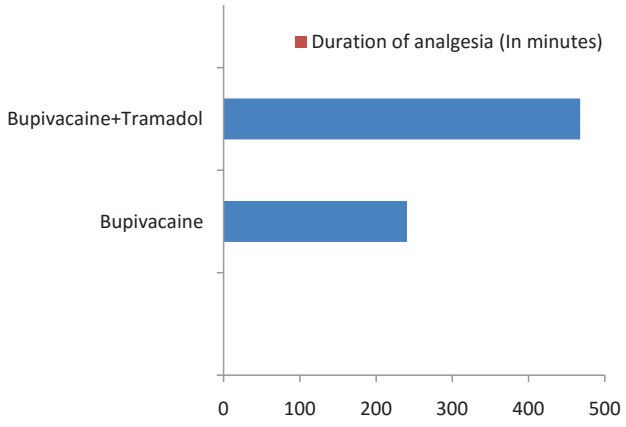

Figure 2: Duration of analgesia

Discussion

Uncontrolled postoperative pain can lead to various unwanted effects like delayed recovery from surgery, restriction of mobility, the risk of thromboembolism, and increased level of blood glucose.These effects cause poor wound healing, immune dysfunction and paralytic ileus. Patients with inadequate analgesia cannot breathe deeply, have an ineffective cough, which leads to various postoperative pulmonary complications. So by preventing the stress response that occurs during surgery through reduction of nociceptive input to the central nervous system and maintaining perioperative analgesia decreases complications and facilitates early recovery.

Regional anaesthetic techniques are used effectively to manage acute pain after a variety of surgeries. The benefits of regional anaesthetic techniques include avoidance of perioperative opioids and their adverse effects, early ambulation, and excellent analgesia. Caudal anaesthesia is the most popular regional anaesthesia technique with a predictable level of blockade for children. Various drugs can be added to local anesthetics as an adjuvant to prolong the duration of caudal analgesia provided by a single injection. Tramadol is one of them used along with Bupivacaine in the caudal block which is an opioid analgesic equipotent to Pethidine with the striking lack of respiratory depressant effect and cost effective also that can be used in our set up for the benefit of the patients undergoing different surgeries.

It was found in this study that Tramadol 1 mg/kg can be used

as an adjunct to 0.25% Bupivacaine for caudal analgesia in children with total volume of 1 ml/kg for increasing the duration of postoperative analgesia without an increase of adverse effects. Similar results were reported by Md Shafiqul Islam et al[5] in a study of children undergoing sub umbilical surgeries with the caudally administered mixture of Tramadol and Bupivacaine. They found that mean duration of pain relief was significantly longer (P<0.001) when the mixture of Tramadol and Bupivacaine was used compared to Bupivacaine alone.

Meena Doda et al[4] did a study in children to compare the quality and duration of pain relief after a single shot caudal block with 0.5 ml/kg of 0.25% Bupivacaine alone and 0.25% Bupivacaine plus Tramadol 2 mg/kg. It was found that the mean duration of the time interval between the caudal block and the first dose of analgesic was significantly longer when the combination of Bupivacaine and Tramadol was used. The dose of Tramadol used by them is greater and the total volume is smaller, however, the concentration of Bupivacaine is similar as compared to our study. A similar result was found by Laiq N et al[6] in a study done in children undergoing hypospadias surgery to compare the effectiveness of Bupivacaine and Bupivacaine-Tramadol mixture administered caudally for postoperative analgesia. They concluded that Tramadol 1 mg/kg with 0.25% Bupivacaine caudally, when given in a total volume of 0.5 ml/kg, provides prolonged and good quality postoperative analgesia compared to Bupivacaine only. The total volume of the drug used in their study was less than that in our study with a similar dose of Tramadol.

Another study was done by Shrestha SK et al[7] and they also concluded that the addition of Tramadol 1 mg/kg to 0.25% Bupivacaine caudally provided longer duration of analgesia and lesser need for rescue analgesics postoperatively compared to Bupivacaine only with total volume being 0.5 ml/kg. The increase in duration of analgesia when Tramadol was added is less in Shrestha's study compared to this study. This might be because of the lower volume of the drug used by them although the concentration of Bupivacaine and the dose of Tramadol are same. Similar results were also found in the study done by S Prakash et al[8] and A.C. Senel[9] et al.

The most frequent side effects of epidural Tramadol are nausea and vomiting. But the incidence of vomiting was same in both groups in our study which was 3.3%. Contradictory to our study, the study done by Shahid Khan et al[10] showed increased incidence of vomiting when Bupivacaine-Tramadol combination was used. The incidence of vomiting was 10% in the combination group compared to 6.66% in the group receiving Bupivacaine only.

None of the patients in our study in either group has developed other adverse effects like arrhythmia, hypotension, bradycardia, seizure, respiratory depression or urinary retention. Similar results were seen in a study done by S Prakash et al[8] to evaluate the analgesic efficacy of three doses of Tramadol administered caudally with Bupivacaine.

Drug volume injected was 1 ml/kg to all the patients regardless of the type and extent of the surgery. This might be the limitation of this study.

This study concludes that Tramadol 1 mg/kg can be added to 0.25% Bupivacaine for caudal analgesia with total volume of 1 ml/kg to prolong the duration of postoperative analgesia in children undergoing lower abdominal, urological, lower extremity surgery without an increase of adverse effects.

Consent: Informed consent was obtained from parents/ guardians of all the participants of the study.

Conflicts of interest: UK Regmi and have filled the ICMJE conflict of Interest form and declare that they have nothing to disclose. S Sapkota is a member of the editorial board of this journal and did not participate in the editorial process of this article.

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