Original Article

Efficacy of two doses of tramadol versus bupivacaine in perioperative caudal analgesia in adult hemorrhoidectomy

ABSTRACT

Background: The study was conducted to evaluate the perioperative analgesic efficacy of the two doses of caudally administered tramadol versus bupivacaine in adult hemorrhoidectomy.

Patients and Methods: A total of 90 patients, aged 20-50 years, undergoing hemorrhoidectomy were randomly scheduled to receive bupivacaine 0.25% in 20 ml (Group B; $n = 30$), tramadol 1 mg/kg in 20 ml (Group T_1; $n = 30$), tramadol 2 mg/kg in 20 ml (Group T_2; $n = 30$) through caudal route after induction of general anesthesia. Postoperative pain was assessed every hour until the visual analog scale was 6, which is 1st time for rescue analgesia. Postoperative sedation, hemodynamic changes, serum cortisol, and epinephrine levels and incidence of side effects were also evaluated.

Results: Duration of analgesia was longer in Group T_2 (20 [1.14] h) compared with the Group B (7 [1.2] h) or Group T_1 (12 [0.75] h); all $P < 0.001$. There were no significant hemodynamic changes. There were not incidences of side effects.

Conclusion: Caudal tramadol 2 mg/kg provided a longer duration of postoperative analgesia with rapid onset and no incidence of complications or adverse effects in adult hemorrhoidectomy.

Key words: Analgesia; bupivacaine; caudal; hemorrhoidectomy; tramadol

Introduction

Pain is a highly unpleasant sensory and emotional experience. Hemorrhoidectomy is generally associated with pain of long duration. Treatment of perioperative acute pain is an important goal for anesthetists to satisfy their patients. The caudal epidural block is considered a simple, safe, and popular anesthetic technique to control such pain. Some members of local anesthetics have been used but still their duration of action need to be prolonged to meet patients' requirements. Bupivacaine is the currently available local anesthetic with long duration of action.[1] Its maximum analgesic effect is up to 6-12 h.[2] Various methods have been devised to extend the duration of regional analgesia with local anesthetics. Placement of catheter invites a high risk of infection.[3] Many drugs including epinephrine,[3] opioids,[4] clonidine,[5] ketamine,[6] midazolam,[6] neostigmine,[6] have been tried as adjuvants with caudal bupivacaine to improve the quality of analgesia and extend its duration. Each of these adjuvants has its merits and demerits. For instance, caudal midazolam has been associated with prolonged sedation.[6] Behavioral changes have been noted with the use of caudal ketamine.[6] Caudal clonidine has been associated with postoperative

Hanan M. Farag, Ibrahim M. Esmat

Department of Anesthesia and Intensive Care and Pain Management, Ain Shams University, Cairo, Egypt

Address for correspondence: Dr. Hanan Mahmoud Farag, Department of Anesthesia and Intensive Care and Pain Management, Ain Shams University, Cairo, Egypt. E-mail: hananfarag@med.asu.edu.eg

hypotension.[5] Caudal morphine and pethidine along with bupivacaine caused nausea, vomiting, pruritus, itching, flushing, urine retention, and respiratory depression.[4] The aim of this study was to assess the efficacy of two different doses of tramadol in perioperative caudal analgesia and to identify which dose had maximum duration of caudal analgesia with minimal adverse effects in adult patients undergoing hemorrhoidectomy.

Patients and Methods

After approval of our local Ethical Committee and obtaining written informed consents from adult patients aged between 20 and 50 years old of both sexes of American Society of Anesthesiologists I and II, this study was conducted in a double-blind, randomized fashion. The patients were scheduled for an elective hemorrhoidectomy. Our exclusion criteria were patients having infection at the site of injection, bleeding disorders, preexisting neurological or spinal disease, abnormalities of the sacrum, and finally patients receiving medications likely to have interaction with opioids or cause sedation. All the patients were examined the day before the operation. All patients were premedicated with 1 mg midazolam intravenous (I.V.) 1 h before the operation. There was no intraoperative use of opioids or any other analgesic. All patients were continuously monitored with three lead electrocardiogram (ECG), noninvasive arterial blood pressure, pulse oximetry, and capnography. An I.V. cannula 18 or 20 gauge was inserted. Induction was started using 2-3 mg/kg propofol while the patient is in the left lateral position. Anesthesia was maintained at this position by an independent anesthetist using isoflurane 1.5-2 volume % via a face mask. Then, caudal space was identified, cleaned with antiseptic solution and draped. A 22 gauge needle was inserted into the epidural space. After negative aspiration for blood or cerebrospinal fluid, and confirmation of the caudal epidural space by modified swoosh test, either of the study preparations was injected into the caudal epidural space. They were randomly divided into three equal groups, 30 patients each. Group B included patients who were injected 20 ml of 0.25% plain bupivacaine in caudal epidural space. Group T_1 included patients who were injected 1 mg/kg tramadol in 20 ml normal saline. Group T_2 included patients who were injected 2 mg/kg tramadol in 20 ml normal saline. By the end of injection of the suggested preparation for each patient, the patient is turned immediately to supine position and a laryngeal mask is inserted. The patient is breathing spontaneously. The patients were monitored for perfusion index (PI) using Masimo Radical-7 SET (Masimo Corporation, Irvine, CA, USA). The pulse oximeter probe monitoring PI was placed on the big toe of either leg and was wrapped in a towel to minimize heat loss and to avoid light interference from operating room. A 100% rise of PI value from baseline is considered the onset of the success of caudal block. Positioning of the patient is done (lithotomy position), and surgery starts. By that time, the isoflurane concentration was reduced to 1-1.5 volume %. The effectiveness of the block was evaluated by respiratory rate (RR), hemodynamic stability, and decreased the requirement for inhalational anesthetic. Block was considered adequate when there was no increase of RR, heart rate (HR), and systolic blood pressure (SBP) by 15% after surgical incision compared to preoperative values. At the end of surgery, isoflurane was discontinued, and the laryngeal mask was removed. The patient was transferred to the postanesthesia care unit (PACU) after full recovery. The duration of the operation was recorded. In the recovery room, all patients were observed for 2 h with continuous monitoring of ECG and SaO_2. HR and blood pressure were recorded before induction of anesthesia (1), after anesthesia has been accomplished (2), after skin incision (3), at the end of the surgery (4), and after recovery before transfer to PACU (5). The postoperative pain was assessed using visual analog scale (VAS) hourly (0 = no pain (the patient is sleeping and lying comfortably), 10 = worst pain felt, 6 = moderate pain (the patient is asking for analgesia but still pain was bearable). If the VAS was 6, rescue dose of analgesic was given. The duration of analgesia was defined as the time interval between placement of the caudal block to the first demand for rescue analgesia. Sedation was assessed according to sedation score where 0 = alert, 1 = sleepy and arousable by verbal command, 2 = sleepy and arousable by tactile stimulation, and 3 = sleepy and arousable by painful stimulation. The degree of motor block was evaluated using the Bromage scale. Bradycardia, 20% decrease in HR compared to preoperative values, was to be treated with atropine 0.6 mg I.V. Hypotension, defined as a 20% decrease in mean arterial pressure compared to preoperative values, was to be treated with ephedrine 5 mg I.V. Follow-up of incidence of complications in the form of respiratory depression, nausea and vomiting, urine retention, pruritus or constipation has been done.

Hormonal stress response was assessed through recording preoperative (before the start of surgery) plasma cortisol (mg/dl) and epinephrine (Pico/ml) levels and recording postoperative (2 h postoperative) plasma cortisol and epinephrine levels. Epinephrine was measured using a noncompetitive enzyme-linked immunosorbent assay (Cat Combi ELISA) kit for the measurement of epinephrine. Serum cortisol was measured by a fluorescence polarization immunoassay technology by the Abbott Axsym system.

Results

Analysis of data

Using PASS 13 for sample size calculation, it was calculated that a sample size of 25 patients per group will achieve 80% power to detect difference in the meantime of analgesia between the three groups using an *F*-test with a 0.05 significance level. The size of the variation in the means is represented by their standard deviation (SD), which is 3.68. The common SD within a group is assumed to be 10.06, 30 patients per group were included to replace any drop-outs.

Data were analyzed using SPSS 18.0 for Windows (SPSS, Chicago, IL, USA). Analysis of variance was used to compare quantitative parametric data with Tukey's test as a *post hoc* test. Kruskal-Wallis test was used for quantitative nonparametric data. The chi-square test was used for comparison of qualitative data. Continuous parametric data were presented as mean ± SD, nonparametric data as median (interquartile range [IQR]), and categorical data were presented as number of patients. $P < 0.05$ were considered as statistically significant.

Ninety patients passed successfully through our study. There was no significant difference in the demographic data of the three groups as regard age, weight, gender (male to female ratio), and the duration of surgery in minutes [Table 1].

The onset of the caudal block in Group T_2 is significantly earlier compared to Group B and Group T_1 [Table 2].

There was a significant difference with respect to the mean duration of analgesia in hours between the three groups [Table 2]. Group T_2 showed the significantly longest mean duration of analgesia while the mean duration of analgesia was significantly longer in Group T_1 than that in Group B.

There was not a significant difference in the mean HR among the three groups. The three groups showed a significant

decrease of the mean HR2 after anesthesia has been accomplished. There was not any significant change in the mean HR after skin incision (HR3) until transfer to PACU for the three groups [Figure 1].

There was not a significant difference in the mean SBP among the three groups [Figure 2].

The three groups showed a significant decrease of the mean SBP2 after the accomplishment of anesthesia. There was not any significant change in the mean SBP after skin incision (SBP3) until transfer to PACU for the three groups.

The three groups showed a significant decrease of the mean RR2 after the accomplishment of anesthesia [Figure 3]. There was not any significant change in the mean RR after skin incision (R3) until transfer to PACU for the three groups.

The middle line in each box represents the median, the outer margins of the box represent the IQR and whiskers represent minimum and maximum [Figure 3].

Table 1: Demographic data and duration of surgery

	Group B	Group T₁	Group T₂	P
Age	30.2±5.7	27.7±4.9	28±5.2	0.4
Weight (kg)	67.4±7	65.4±6.5	63.8±7.2	0.139
Gender ratio (male:female)	13/17	14/16	12/18	0.796
Duration of surgery (min)	44.07±6.2	43.9±5.9	40.1±5.3	0.2

Data are presented as mean ± SD or ratio, P > 0.05 is considered statistically nonsignificant between the three groups. SD: Standard deviation

Table 2: Onset of block and duration of analgesia

	Group A	Group T₁	Group T₂	P
Onset of block in minutes	20.9±1.7	33.4±1.5	17.07±1.1	<0.001*
Duration of analgesia in hours	7±1.2	12.3±0.75	20±1.14	<0.001*

Data are presented as mean ± SD, *P < 0.001 is considered statistically significant between the three groups. SD: Standard deviation
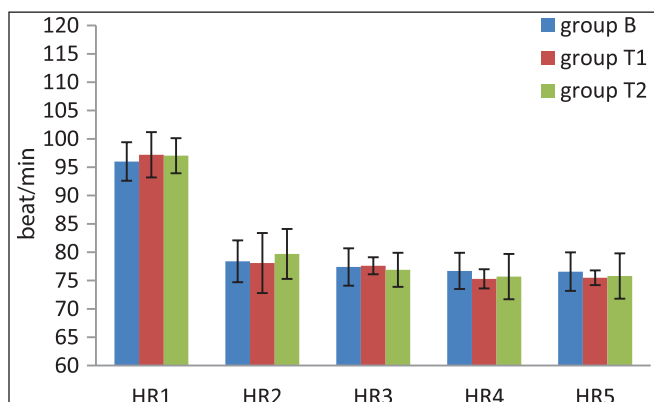

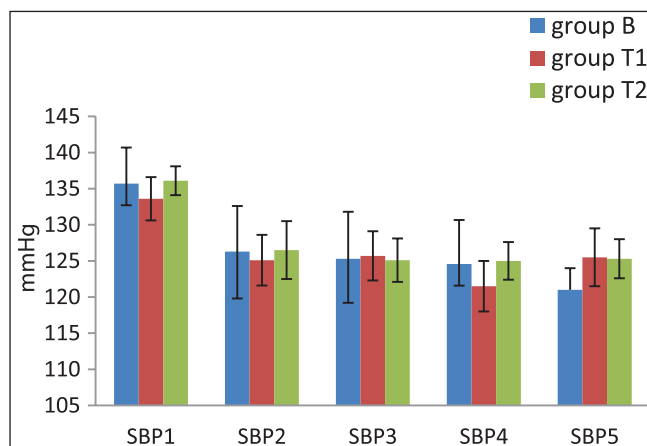**Figure 1: Heart rate changes during the study period in all groups**

Figure 2: Systolic blood pressure changes during the study period in all groups
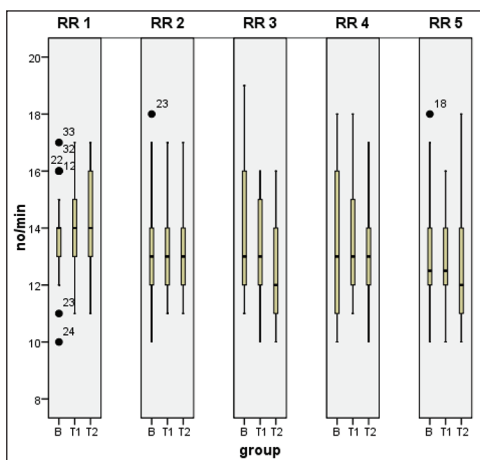
Figure 3: Respiratory rate changes during the study period in all groups

Table 3: cortisol and epinephrine level

	Group B	Group T$_1$	Group T$_2$	P
Preoperative mean cortisol (mg/dl)	23.5±8	23.6±9	23.6±6	0.172
Postoperative mean cortisol (mg/dl)	26.7±5	24.7±6	23.5±5‡	<0.001*
Preoperative mean epinephrine level (pg/ml)	52.4±63	50.5±8.6	52.4±4	0.149
Postoperative mean epinephrine level (pg/ml)	56±8	54.4±4	51.4±4‡	<0.001*

Data are presented as mean ± SD, *$P < 0.001$ is considered statistically significant between the three groups; ‡$P < 0.05$ is considered statistically significant between group 3 and groups 1 and 2, SD: Standard deviation

Table 3 shows a statistically nonsignificant rise of mean postoperative plasma cortisol and epinephrine levels compared to the mean preoperative values in the three groups. The rise of mean plasma cortisol and epinephrine levels is statistically less significant in Group T$_2$ compared to that of Group B and Group T$_1$. There was no statistically significant difference between Group B and Group T$_1$ as regard the mean postoperative plasma cortisol and epinephrine levels.

With respect to sedation assessment, all of the three groups were alert, that is, sedation score = 0. None of the patients developed any episode of hypotension or bradycardia throughout the study. None of our patients had a motor block on emergence from anesthesia. There was not any incidence of respiratory depression, urine retention, nausea, vomiting or pruritus for any patient of the three groups.

Discussion

Hemorrhoidectomy is associated with postoperative severe, unpleasant pain. The golden goal for the anesthetist is to support his patient with a simple and inexpensive method of pain relief.

The result of the current study showed that the mean duration of the postoperative analgesia was 7 ± 1.2, 12.3 ± 0.75, 20 ± 1.14 h for Groups B, T$_1$, T$_2$, respectively. This means that caudal tramadol 2 mg/kg showed the longest duration of postoperative analgesia. Group T$_2$ showed the least hormonal stress response indicating the best quality of analgesia. There was no significant difference in the quality of analgesia between Group B and Group T$_1$.

Activation of the hypothalamo-pituitary-adrenal axis and rise of cortisol and epinephrine plasma levels associated with surgical trauma are very important perioperative stress responses. In our study, cortisol and epinephrine showed insignificant rise 2 h postoperatively compared with the preoperative values of the three groups. However, still their values are significantly higher in Group B and Group T$_1$ than Group T$_2$. This means that the endocrine stress response has been successfully modified in the three groups, but more modified in Group T$_2$.

Gunduz et al.[7] found that caudally administered tramadol is as effective as bupivacaine and administration of tramadol to bupivacaine did not prolong the duration of bupivacaine.

Prosser et al.[8] found no statistically significant difference in duration of analgesia of both bupivacaine (2 mg/kg) and tramadol (2 mg/kg).

Prakash et al.[9] found a dose-related increase in the postoperative analgesia of caudally co-administered tramadol with bupivacaine. The previous studies are partially consistent with our study.

The study of Buhtta and Tarik[10] demonstrated results inconsistent to ours. They stated that bupivacaine provided a longer duration of analgesia (10.5 ± 2.02 h) compared to tramadol (7.14 ± 1.77 h). They achieved a good quality of analgesia without respiratory depression in tramadol group (100 mg, 20 ml).

Ozkan et al.[11] found caudal tramadol has more analgesic efficacy than bupivacaine.

Batra et al.[12] worked on the analgesic duration of bupivacaine and tramadol. They stated a significantly lower pain score with caudal bupivacaine in the immediate postoperative period (rapid onset) where caudal tramadol showed significantly lower pain score in the late postoperative period, and longer duration of action compared to caudal bupivacaine.

Grond and Sablotzki[13] stated that in equipotent analgesic doses tramadol to morphine is free of respiratory depression.

Conclusion

Our study concluded that both caudally administered bupivacaine and tramadol provide efficient and safe postoperative analgesia. However, caudal tramadol (2 mg/kg, 20 ml) gives postoperative efficient analgesia with longer duration and free from any incidence of respiratory depression, nausea, vomiting and urine retention.

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Conflicts of interest
There are no conflicts of interest.

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