Original Article

Ketamine versus magnesium sulfate with caudal bupivacaine block in pediatric inguinoscrotal surgery: A prospective randomized observer-blinded study

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Abstract

Introduction: Possible approaches for postoperative analgesia after pediatric inguinoscrotal surgery are caudal block by bupivacaine/ketamine (BK) and bupivacaine/magnesium sulfate (BM).

Aim: The purpose of the following study is to compare the analgesic efficacy and safety of ketamine and magnesium sulfate in combination with bupivacaine for caudal blockade in pediatric patients after inguinoscrotal operations.

Materials and Methods: Patients randomly received one of the two solutions for caudal epidural injection after induction of general anesthesia. Group-BK: Were given a mixture of 0.25% bupivacaine and 0.5 mg/kg of ketamine. Group-BM: Were given a mixture of 0.25% bupivacaine and 50 mg magnesium sulfate. Postoperatively, a blinded post-anesthesia care unit nurse assessed the quality of analgesia with a visual pain analog scale (VPAS). Significant pain is defined as one that has a VAPS of ≥3.

Results: Forty American Society of Anesthesiologists I-II children (20 in each group) completed the study. The two groups were comparable regards age, sex, body mass index, anesthesia and surgery durations, recovery time and sevoflurane concentration. The mean duration of caudal analgesia ± standard deviation was 462 ± 17.2 min versus 398.05 ± 12.9 min for BK and BM groups, receptively ($P < 0.001$). Supplemental rectal paracetamol within 12 h postoperatively were 15% for BK group versus 25% for BM ($P = 0.05$). Four patients in BK group only experienced postoperative nausea and vomiting ($P = 0.053$).

Conclusion: Caudal administration of BK is efficient and safe for pediatric inguinoscrotal operations with longer postoperative analgesia than BM sulfate.

Key Words: Ingunoscrotal surgery, ketamine, magnesium sulphate, pediatric caudal block

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INTRODUCTION

Regional anesthetic techniques have considered being popular for pediatric patients. Lowering general anesthetic requirements intraoperatively and providing adequate postoperative pain relief are stated as major two benefits of regional supplementation.[1] Of the regional blocks, caudal epidural analgesia is one of the most commonly performed in the pediatric population. It is a reliable and safe technique that can be used in patients undergoing abdominal and lower-limb surgery.[2] Many anesthetic agents have been used for caudal analgesia in pediatric patients, with lignocaine and bupivacaine being most common.[1] Bupivacaine has been in clinical use for more than 25 years and is widely used for pediatric caudal epidural analgesia because of its long duration of action and preferential sensory than motor blocks.[3] The relative short duration of action after a single

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injection of local anesthetic solution is the main disadvantage of caudal anesthesia. Prolongation of caudal analgesia using a "single-shot" technique has also been achieved by the addition of various adjuvants.[4] Ketamine is an anesthetic and analgesic agent with a wide range of applications in pediatric anesthesia.[5] It exerts its effects by binding non-competitively to a subset of glutamate receptors stimulated by the excitatory amine N-methyl D-aspartate (NMDA), blockade of which leads to a decrease in the activation of dorsal horn neurons. These receptors are located throughout the central nervous system as well as in the substantia gelatinosa in the spinal cord and play an important role in central pain processing and in neural plasticity in the spinal cord.[6] Magnesium is an antagonist of NMDA receptor ion channel and this may explain part of its analgesic activity and it has been called physiological calcium channel blocker.[7]

The aim of this study was to compare the analgesic efficacy and side effects of ketamine and magnesium sulfate in combination with bupivacaine for caudal blockade in pediatric patients after inguinoscrotal operations.

MATERIALS AND METHODS

Patient's criteria

Unpremedicated children aged 3-10 years of American Society of Anesthesiologists (I and II); undergoing inguinoscrotal surgery in our hospital, between January 2011 and January 2012, were included in this study. Those with allergic history to bupivacaine/ketamine (BK) and children with any absolute or relative contraindication for central neuro-axial block were excluded from the study. Sample size calculation was carried out using Epi-info TM, version 3.5 (CDC, 2008; Atlanta, GA, USA). A calculated sample of 40 was needed to detect an effect size of 0.3 between the two groups (20 from the BK group and 20 from the bupivacaine/magnesium [BM] group), with a $P < 0.05$ and 80% power.

After receiving informed consent from parents, the children were allocated to receive one of the two solutions for caudal epidural injection after induction of general anesthesia. The patients were quasi-randomized into two treatment groups according to the order of presentation; those who were odd cases received BK and even cases received BM. Group-BK; were given a mixture of 0.25% bupivacaine and 0.5 mg/kg of preservative free ketamine at a volume of 0.5 mL/kg. Group-BM; were given a mixture of 0.25% bupivacaine and 50 mg magnesium sulfate at a volume of 0.5 mL/kg. Anesthesia was induced either with Propofol 2 mg/kg via a 20 or 22-gauge intravenous (i.v.) cannula, or with inhalation of nitrous oxide, oxygen and sevoflurane. Anesthesia was maintained using nitrous oxide 50%, oxygen 50% and sevoflurane delivered to the trachea through Laryngeal Mask Airway via Modified Ayre's T-piece with spontaneous breathing. Intraoperative sevoflurane concentration was adjusted and other maintenance doses of Propofol were injected on needed.

Caudal analgesia technique

Patients were placed in left lateral position after induction of general anesthesia. The back of the patient including the sacral hiatus was carefully sterilized with an antiseptic solution; sterile drapes were placed around the injection site. The technique was done by introducing a 23-gauge hypodermic needle perpendicular to the sacrococcygeal membrane with the bevel in the direction of the long fibers of the membrane. The needle was inserted until there is release of impedance as it pierced the sacrococcygeal membrane. Then, it was directed upwards so that it made an angle of 20-30° with the skin about 2 mm so that the whole bevel will be inside the sacral canal. The injection was made over a period of about 60 s and then a small elastoplast dressing was placed over the injection site and the child was placed supine. Intraoperative analgesic supplement was not given.

Standard monitoring was used during anesthesia and surgery (non-invasive blood pressure, heart rate [HR], arterial oxygen saturation and end-tidal carbon dioxide). The volatile agent concentration will be reduced toward the end of surgery in order to shorten the recovery time. All patients were admitted for at least 1 h to the recovery room and were returned to the ward when they were fully awake and pain free.

Measurements

hemodynamic and respiratory data including; HR, mean arterial blood pressure (MABP), respiratory rate (RR) and arterial oxygen saturation (SaO_2) were recorded preoperative, intraoperative (before and after caudal block), these variables were recorded every 5 min until the end of surgery and postoperative (time frame: 12 h). Postoperatively, a blinded post-anesthesia care unit nurse assessed the quality of analgesia with a VAPS graded from 0 to 10 (0 = No pain, 10 = The worst possible pain) at rest and on movement. Sedation was assessed using a four-point sedation score (0 = Eyes open spontaneously; 1 = Eyes open to speech; 2 = Eyes open when shaken; 3 = Unrousable). Assessment was made at 15-min intervals for the first 1 h, 30-min intervals for the next 1 h and then every hour till the end of 12-h postoperative. Significant pain is defined as one that has a VAPS of 3 or more and necessitates a dose of analgesia. A pain score (3-6/10) was the indication for analgesic that was provided by rectal paracetamol 15 mg/kg, while a pain score (>6/10) was the indication for additional analgesics that was provided by i.v. Pethidine (1 mg/kg). The time from induction of anesthesia till the anesthetic agent was discontinued when surgery is finished (Anesthesia duration) and the time from discontinuation of anesthesia to eyes' opening on tactile stimulus (Recovery time) were recorded. The duration of caudal

analgesia was defined from the time of caudal injection until the time of first postoperative analgesic requirement. The incidence of adverse effects such as nausea, vomiting, urinary retention and any side effects related to injection of ketamine, magnesium sulfate, or bupivacaine were recorded.

Data analysis

All statistical analyses were carried out using SPSS statistical package (SPSS 16 for Windows [SPSS, Inc., Chicago, IL]). Analysis of Variance with multiple comparisons was used for comparisons between groups. Paired *t*-test was applied to compare between the basal (preoperative) reading and the subsequent readings (intraoperative and postoperative) inside the same group. The results were expressed as mean ± standard deviation (SD) and $P < 0.05$ was regarded as statistically significant.

RESULTS

The demographic data in the two groups were comparable in age, weight, height and sex. Most of the patients had congenital inguinal hernias (BK: 70%, BM: 90%), while the remaining had inguninal undescended testes (BK: 20%, BM: 10%) and glandular hypospadias (BK: 10, BM: 0%). None of our patients had a urethral catheter insertion at the end of the operation. There were no significant differences between the two groups as regard to anesthesia and surgery duration, recovery time and sevoflurane concentration [Table 1].

There was a significant decrease among groups for HR in the study period (intraoperative and postoperative), compared with the mean baseline value measured before induction of anesthesia. The MABP and RR showed a significant decrease in its mean value in both groups only intraoperative, whereas postoperative values were insignificant in both groups when compared with the mean baseline value. None of the children suffered from hypotension or bradycardia and SaO_2 was within the clinically accepted value through the study period. Basal, intraoperative and postoperative readings for these four vital signs were comparable for both groups ($P > 0.05$) [Table 2].

Table 1: Demographic and operative data (mean±SD)

Variable	Group (*n*=20)	
	BK	BM
Age (year)	6.7±2.3	6.4±2.1
Weight (kg)	26.5±5.6	24.3±8.4
Height (cm)	112.5±12.2	108.8±14.2
Sex		
Male/female	19/1	20/0
Surgery duration (min)	40.85±8.84	41.25±8.39
Anesthesia duration (min)	53.45±9.90	54.95±8.66
Recovery time (min)	13.6±4.2	14.7±5.1
Sevoflurane concentration (%)	1.03±0.17	1.22±0.24

BK: Bupivacaine/ketamine, BM: Bupivacaine/magnesium, SD: Standard deviation

According to the quality of postoperative analgesia; patients in Group BK had significant decreased visual analog score (VAS) [Figure 1 and Table 3], at 8 h (mean ± SD was 3.0 ± 0.9/10, $P = 0.001$) and at 12 h (mean ± SD was 4.9 ± 0.9/10, $P = 0.04$) postoperatively when compared to Group BM. The four-point sedation score was statistically insignificant when we compared between the two groups. As it has shown in Figure 2, the duration of caudal analgesia was significantly prolonged in Group BK (462 ± 17.2 min) compared with Group BM (398.05 ± 12.9 min) and $P < 0.001$. Supplemental analgesia requirements with rectal paracetamol within 12 h postoperatively were 15% for BK group versus 25% for MB ($P = 0.05$). No subject in both groups was required supplemental i.v. pethedine.

The incidence of postoperative side effects was compared between the groups. Four patients (20%) in the BK group and no patient (0%) in the BM group experienced postoperative nausea and vomiting ($P = 0.053$). No patient in either group was suffered from postoperative urinary retention. There were no instances of residual paralysis or toxic reactions to BK, BM sulfate during or after administration of the caudal block.

DISCUSSION

We designed this study to compare whether the addition of ketamine or magnesium sulfate to bupivacaine, when administered caudally, would prolong the duration of postoperative analgesia in children undergoing inguinal

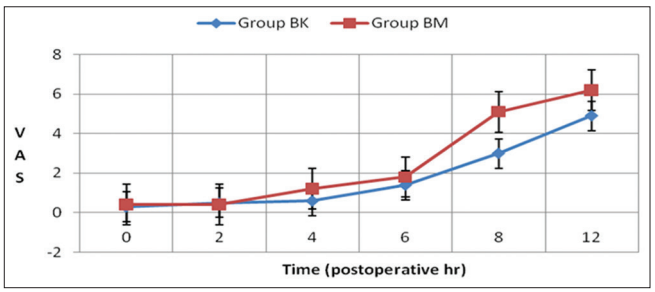

Figure 1: Postoperative visual pain analogue scale (VPAS)

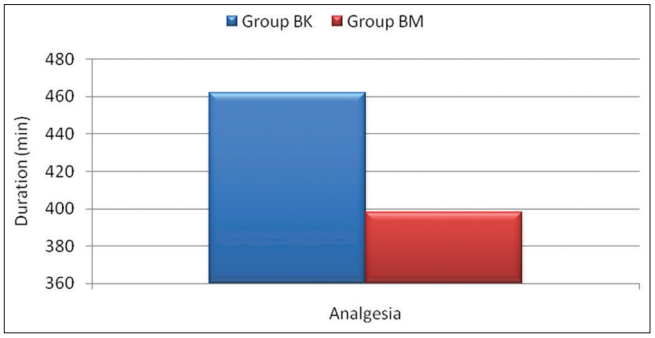

Figure 2: Postoperative caudal analgesia

Table 2: Hemodynamic and respiratory data (mean±SD)

Variable	Group BK (*P* value)			Group BM (*P* value)		
	Pre-operative	Intra-operative	Post-operative	Pre-operative	Intra-operative	Post-operative
HR/min	102.2±7.6	88.0±4.8* (0.00)	94.2±5.0* (0.04)	101.8±10.1	86.0±7.4* (0.002)	92.3±7.8* (0.002)
MABP (mmHg)	76.4±4.2	68.9±4.9* (0.007)	72.6±4.5 (0.11)	74.9±5.4	67.2±6.7* (0.00)	73.8±5.2 (0.27)
RR/min	23.2±4.1	18.0±1.8* (0.003)	22.4±3.2 (0.44)	25.2±4.6	20.2±3.9* (0.001)	23.0±2.8 (0.17)
SaO_2 (%)	98.0±0.6	98.7±0.4 (0.32)	98.1±0.9 (0.64)	97.7±0.8	98.5±0.7 (0.16)	97.9±0.9 (0.62)

BK: Bupivacaine/ketamine, BM: Bupivacaine/magnesium, SD: Standard deviation, HR: Heart rate, MABP: Mean arterial pressure, RR: Respiratory rate, SaO_2: Arterial oxygen saturation. *Significant compared to baseline in the same group ($P<0.05$)

Table 3: Post-operative pain score (VAPS) and 4-points sedation score (mean±SD [range])

Time	Variable					
	VAPS			4-points sedation score		
	Group BK	Group BM	*P* value	Group BK	Group BM	*P* value
30 min	0.3±0.48 (0-1)	0.4±0.51 (0-1)	0.67	1.7±0.9 (1-3)	1.4±0.6 (1-3)	0.46
2 h	0.5±0.52 (0-1)	0.4±0.69 (0-2)	0.11	0.30±0.48 (0-1)	0.20±0.42 (0-1)	0.59
4 h	0.6±0.69 (0-2)	1.20±1.22 (0-3)	0.16	0.2±0.42 (0-1)	0.1±0.31 (0-1)	0.59
6 h	1.4±1.07 (0-3)	1.8±1.5 (0-4)	0.26	0.0±0.0 (0-0)	0.0±0.0 (0-0)	-
8 h	3.0±0.9 (2-4)	5.1±1.1 (4-6)	0.001*	0.0±0.0 (0-0)	0.0±0.0 (0-0)	-
12 h	4.9±0.9 (4-6)	6.2±1.3 (4-8)	0.04*	0.0±0.0 (0-0)	0.0±0.0 (0-0)	-

VPAS: Visual pain analogue scale, BK: Bupivacaine/ketamine, BM: Bupivacaine/magnesium, SD: Standard deviation. *Significant regarding comparison between two groups ($P<0.05$)

orchidopexy, distal hypospadias surgery or inguinal herniorrhaphy. Our results revealed that caudal administration of 0.5 mg/kg ketamine with bupivacaine (0.25%) in a total volume 0.5 mg/kg significantly prolonged the mean duration of postoperative analgesia by about 8 h compared with caudal injection of a mixture of 0.25% bupivacaine and 50 mg of magnesium sulfate at a volume of 0.5 mL/kg (up to 6.5 h). Caudal administration of bupivacaine alone at a dose of 2-2.5 mg/kg can provide adequate analgesia in the early postoperative period only for the duration of the local anesthetic; 2-4 h.[8,9] Hence, early postoperative adjuvant systemic analgesia is usually required.

The efficacy of caudal epidural ketamine in children has been demonstrated in a number of studies.[10] In a double-blind study, Naguib *et al.* compared the analgesic effects of bupivacaine 0.25% (1 mL/kg) with and without ketamine 0.5 mg/kg in children undergoing inguinal herniotomy; although there was no significant difference in the quality of analgesia between the groups, only 7% of patients who received the BK combination required further analgesia in the first 24 h after surgery.[11] Such finding was comparable with our study, in which 15% of children received caudal BK required supplemental analgesia by rectal paracetamol in the first 12 h postoperative. Although different doses of ketamine have been used in combination with local anesthetics, the optimal dose is probably 0.5 mg/kg.[12] In determining this dose, Semple *et al.*, found that after orchidopexy, bupivacaine 0.25% (1 mL/kg) combined with ketamine 0.25 mg/kg, 0.50 mg/kg or 1.0 mg/kg produced a median duration of analgesia of 7.9 h, 11 h and 16.5 h, respectively.[13] Another study done by Weber and Wulf and they concluded that addition of preservative free s- ketamine 0.5 mg/kg to caudal bupivacaine 0.125% 1 mL/kg provides significant prolongation of analgesia without producing negative side effects.[14] Another potential benefit of central ketamine is that it may counteract local anesthetic-induced hypotension by an inhibitory effect on the sympathetic nerve activity and tends to increase the RR.[15] In our study, the observed relative stability of perioperative hemodynamics with the use of caudal bupivacaine plus ketamine supports this concept.

Intrathecal administration of magnesium has been reported as adjunct to both anesthesia and postoperative analgesia. The possible analgesic effect of magnesium sulfate occurred at the central level and might be due to its absorption to the systemic circulation.[16] Perioperative efficacy of adjuvant addition of magnesium (10 mL of 5% magnesium sulfate) to epidural bupivacaine (10 mL of 0.25% plain bupivacaine) and fentanyl (100 μg) was demonstrated in women undergoing elective caesarean section.[17] Ghatak *et al.* evaluate the effect of 50 mg magnesium sulfate versus 150 mg clonidine as adjunct to 19 mL of epidural bupivacaine on 90 patients undergoing lower abdominal and lower limb surgeries; the onset of anesthesia in the magnesium group was faster. No statistically significant differences for both groups regard perioperative hemodynamics and postoperative side effects. Onset of anesthesia was more rapid with magnesium sulfate group.[18]

Our study revealed that, there was no significant difference between the two groups regards postoperative sedation score. Similar results were demonstrated with Siddiqui and Chowdhury for both bupivacaine and ketamine either alone or in combination, the sedation score did not differ significantly within the first 2 h of recovery.[8]

In this study, we investigated the incidence of side effects and found only four patients (20%), in BK group suffering from nausea and vomiting, 0% in group BM, and no additional problems with urinary retention or residual paralysis postsurgical were seen in both groups. Kumar *et al.* showed that the incidence of vomiting was not significantly different among bupivacaine versus BK groups; two patients in each group had postoperative vomiting.[19] A transient motor block was developed in one report with inadvertent intrathecal injection of very high dose (1 g) of magnesium sulfate.[20]

CONCLUSION

This study demonstrated that caudal administration of BK (0.5 mg/kg), with 0.5 mL/kg volume provided adequate postoperative analgesia of similar quality and longer duration than caudal injection of bupivacaine with magnesium sulfate (50 mg) in pediatric patients after inguinoscrotal operations without producing many side effects.

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