Caudal Analgesia In Paediatrics: A Comparison Between Bupivacaine And Ketamine

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Citation

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Abstract

Sixty children undergoing subumbillical operations were randomly allocated to three groups to receive a caudal injection of either 0.25% bupivacaine 1 $ml.kg^{-1}$ with or without ketamine 0.5 $mg.kg^{-1}$ or ketamine 1 $mg.kg^{-1}$ with normal saline 1 $ml.kg^{-1}$. Pain scores (TPPPS), sedation scores, analgesic requirements and associated side effects were recorded for the first 24 hours after operation. The bupivacaine-ketamine mixture and the ketamine alone provided significantly better quality of pain relief. The bupivacaine group received more doses of analgesic supplements with paracetamol than bupivacaine-ketamine or ketamine only groups in order to remain pain-free in the first 24 hours after recovery from anaesthesia ($P<0.001$). Mean duration of time intervals between the recovery from anaesthesia and the first dose of analgesia given for bupivacaine-ketamine and ketamine only groups are comparable (12.04 & 12.70 h respectively) whereas recovery-analgesia time was significantly shorter (3.26 h) in the bupivacaine group ($P<0.001$). Side effects such as motor weakness and urinary retention were not observed in the ketamine group. However, nystagmus occurred in four patients (20%) of the ketamine group and in one patient (5%) of the bupivacaine-ketamine group.

INTRODUCTION

Regional anesthetic techniques have gained considerable popularity for use with pediatric patients. The primary advantage of regional supplementation are lowering general anesthetic requirements intraoperatively and providing good postoperative pain relief[1].

Caudal anesthesia is the most frequently used regional technique in children, accounting for almost 50% of all regional techniques[2]. Many anesthetic agents have been used for caudal analgesia in pediatric patients, with lignocaine and bupivacaine being most common[1]. But a single caudal injection provides analgesia only for the duration of action of the local anesthetic. Most of the children undergoing subumbillical operations require further analgesia during the post operative period which influenced many authors to search for means to prolong the duration of caudal analgesia. The addition of opioids to the local anesthetic mixture is known to prolong the duration of caudal analgesia but the possibility of respiratory depression along with itching, vomiting, and postoperative retention of urine has limited the use of such mixtures.

Ketamine binds to a subset of glutamate receptors stimulated by the agonist N-methyl D-aspartate (NMDA) and thus exerts its analgesic action[3]. These receptors are found throughout the central nervous system, including the lumbar spinal cord. Ketamine has a potent analgesic action when used in subdissociative doses[3]. Moreover, it does not cause respiratory depression[4] and therefore seems to be a suitable drug for pain relief.

The caudal administration of 1 $ml.kg^{-1}$ of a solution of 0.5 $mg.kg^{-1}$ of ketamine, diluted in normal saline, has been studied[5]. The secondary effects reported by the authors were less than those following administration of 1 $ml.kg^{-1}$ of 0.25% bupivacaine were, while the analgesic effect was comparable. On the other hand, a combination of ketamine and bupivacaine increases the potency of analgesia. In the above-mentioned study performed by Naguib et al, the same dose of ketamine was used in combination with bupivacaine and when ketamine was used alone. No patient in the caudal ketamine group had urinary retention or any sign of motor weakness in contrast to the other two groups (bupivacaine with or without ketamine).

We assume that increasing the dose of ketamine when used as a sole agent will increase the potency of analgesia while providing the advantages mentioned in the study. This double-blind study is designed to compare the analgesic

effectiveness of caudal administration of ketamine (1 $mg.kg^{-1}$ with 1 $ml.kg^{-1}$ of normal saline), bupivacaine (1 $ml.kg^{-1}$ of 0.25%) or a mixture of both drugs (0.5 $mg.kg^{-1}$ of ketamine with 1 $ml.kg^{-1}$ of 0.25% bupivacaine) in the treatment of pain after subumbillical operations in children.

MATERIALS AND METHODS

Our institutional review board approved the enrolled patients. 60 children aged 2–6 years of ASA (American Society of Anesthesiologists classification) physical status 1 and 2, randomly collected during January to December 2001, undergoing subumbillical operations (inguinal herniotomy, herniorrhaphy, orchidopexy and hypospadias repair) in Chittagong Medical College Hospital were randomly allocated to receive one of the three solutions for caudal epidural injection. Children with history of allergic reaction to bupivacaine or ketamine and those with any contra-indication for central neuroaxial blockade (either absolute or relative) were excluded from the study.

After taking informed consent from their parents or guardian, the children were given one of the three solutions caudally after induction of anesthesia. The children were divided into three groups using a random number table. Group B were given 1 $ml.kg^{-1}$ of 0.25% bupivacaine, Group BK were given a mixture of 0.25% bupivacaine and 0.5 $mg.kg^{-1}$ of ketamine at a volume of 1 $ml.kg^{-1}$ while Group K were given 1 $mg.kg^{-1}$ of ketamine only with 1 $ml.kg^{-1}$ of normal saline. Preservative free ketamine were used which was confirmed not to be neurotoxic after repeated intrathecal administration in the rabbit[6].

No premedication was given and all operations were performed under general anaesthesia. Anaesthesia was induced either with thiopentone 5 $mg.kg^{-1}$ via a 21 or 23-gauge i/v cannula, or with inhalation of nitrous oxide, oxygen and halothane. Tracheal intubations were facilitated using atracurium 0.5 $mg.kg^{-1}$. Anaesthesia were maintained using nitrous oxide 67%, oxygen 33% and halothane delivered via a Bain coaxial system or modified Ayre's T-piece with controlled ventilation.

After induction of general anesthesia, patients were given caudal injections in left lateral position by the same investigator using a 23-gauge needle. The area was carefully and thoroughly cleaned with an antiseptic solution, especially because the site of puncture is so close to the anus – particularly in children lacking sphincter control. Sterile drapes were placed around the site. Due to unavailability of the appropriate needle recommended by Dalens[2], a 23-gauge hypodermic needle is used. The technique was performed in the simplest way to penetrate the sacrococcygeal membrane by introducing the needle perpendicular to it with the bevel parallel to the long fibers of the membrane. The needle was advanced until there was loss of resistance as it pierced the sacrococcygeal membrane. Once the needle crossed the membrane, it was directed upwards so that it made an angle of 20–30 degrees with the skin. The needle was then advanced for 2 to 3 mm so as to ensure that the entire bevel was within the sacral canal. The entire volume of injection was made over a period of 60 to 90 seconds and after completion of the injection the child was placed supine after placing a small Elastoplast dressing over the site of the sacral hiatus.

Intraoperative analgesic supplement was not given. Standard monitoring was used during anesthesia and surgery. The concentration of volatile agent was reduced towards the end of surgery in order to achieve rapid awakening before return to the recovery ward. Residual neuromuscular block was antagonized with neostigmine 50 $g.kg^{-1}$, given together with atropine 20 $g.kg^{-1}$, and the patient's trachea was extubated. All patients were admitted to the recovery ward for al least 2 hours and, when fully awake and pain free, were returned to the children's ward. Heart rate and arterial pressure were recorded before operation. After caudal block, these two variables were recorded every 5 min till the end of surgery. The time from induction of anesthesia to the end of surgery when the anesthetic agent was discontinued was recorded, and the time from end of surgery to opening the eyes on calling the patient's name or on tactile stimulus was noted. The duration of caudal analgesia is defined from the time of caudal injection to the time the child first complains of pain or time of first postoperative analgesic requirement.

During the first 24 h after operation, the following variables were recorded: heart rate, arterial pressure, ventilatory frequency, a four-point sedation score (0 = eyes open spontaneously; 1 = eyes open to speech; 2 = eyes open when shaken; 3 = unrousable) and a modified TPPPS pain score[7]. Assessment was made at 15-min intervals for the first 1 h, 30-min intervals for the next 1 h and 3, 4, 6 and 24 h after recovery from anesthesia. A TPPPS pain score modified to give a maximum score of 10 was used to assess pain over a 5-min period. A pain score >3/10 was the indication for additional analgesics that was provided by either i.m. pethidine 1 $mg.kg^{-1}$ or oral paracetamol 20 $mg.kg^{-1}$, as it was deemed appropriate. Episodes of nausea, vomiting, sleep

disturbance and incidence of behavioral side effects and abnormal effect, if they occurred, were noted.

DATA PROCESSING

All statistical analyses were carried out using SPSS statistical package (SPSS 10.0 for Windows Student Version). ANOVA with multiple comparisons was used for comparisons between the groups. Using Chi squared (^{2}) test compared the non-parametric data. P<0.05 was regarded as statistically significant.

RESULTS

The three groups were comparable in age, weight and duration of their surgeries (table I). While comparing the quality of postoperative analgesia between the groups it revealed that caudal administration of ketamine only and bupivacaine with the addition of ketamine resulted in superior analgesia compared with caudal injection of bupivacaine alone. A significant number of patients in the bupivacaine group had 'significant pain' at 2 hours after recovery from anesthesia. Significant pain is defined as one that has a TPPPS score of 3 or above and as a consequence required a supplementary dose of analgesia. Furthermore, the bupivacaine group received significantly (P<0.001) more doses of analgesic supplements with paracetamol than bupivacaine-ketamine or ketamine only groups in order to remain pain-free in the first 24 hours after recovery from anaesthesia (table II). There was no significant difference between the caudal ketamine group compared with the bupivacaine-ketamine group in the number of analgesic doses required in the first 24 hours.

Figure 1

Table 1: Patient data and duration of surgery [mean (std. deviation)]. *P

	Bupivacaine Group (n=20)	Bupivacaine-ketamine Group (n=20)	Ketamine Group (n=20)
Age (Years)	4.025 (1.208)	3.725 (1.352)	4.000 (1.755)
Weight (kg)	12.675 (2.520)	11.450 (2.559)	13.200 (3.298)
Duration of Surgery (min)	48.10 (17.75)	50.85 (18.13)	52.45 (20.95)

Figure 2

Table 2: Frequency of analgesia given during the first 24 hours after operation. Number (%) of patients receiving 1-5 doses of oral paracetamol syrup 20 mg.kg body weight. ***P

Analgesia (No. of Doses)	Patients receiving analgesia		
	Bupivacaine group (n =20)	Bupivacaine- Ketamine group (n =20)	Ketamine group (n =20)
1	0	1 (5)	1 (5)
2	0	14 (70)	18 (90)
3	9 (45)	4 (20)	0
4	10 (50)	1 (5)	1 (5)
5	1 (5)	0	0

The time interval between the recovery from anaesthesia and the first dose of analgesia given is displayed as mean and standard deviation for the three groups in table III. Mean duration of time intervals for bupivacaine-ketamine and ketamine only groups are comparable (12.04 & 12.70 h respectively) whereas recovery-analgesia time was significantly (P<0.001) shorter (3.26 h) in the bupivacaine group.

Figure 3

Table 3: Time interval between the recovery and first dose of analgesia given. ***P

Patient group	Mean duration (hours)	Standard deviation
Bupivacaine (n =20)	3.26	2.05
Bupivacaine- Ketamine (n =20)	12.04	3.31
Ketamine (n =20)	12.70	3.54

The sedation score did not differ significantly between the bupivacaine, the bupivacaine-ketamine and the ketamine groups during the first 2 hours of recovery. More patients who had received caudal bupivacaine were more wakeful with less sedation score as compared with the other 2 groups but the difference was not statistically significant (P>0.05).

Incidences of side effects were compared between the groups (table IV). Motor weakness after 6 hours from recovery occurred in two (10%) and one (5%) patients in the caudal bupivacaine and bupivacaine-ketamine groups, respectively. Postoperative urinary retention was noted in three patients in the bupivacaine (15%) and two patients in the bupivacaine-ketamine (10%) groups. However, no patient in the caudal ketamine group had urinary retention or any sign of motor weakness. Six patients (30%) in the caudal bupivacaine group, four patients (20%) in the caudal bupivacaine-ketamine group and two patients (10%) in the caudal ketamine group experienced postoperative vomiting.

Figure 4

Table 4: Incidence of side effects in the three groups during the first 24 hours after recovery from anesthesia.

Incidence of side effects n (%)	Patient Group		
	Bupivacaine	Bupivacaine-Ketamine	Ketamine
Motor weakness after 6 hrs of recovery	2 (10)	1 (5)	0 (00)
Urinary retention	3 (15)	2 (10)	0 (00)
Vomiting	6 (30)	4 (20)	2 (10)
Nystagmus	0 (00)	1 (5)	4 (20)

Nystagmus occurred in four patients (20%) of the ketamine group and in one patient (5%) of the bupivacaine-ketamine group. In contrast, no patient from the caudal bupivacaine group had abnormal eye movement in the first 24 hours after operation.

There were no instances of hypotension, bradycardia, residual paralysis or toxic reactions to bupivacaine or ketamine during or after administration of the caudal blocks.

DISCUSSION

The modulatory influences of extradural ketamine on postoperative pain mechanisms were confirmed by several previous studies[5,8,9]. There are obvious advantages, especially in children, in prolonging the duration of postoperative analgesia with the use of caudal ketamine and thus reducing the frequency of analgesic supplementation. In this study, caudal administration of ketamine 1 $mg.kg^{-1}$ produced postoperative analgesia comparable to that associated with caudal injection of 0.25% bupivacaine 1 $ml.kg^{-1}$ with ketamine 0.5 $mg.kg^{-1}$ whereas superior in quality to the analgesia produced by 1 $ml.kg^{-1}$ of caudal bupivacaine 0.25%.

Caudal administration of bupivacaine alone can provide adequate analgesia in the early postoperative period, but a single caudal injection provides analgesia only for the duration of action of the local anaesthetic. Bupivacaine 2-2.5 $mg.kg^{-1}$ has duration of action of only 2-4 hours[10]. As a result, systemic analgesia is usually required as the block wears off. In the present study, no patient in any of the groups was found not requiring additional analgesic. But the mean of the number of doses of oral paracetamol in bupivacaine group (3.6) was significantly higher than that of bupivacaine-ketamine group (2.25) or that of ketamine only group (2.05).

A combination of ketamine and bupivacaine increases the potency and duration of caudal analgesia. The addition of ketamine 0.5 $mg.kg^{-1}$ to bupivacaine, in our study, improved significantly both quality and duration of analgesia (mean duration of 12.04 hours) compared with administration of bupivacaine solution alone (mean duration of 3.26 hours). This finding is similar to the previous report[10], in which the median duration of caudal analgesia was 12.5 hours when bupivacaine and ketamine were used. In addition, we found that ketamine alone in a dose of 1 $mg.kg^{-1}$ diluted in 1 $ml.kg^{-1}$ of normal saline can provide the quality and duration of caudal analgesia (mean duration of 12.70 hours) as well as bupivacaine and ketamine mixture. The caudal administration of 1 $ml.kg^{-1}$ of a solution of 0.5 $mg.kg^{-1}$ of ketamine, diluted in normal saline, has also been studied before[5]. The secondary effects reported by the authors were less than those following administration of 1 $ml.kg^{-1}$ of 0.25% bupivacaine were, while the analgesic effect was comparable. In the above-mentioned study performed by Naguib et al, the same dose of ketamine was used in combination with bupivacaine and when ketamine was used alone. In contrast, we increased the dose of ketamine to 1 $mg.kg^{-1}$ while using it as a sole agent, which perhaps increased the potency of analgesia. One other study using the same dose has shown a median duration of 16.5 hours[10].

The degree of sedation was comparable between the three groups as it is described in the previous studies[10,11].

The higher dose of ketamine caused a higher incidence of behavioural side effects including slightly odd behaviour, vacant stares and abnormal effect in the previous study[11]. We investigated for those in our study and found higher incidence of nystagmus (20%) in comparison to the bupivacaine-ketamine group (5%) and bupivacaine group (0%).

We found no additional problems with motor block as shown by leg weakness or urinary retention in the ketamine group. On the other hand, significant number of patients from the other two groups showed signs of motor weakness after 6 hours of recovery from anaesthesia. The incidence of postoperative vomiting, however, was comparable between the three groups.

CONCLUSION

Caudal administration of ketamine 1 $mg.kg^{-1}$ in children provided adequate postoperative analgesia after subumbillical operations without producing many side effects. The quality and duration of analgesia did not differ significantly from that associated with the caudal injection of

0.25% bupivacaine 1 $ml.kg^{-1}$ with ketamine 0.5 $mg.kg^{-1}$ whereas it is proved to be superior in those respects from the caudal administration of 1 $ml.kg^{-1}$ of bupivacaine 0.25% alone.

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