KETAMINE FOR CAUDAL ANALGESIA IN CHILDREN: COMPARISON WITH CAUDAL BUPIVACAINE

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SUMMARY
Fifty children undergoing inguinal herniotomy were allocated randomly 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 0.5 mg kg⁻¹ with normal saline 1 ml kg⁻¹. There was no significant difference in quality of pain relief, postoperative behaviour or analgesic requirements between the ketamine group and the two other groups. The bupivacaine-ketamine mixture provided better analgesia than the bupivacaine solution alone. Side effects such as motor weakness or urinary retention were not observed in the ketamine group.

KEY WORDS

Caudal analgesia with bupivacaine is used commonly for pain relief in children [1]. More recently, the use of caudal morphine has been extended to children and has also been demonstrated to result in good analgesia [2], but has been associated with side effects, in particular, delayed respiratory depression [2, 3].

Ketamine has analgesic properties which are mediated by different mechanisms. Analgesia after periaqueductal administration of ketamine and its antagonism by naloxone suggested an opioid mechanism of analgesia [4]. This was disputed by Tung and Yaksh, who found that analgesia was reversed by methysergide but not by naloxone, suggesting a serotonergic mechanism [5]. Further, it has been shown that ketamine and phencyclidine selectively reduced responses of central neurones to N-methyl-aspartate [6], but this effect is not known to mediate analgesia.

Animal experiments [7] showed that intrathecal administration of ketamine preserved with benzethonium chloride was not associated with evidence of macroscopic or microscopic abnormalities in the spinal cord. Ketamine produces potent analgesia [8] without respiratory depression [9] and would therefore seem to be a suitable drug for pain relief. Extradural administration of ketamine has been studied by several investigators [10, 11] as an alternative to local analgesics and opioids, which are not ideal by virtue of their unwanted side effects [2, 3, 12, 13]. Extradural ketamine seemed to be a potent and safe method for postoperative analgesia in adults [10, 11].

This double-blind study was designed to compare the analgesic effectiveness of caudal administration of ketamine, bupivacaine or a mixture of both drugs in the treatment of pain after herniotomy in children.

PATIENTS AND METHODS
Institutional Review Board approval and informed consent from parents or guardians were obtained. We studied 50 boys, ASA physical status I, undergoing unilateral inguinal herniotomy. Patients were excluded from the study if a history of allergic reactions to local anaesthetics,
TABLE I. Patient data and duration of surgery (median (range or SE median))

<table>
<thead>
<tr>
<th></th>
<th>Bupivacaine group (n = 20)</th>
<th>Bupivacaine–ketamine group (n = 15)</th>
<th>Ketamine group (n = 15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (months)</td>
<td>36 (24–84)</td>
<td>42 (20–72)</td>
<td>36 (24–72)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>14.6 (0.9)</td>
<td>15 (0.7)</td>
<td>16 (0.3)</td>
</tr>
<tr>
<td>Duration of surgery (min)</td>
<td>30 (4.3)</td>
<td>30 (5.7)</td>
<td>40 (2.8)</td>
</tr>
</tbody>
</table>

bleeding diathesis, aspirin ingestion in the preceding week, or pre-existing neurological or spinal disease were present.

No premedication was given and all operations were carried out under general anaesthesia, induced with thiopentone 5–6 mg kg\(^{-1}\) i.v. or with inhalation of nitrous oxide and halothane in oxygen. In all patients, anaesthesia was maintained with 70 % nitrous oxide and halothane in oxygen delivered via an Ayre’s T-piece with spontaneous ventilation. No intraoperative sedatives or opioids were administered.

After induction of general anaesthesia, patients were allocated randomly to one of three groups. Children in group I received a caudal injection of plain 0.25% bupivacaine 1 ml kg\(^{-1}\). Group II received an identical local anaesthetic dosage mixed with ketamine 0.5 mg kg\(^{-1}\) and group III received caudal ketamine 0.5 mg kg\(^{-1}\) in 0.9 % sodium chloride using the same weight-related volumes. All blocks were performed by one investigator with the patient in the left lateral position, using a 23-gauge needle under sterile conditions. Ketamine with benzethonium chloride as the preservative was used. A small Elastoplast dressing was placed over the site of sacral hiatus in all patients.

After administration of the caudal block, heart rate and pulse oximetry were monitored continuously and arterial pressure was monitored every 5 min by an electronic oscillotonometer.

After operation the duration of surgery was noted and the patient was transferred to the recovery room. All patients were observed for 2 h in the recovery room before returning to the ward. When the child was awake, objective pain assessments, ventilatory frequency, arterial pressure and heart rate were recorded by one investigator unaware of the treatment given. Assessments were 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 anaesthesia. The observer scored pain on each occasion with reference to a three-point scale (none/insignificant pain; moderate pain; severe pain) and demeanour was scored similarly (cheerful and calm; restless; tense or tearful). Side effects were recorded by the observer in addition to the time at which analgesia, if any, was first received (recovery–analgesia time), and the total number of analgesic doses required in the first 24 h after operation. The patient’s ability to stand unaided was assessed 6 h after operation.

Postoperative analgesia (paracetamol suppository 125 mg) was prescribed for each patient and was given as required at the discretion of the nursing staff, who were unaware of the group allocation of the patients.

Further assessment 24 h after operation was made by nurses and mothers. They were asked to assess the child’s behaviour at bed time on the day of operation and on the following morning, with respect to pain and quality of overnight sleep.

Data processing

All statistical analyses were carried out using BMDP (1990) statistical package (University of California Press). Kruskal–Wallis test with multiple comparisons was used for comparisons between the groups. In multiple comparisons the null hypothesis was rejected if \( Z \) stat is larger than the critical value \( Z_C \):

\[
1 - \Phi(Z_C) = \alpha[K(K-1)]
\]

where \( \Phi \) = cumulative standard normal distribution function, \( \alpha = \) desired overall significance level, and \( K = \) number of groups compared.

The times at which analgesia was given were treated as being analogous to survival data. “Survival” curves were plotted to indicate the proportion of patients in each group who had received no analgesia by a given time after operation. The times at which analgesia was first received for the three groups were compared using four non-parametric linear rank tests: The Mantel–Cox (log-rank), Tarone–Ware, Breslow, and Peto–Prentice statistics. These tests compare the observed rate at which patients needed
CAUDAL KETAMINE FOR POSTOPERATIVE ANALGESIA

The groups were comparable in age, weight and duration of their operations (table I).

The quality of analgesia in the group which had received a caudal injection of ketamine did not differ from the two other groups (fig. 1). Caudal administration of bupivacaine with the addition of ketamine resulted in superior analgesia compared with caudal injection of bupivacaine alone. Significantly fewer patients in the latter group had no or insignificant pain at 60 min after recovery from anaesthesia (fig. 1). In addition, the bupivacaine group received significantly more doses of paracetamol than the bupivacaine–ketamine group in order to maintain analgesia in the first 24 h after recovery from anaesthesia (table II).

The times at which analgesia was first given are displayed in the form of survival curves in figure 2. The curves indicate the proportion of patients who received no analgesia by a given elapsed time after recovery from anaesthesia. Recovery–analgesia times were significantly longer in the bupivacaine–ketamine group than in the bupivacaine group.

There was no significant difference between the caudal ketamine group compared with the two other groups in time to first analgesia and the number of analgesic doses required in the first 24 h.

Administration of ketamine caudally either alone or in combination with bupivacaine was not associated with changes in postoperative behaviour. Significantly more patients who had received caudal ketamine either alone or with bupivacaine were described as cheerful and calm 60 and 90 min after recovery from anaesthesia (fig. 3) compared with those in the bupivacaine group.

The results from mothers' and nurses' assessments 24 h after operation showed no significant difference between the three groups with respect to pain and quality of overnight sleep. Vomiting occurred after operation in five (25 %), four (27 %) and two (13 %) patients in the caudal bupivacaine, bupivacaine–ketamine and ketamine groups, respectively (ns).

Postoperative urinary retention was noted in two patients in the bupivacaine (10 %) and

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**Table II. Requirement for analgesia during the first 24 h after operation. Number (%) of patients receiving 0–3 doses of paracetamol suppository 125 mg. *P < 0.05 vs caudal bupivacaine group**

<table>
<thead>
<tr>
<th>Analgesia (No. of doses)</th>
<th>Bupivacaine group (n = 20)</th>
<th>Bupivacaine–ketamine* group (n = 15)</th>
<th>Ketamine group (n = 15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>10 (50)</td>
<td>14 (93)</td>
<td>12 (80)</td>
</tr>
<tr>
<td>1</td>
<td>6 (30)</td>
<td>1 (7)</td>
<td>3 (20)</td>
</tr>
<tr>
<td>2</td>
<td>3 (15)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>1 (5)</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

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analgesia with the rate which might be expected if caudal administration of bupivacaine, bupivacaine–ketamine and ketamine were equally effective. *P < 0.05 was regarded as statistically significant.

**RESULTS**

The groups were comparable in age, weight and duration of their operations (table I).

The quality of analgesia in the group which had received a caudal injection of ketamine did not
bupivacaine-ketamine (13%) groups, 6 h after recovery from anaesthesia. Two patients (10%) in the caudal bupivacaine group and one patient (7%) in the caudal bupivacaine-ketamine group were unable to stand 6 h after operation. In contrast, no patient in the caudal ketamine group had urinary retention or any sign of motor weakness.

No child in the first 24 h after operation had a recorded ventilatory frequency less than 12 b.p.m. or showed any significant changes in heart rate and arterial pressure. 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**

There is considerable evidence implicating ketamine in the spinal inhibition of nociceptive transmission [4, 5, 14]. The results of the present study confirm previous reports that extradural administration of ketamine exerts modulatory influences on postoperative pain mechanisms [10, 11]. In this study, caudal administration of ketamine 0.5 mg kg⁻¹ produced postoperative analgesia comparable to that associated with caudal injection of 0.25% bupivacaine 1 ml kg⁻¹ with or without ketamine.

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**FIG. 2.** "Survival" curves for the bupivacaine, bupivacaine-ketamine and ketamine groups. Proportion of patients in each group who had not required any analgesia since recovery from anaesthesia.

**FIG. 3.** Behaviour in the first 24 h after recovery from anaesthesia. Calm and cheerful; restless; tense or tearful. *P < 0.05 vs caudal bupivacaine group.
It was noted in adults that a lesser dose of extradural ketamine (4–8 mg) did not produce significant analgesic effects [15, 16]. This observation was reported earlier by Naguib and colleagues [11], who found that ketamine 10 mg in saline 10 ml administered extradurally was ineffective in producing analgesia and all of the patients in that group required additional doses. In contrast, by increasing the dose of ketamine to 30 mg, 54% of the patients had adequate analgesia for 24 h after a single extradural injection [11].

Caudal block with bupivacaine alone can provide adequate analgesia in the early postoperative period, but as the block wears off, systemic analgesia is often required [17]. In the present study, 20% and 50% of patients in the caudal ketamine and bupivacaine groups, respectively, required additional analgesia during the first 24 h after surgery (table II). These results are similar to those of a previous report on herniotomy [18], in which 55% of patients who had caudal block with 0.25% bupivacaine 1 ml kg⁻¹ required further analgesia.

The addition of ketamine 0.5 mg kg⁻¹ to bupivacaine improved significantly both quality and duration of analgesia compared with administration of bupivacaine solution alone, without an increase in the incidence of side effects. There was a significant reduction in the amount of postoperative analgesia required by the children in the bupivacaine–ketamine group compared with those receiving bupivacaine alone. In addition, the recovery–analgesia times were significantly shorter in the latter group (fig. 2).

The overall incidence of side effects observed in the bupivacaine and bupivacaine–ketamine groups was comparable to that reported previously in children who received caudal bupivacaine [18, 19].

Respiratory depression, urinary retention and pruritis have been described in children after caudal administration of opioids [2, 3, 17], but these side effects were not encountered in this study after caudal injection of ketamine 0.5 mg kg⁻¹. Caudal ketamine was not associated with motor block, and rapid mobilization was possible in that group.

We conclude that caudal administration of ketamine 0.5 mg kg⁻¹ in children produced satisfactory postoperative analgesia after inguinal herniotomy without respiratory depression or other side effects. The quality of analgesia did not differ significantly from that associated with caudal injection of 0.25% bupivacaine 1 ml kg⁻¹ with or without ketamine.

REFERENCES