

Caudal Morphine in Paediatric Patients: A Comparison of Two Different Doses in Children after Major Urogenital Surgery

C K Leong,**MBBS, M Med (Anaes)*, A S B Ng,***MBBS, M Med (Anaes)*, S L Chew,****MBBS, M Med (Anaes), FANZCA*

Abstract

We compared the duration of postoperative analgesia and the occurrence of side-effects of two different doses of caudal morphine in children undergoing major urogenital surgery. Fifty-two children aged between 1 and 12 years were randomly selected to receive caudal morphine, either 25 $\mu\text{g.kg}^{-1}$ (Group A) or 50 $\mu\text{g.kg}^{-1}$ (Group B) with 0.5 ml kg^{-1} of 0.25% plain bupivacaine immediately before surgery. They were monitored for 24 hours in a high dependency area for known complications of epidural morphine. There was no significant difference in postoperative analgesia between the two doses of caudal morphine. Clinically significant respiratory depression or sedation was not detected in either group. The occurrence of vomiting and pruritus was similar in both groups. Urinary retention was not recorded as all children had an indwelling catheter as required by the surgical procedure. We concluded that 25 $\mu\text{g.kg}^{-1}$ of caudal morphine is as effective as 50 $\mu\text{g.kg}^{-1}$ for providing postoperative analgesia in children undergoing urogenital surgery.

Ann Acad Med Singapore 1998; 27:371-5

Key words: Bupivacaine-morphine mixture, Epidural opioid, Postoperative analgesia, Pre-surgery caudal injection

Introduction

The use of caudal preservative-free morphine for postoperative analgesia in children has gained popularity since it was first described by Jensen.¹ Several studies have reviewed its use for inguinal and genital surgery in children.^{2,3} These studies showed that 50 to 100 $\mu\text{g.kg}^{-1}$ of caudal morphine could be expected to provide prolonged analgesia (8 to 24 hours) with an acceptable incidence of side-effects. Krane et al⁴ compared 33 $\mu\text{g.kg}^{-1}$, 67 $\mu\text{g.kg}^{-1}$ and 100 $\mu\text{g.kg}^{-1}$ of caudal morphine after major abdominal, genitourinary or orthopaedic surgery and found that all three doses provided prolonged postoperative analgesia (greater than 8 hours) but the duration of analgesia was greatest in children who received 100 $\mu\text{g.kg}^{-1}$.

In our institution, we have adopted caudal administration of morphine as part of our anaesthetic technique for children undergoing major urogenital surgery. A preliminary study showed that 25 $\mu\text{g.kg}^{-1}$ of caudal morphine was effective in providing prolonged analgesia. A dose as low as 25 $\mu\text{g.kg}^{-1}$ had not been used in previous studies. Hence, we undertook a prospective,

randomised study to compare the effects of two doses of caudal morphine, 25 $\mu\text{g.kg}^{-1}$ and 50 $\mu\text{g.kg}^{-1}$, in children following major urogenital surgery.

Materials and Methods

Study Protocol

Institutional Ethics Committee approval and informed consent were obtained. Children, aged 1 to 12 years, ASA physical status I-2, who were scheduled for major urogenital surgery were randomly assigned to receive 25 $\mu\text{g.kg}^{-1}$ or 50 $\mu\text{g.kg}^{-1}$ of caudal preservative-free morphine with 0.5 ml kg^{-1} of 0.25% plain bupivacaine. Children with a history of allergy to opioids or bupivacaine were excluded from the study.

The children were given a non-opioid based oral premedication; either a benzodiazepine or phenothiazine. Baseline heart rate and blood pressure were recorded prior to induction of general anaesthesia. General anaesthesia was induced either with an inhalational agent (halothane 2 to 3% in oxygen) or an intravenous agent (sodium thiopental 4 to 5 mg.kg^{-1}) depending on the degree of co-operation of the child; followed by main-

* Consultant

Department of Anaesthesia & Surgical Intensive Care
Singapore General Hospital

** Head and Consultant

Department of Paediatric Anaesthesia
KK Women's and Children's Hospital

*** Consultant

Gleneagles Medical Centre

Address for Reprints: Dr Leong Choy Kuen, Department of Anaesthesia & Surgical Intensive Care, Singapore General Hospital, 1 Hospital Drive, Singapore 169608.

nance with nitrous oxide in 66% oxygen and halothane (0.2 to 1%). Intubation and intermittent positive pressure ventilation was facilitated by the use of atracurium 0.5 mg.kg^{-1} .

Following induction of general anaesthesia, caudal injection of morphine and bupivacaine was performed prior to surgery. Using an aseptic technique, morphine $25 \mu\text{g.kg}^{-1}$ (in Group A) or $50 \mu\text{g.kg}^{-1}$ (in Group B) mixed with bupivacaine (0.25% without adrenaline) 0.5 ml.kg^{-1} was injected into the caudal epidural space via a 21 or 23 gauge needle after negative aspiration for cerebrospinal fluid or blood. Intraoperative measurements of heart rate and blood pressure were recorded at 5 minutes intervals and used to assess the success of caudal injection. Presence of hypertension and tachycardia (30% more than baseline) in the absence of other known causes was assumed to be due to technical failure and the child would be removed from the study. Intraoperative opioids, apart from the caudal route, were not administered to any patient. At the end of the operation, general anaesthesia was reversed and all the children were extubated.

Postoperatively, the children were monitored for 24 hours in a high dependency area in the paediatric surgical ward. Monitoring included continuous pulse oximetry, hourly blood pressure, heart rate and respiratory rate. We had adopted the pain / discomfort scoring sys-

tem developed by Hannallah and colleagues (Table I)⁵ for scoring postoperative pain. This is a useful system to score pain objectively in young children who are unable to verbalise. It was completed hourly by nursing staff who was unaware of the morphine dose administered. Pain was deemed present if the pain score was 4 and above (with a maximum possible score of 10), or in the older children when they complained of pain. Paracetamol was given as the supplement analgesic when pain occurred. The time when paracetamol was first served was recorded and this was taken to be the duration of postoperative analgesia conferred by caudal morphine.

The occurrence of known complications of epidural opioids: nausea and vomiting, pruritus, excessive sedation, and respiratory depression were recorded hourly for 24 hours. Respiratory depression was defined as: apnoea (not breathing for more than 10 seconds), bradycardia, episodes of desaturation ($\text{SpO}_2 < 90\%$) with bradycardia or excessive sedation, or decreased respiratory rate (6 months to 1 year of age, rate $< 22/\text{minute}$, 1 to 4 years of age, rate $< 15/\text{minute}$, 4 to 12 years of age, rate $< 12/\text{minute}$). Excessive sedation was defined as unarousability; this was determined by nursing staff hourly by gently stimulating the child during sleep until the child was aroused. Urinary retention was not monitored as all the children had an indwelling catheter as required by the surgical procedure.

Oxygen was available at each patient's bedside. Naloxone, oral airways, face masks and an Ambu bag were available at the nurses' station in the high dependency area. Intravenous metoclopramide ($150 \mu\text{g.kg}^{-1}$) was used to treat vomiting; intravenous promethazine (0.2 to 0.5 mg.kg^{-1} , maximum 25 mg) was used to treat severe pruritus (defined as pruritus which caused disturbance in sleeping pattern).

Statistical Analysis

The ages and weights of the children were compared using the Mann-Whitney U-test. Reception of premedication, need for paracetamol and occurrence of side-effects were compared using Fisher's exact test. The difference in duration of postoperative analgesia between the treatment groups was assessed using the Mann-Whitney U-test. A *P* value of ≤ 0.05 was considered statistically significant. Statistical analysis was performed using a commercial software programme (SPSS for windows, version 6.1, SPSS, Chicago, IL).

Results

Fifty-two children were studied, 25 in Group A and 27 in Group B. There were no failed caudals. The study groups were comparable in age, weight and sexual distribution (Table II). The boys had undergone repair of hypospadias surgery while the only female child studied had a rectovaginal fistula repaired. Eighteen (72%)

TABLE I: PAIN/DISCOMFORT SCORE

Observation	Criteria	Score
Blood Pressure	$\pm 10\%$ preoperative value	0
	$> 20\%$ preoperative value	1
	$> 30\%$ preoperative value	2
Crying	Not crying	0
	Crying, respond to tender loving care (TLC)	1
	Crying and does not respond to TLC	2
Movement	None	0
	Restless	1
	Thrashing	2
Agitation	Asleep or calm	0
	Mild	1
	Hysterical	2
Posture	No special posture	0
	Flexing legs and thighs	1
	Holding scrotum or groin	2
Complaints of pain (if able to do so)	Asleep, or states no pain	0
	Cannot localise	1
	Can localise	2

Reproduced with permission from: Hannallah R S, Broadman L M, Belman B, Abramowitz M D, Epstein B S. Comparison of caudal and ilioinguinal/iliohypogastric nerve blocks for control of post-orchidopexy pain in paediatric ambulatory surgery. *Anesthesiology* 1987; 66:832-4.⁵

children in Group A and 23 (85%) children in Group B received premedication, the difference did not reach statistical significance (Table II).

Analgesia

Five children in Group A complained of pain while 8 children had pain/discomfort score of more than 4. In Group B, 3 children complained of pain and 9 had pain/discomfort score of more than 4 (Fig. 1). These children were given paracetamol for pain relief (Table III). The need for paracetamol was not significantly different between the two groups ($P = 0.7816$). The maximum score obtained was 5 (in one child). All those who complained of pain were able to localise the site to the operative site.

The duration of postoperative analgesia is presented in Figure 1. The median duration of analgesia in treatment Group A was 23 hours; in treatment Group B was 24 hours (Table III). There was no statistical difference between the two treatment groups ($P = 0.9685$).

Side-effects

Side-effects monitored included nausea and vomiting, pruritus, sedation, and respiratory depression. There was no statistical difference in the occurrence of side-effects between the two doses of caudal morphine

(Table IV). Vomiting and pruritus were not severe enough to require treatment and these resolved spontaneously. All the children studied had routine postoperative bladder catheterisation, hence the occurrence of urinary retention was not noted.

Discussion

The effectiveness of caudal morphine for providing postoperative analgesia in children had been demonstrated in a number of studies.^{1-4,6-9} Doses ranging from $33 \mu\text{g.kg}^{-1}$ to $100 \mu\text{g.kg}^{-1}$ had been used, all providing prolonged postoperative analgesia (greater than 8 hours). The duration of analgesia was greatest in children who received $100 \mu\text{g.kg}^{-1}$ (greater than 12 hours). Krane et al⁴ showed that decreasing the dose of caudal morphine had little effect on the duration of analgesia and might decrease the incidence of side-effects. Our study showed that a dose as low as $25 \mu\text{g.kg}^{-1}$ of caudal morphine was effective in providing prolonged analgesia for children after major urogenital surgery, and compared favourably with a larger dose of $50 \mu\text{g.kg}^{-1}$. The sex distribution was skewed because of the nature of surgery performed (mainly repair of hypospadias). There was no statistically significant difference between the two treatment groups, with respect to the number of children who had pain, and the duration of postoperative analgesia. We have not analysed the exact duration of analgesia provided by caudal morphine in children who have no pain within the first 24 hours after surgery as the observation

TABLE II: CLINICAL CHARACTERISTICS OF THE STUDY GROUPS

	Group A ($25 \mu\text{g.kg}^{-1}$) n = 25	Group B ($50 \mu\text{g.kg}^{-1}$) n = 27	P value
Age (y)*	3 (1-12)	2 (1-10)	0.2488
Weight (kg)*	13 (8-46)	11 (6-35)	0.1346
Male/Female	25/0	26/1	1.0000
Children who received			
1. premedication (%)	18 (72)	23 (85)	0.3169
2. phenothiazines (%)	10 (40)	17 (62)	0.1640

* Median values, range in parenthesis where appropriate.
No significant differences between groups.

TABLE III: NUMBER (%) OF CHILDREN GIVEN PARACETAMOL AND DURATION OF POSTOPERATIVE ANALGESIA BY TREATMENT GROUPS

	Group A ($25 \mu\text{g.kg}^{-1}$)	Group B ($50 \mu\text{g.kg}^{-1}$)	P value
Number (%) of children given paracetamol	13 (52)	12 (44)	0.7816
Number (%) of children who are pain-free 24 hours after operation	12 (48)	15 (56)	
Median (range) duration of postoperative analgesia (h)	23 (3-24)	24 (4-24)	0.9685

No significant difference between the two groups.

TABLE IV: OCCURRENCE (%) OF SIDE-EFFECTS BY TREATMENT GROUP

	Group A ($25 \mu\text{g.kg}^{-1}$)	Group B ($50 \mu\text{g.kg}^{-1}$)	P value
Vomiting	7 (28.0)	5 (18.5)	0.5174
Pruritus	6 (24.0)	4 (14.8)	0.4922
Sedation	0 (0)	0 (0)	
Respiratory depression	0 (0)	0 (0)	

No significant difference between the two groups.

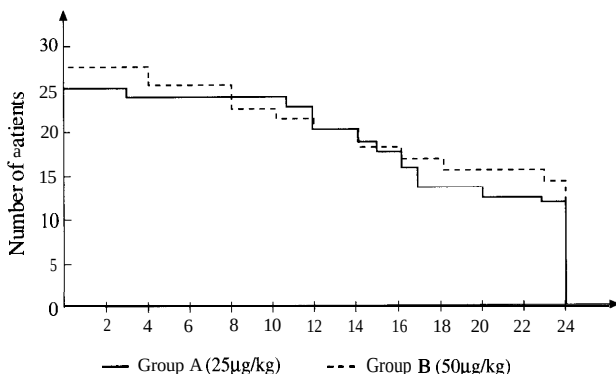


Fig. 1. Duration of postoperative analgesia within the 24-hour observation period.

period was stopped at 24 hours after operation.

Pain assessment can be difficult in children, especially younger pre-verbal children for whom communication of discomfort may not be clearly understood. The differentiation between anxiety and pain may be difficult too. Certainly, the techniques based on self-reporting scales are inadequate. Behavioural observation methods have been developed to circumvent this as they are independent of verbal skills and may be more objective. Hannallah and colleagues⁵ used a scoring system for assessing pain/discomfort in children who had undergone orchidopexy. We have adopted this system to score post-operative pain in our patients who had major urogenital surgery. This is an objective assessment of pain as it combined observation of behaviour (crying, movement, agitation and posture), physiological parameter (blood pressure), and in older children, verbal response.

Caudal bupivacaine alone can provide good post-operative analgesia. However, the duration of analgesia provided is shorter compared to caudal morphine.^{1,2} A study by Wolf et al³ demonstrated that addition of morphine ($50 \mu\text{g.kg}^{-1}$) to a 0.125% solution of bupivacaine significantly improved both quality and duration of pain relief after orchidopexy. We choose to use a mixture of morphine and bupivacaine in the study as the local anaesthetic provides intraoperative analgesia and reduces the requirement of intraoperative narcotics. None of the children in the study received perioperative narcotics apart from the caudal morphine.

Irving et al⁶ showed that caudal morphine injection given prior to surgery significantly prolonged postoperative analgesia when compared to caudal morphine given immediately after surgery. Approximately 50% of the children studied here were pain-free up to 24 hours after operation, following administration of single dose of caudal morphine, which was given immediately prior to surgery. This is a simple and effective means of pain control in children undergoing major urogenital surgery. Postoperatively, the children did not require any other parenteral means of pain relief. They were allowed to feed orally and paracetamol was sufficient for pain relief.

Nausea and vomiting after caudal morphine are common side-effects occurring in approximately 40% of patients.⁴ Pruritus is also common but is rarely severe enough to require treatment. Decreasing the dose of caudal morphine does not seem to reduce the incidence of vomiting or pruritus. Its occurrence is lower in this study, probably related to the fact that a majority of the children were given trimeprazine or promethazine as premedication. These are phenothiazine derivatives with antihistamine and antiemetic properties. We have not compared the incidence of vomiting and pruritus in children who received benzodiazepines with children receiving phenothiazine derivatives. Irving et al⁶ recom-

mended a combination of trimeprazine and droperidol as premedication to reduce the occurrence of vomiting and pruritus. In their series, there was no reported occurrence of vomiting and pruritus. However, oral droperidol is not available locally. Possible prolonged drowsiness caused by this combination may present an unnecessary complication.

Delayed respiratory depression after caudal morphine can occur in children. The ventilatory response to carbon dioxide remains depressed for at least 22 hours.¹⁰ Krane¹¹ reported respiratory depression in one child who received $100 \mu\text{g.kg}^{-1}$ of caudal morphine. Valley and Bailey⁷ reported 11 cases of respiratory depression in 138 administrations of caudal morphine ($70 \mu\text{g.kg}^{-1}$). All were within 12 hours of morphine administration, and 10 were in children 12 months of age or less, and weighing less than 9 kg. The children in our study were 1 year old or older, and we used a lower dose ($25 \mu\text{g.kg}^{-1}$ and $50 \mu\text{g.kg}^{-1}$). None of the children developed respiratory depression. However, Karl et al¹² reported recently that a 15-month-old, 9.8 kg child developed respiratory depression 2 hours after administration of $40 \mu\text{g.kg}^{-1}$ of caudal morphine.

We have adopted a practice of assessing arousability on an hourly basis, for 24 hours following caudal morphine administration. This is based on observations by Ready et al¹³ that excessive sedation is associated with respiratory depression and hypercarbia, and that all reported cases of respiratory depression have occurred within the first 24 hours after starting epidural narcotics. The children who have received caudal morphine are monitored by nurses trained in Pain Management Service in a high dependency area for the first 24 hours after operation. The high dependency area is adequately equipped with monitoring and resuscitative equipment. The nurse to patient ratio is 1:2. In-house anaesthetists are available on a 24-hour basis for consultation should any problem arise.

In conclusion, we have found that a single dose of caudal morphine, $25 \mu\text{g.kg}^{-1}$ or $50 \mu\text{g.kg}^{-1}$, provides prolonged postoperative analgesia in children after major urogenital surgery. There was no difference in terms of duration of postoperative analgesia. Half of the children remained pain-free for up to 24 hours after operation, following administration of caudal morphine immediately prior to surgery. The occurrence of side-effects such as nausea and vomiting, and pruritus was similar in both treatment groups, with no reported occurrence of oversedation and respiratory depression. A period of 24 hours of monitoring in a high dependency area is recommended.

Acknowledgements

The authors would like to thank Ms Stephanie Fook Chong for her invaluable help with statistical analysis.

REFERENCES

1. Jensen B H. Caudal block for postoperative pain relief in children after genital operations. A comparison between bupivacaine and morphine. *Acta Anaesthesiol Scand* 1981; 25:373-5.
2. Krane E J, Jaconson L E, Lynn A M, Parrot C, Tyler D C. Caudal morphine for postoperative analgesia in children: a comparison with caudal bupivacaine and intravenous morphine. *Anesth Analg* 1987; 66:647-53.
3. Wolf A R, Hughes D, Wade A, Matter S J. Postoperative analgesia after paediatric orchidopexy: evaluation of a bupivacaine-morphine mixture. *Br J Anaesth* 1990; 64:430-5.
4. Krane E J, Tyler D C, Jacobson L E. The dose response of caudal morphine in children. *Anesthesiology* 1989; 71:48-52.
5. Hannallah R S, Broadman L M, Belman B, Abramowitz M D, Epstein B S. Comparison of caudal and ilioinguinal/iliohypogastric nerve blocks for control of postoperative orchidopexy pain in paediatric ambulatory surgery. *Anesthesiology* 1987; 66:832-4.
6. Irving G A, Butt A D, Vanderveen B. A comparison of caudal morphine pre- or post- surgery for postoperative analgesia in children. *Paediatr Anaesth* 1993; 3:217-21.
7. Rosen K R, Rosen D A. Caudal epidural morphine for control of pain following open heart surgery in children. *Anesthesiology* 1989; 70:418-21.
8. Shapiro L A, Jedeikin R J, Shaley D, Hoffman S. Epidural morphine analgesia in children. *Anesthesiology* 1984; 61:210-1.
9. Valley R D, Bailey A G. Caudal morphine for postoperative analgesia in infants and children: a report of 138 cases. *Anesth Analg* 1991; 72:120-4.
10. Attia J, Ecoffey C, Sandouk P, Gross J B, Samji K. Epidural morphine in children: Pharmacokinetics and CO₂ sensitivity. *Anesthesiology* 1986; 65:590-4.
11. Krane E J. Delayed respiratory depression in a child after caudal epidural morphine. *Anesth Analg* 1988; 67:79-82.
12. Karl H W, Tyler D C, Krane E J. Respiratory depression after low-dose caudal morphine. *Can J Anaesth* 1996; 43:1065-7.
13. Ready L B, Oden R, Chadwick H S, Benedetti C, Rooke G A, Caplan R, et al. Development of an anesthesiology-based postoperative pain management service. *Anesthesiology* 1988; 68:100-6.