Original Article

Postoperative analgesia in children: A comparison of three different doses of caudal epidural morphine

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Abstract

Background and Aims: Caudal epidural block is the most commonly used neuraxial block in children. Morphine has been used as a caudal additive for more than three decades. The aim of our study was to evaluate the efficacy and duration of analgesia of three different doses of caudal epidural morphine (CEM), and to find out the incidence of side effects.
Material and Methods: This study was conducted on 75 patients of American Society of Anesthesiologists grades I and II, aged 2-12 years, undergoing lower abdominal and urogenital surgeries. Patients were randomly allocated to one of the three groups according to the dose of morphine. Group I received 30 μg/kg, group II 50 μg/kg, and group III 70 μg/kg. Heart rate, blood pressure, oxygen saturation, electrocardiogram, pain score, sedation score, duration of analgesia, and side-effects were noted.
Results: The mean duration of analgesia was 8.63 h in group I, 13.36 h in group II and 19.19 h in group III. Respiratory depression was noted in three patients in group III. One patient in group I had itching. One patient each in groups I, II, and III had nausea/vomiting.
Conclusion: CEM significantly prolongs the duration of analgesia, though with a higher dose the risk of respiratory depression should always be kept in mind.

Key words: Analgesia, caudal, morphine, pediatric, respiratory depression

Introduction

Caudal epidural block (CEB) is the most commonly used neuraxial block in children. The use of preservative free morphine as an adjunct to caudal anesthesia is associated with various side effects such as nausea/vomiting, pruritis, urinary retention and potential life-threatening respiratory depression, discouraging's its use, especially in pediatric age group. This led to the use of various other caudal additives such as clonidine, midazolam, ketamine, and tramadol.[1-4] These were proven to be practically free of the side-effects for which morphine had become notorious, but the quality and duration of analgesia provided by morphine remains unmatched.[5,6] Hence, our study was conducted to compare the efficacy and safety of three different doses of caudal epidural morphine (CEM). Since 50 μg/kg is the standard dose, and 100 μg/kg has been shown to cause respiratory depression, we decided to compare 30, 50, and 70 μg/kg of CEM.[7]

Material and Methods

The prospective double-blind study was conducted on 75 pediatric patients of American Society of Anesthesiologists (ASA) grades I and II between 2 and 12 years of age,

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undergoing lower abdominal and urogenital surgeries, over a period of 1 year. Approval from hospital Ethical Committee and informed consent from parents of each participating child was taken, and a careful preanesthetic examination was performed. Patients were kept fasting for 6 h prior to surgery and were premedicated with oral midazolam 0.5 mg/kg body weight. All procedures were carried under general anesthesia.

Exclusion criteria included history of allergy to any of the study drugs, history of any respiratory illness, presence of any sacral deformity or any localized infection. Patients were randomly allocated to one of the three groups of 25 each, according to computer generated random number chart. Group I received 30 μg/kg of CEM, group II 50 μg/kg, and group III 70 μg/kg. General anesthesia was induced, and no intraoperative sedatives or opioids were administered.

The assigned dose of preservative free morphine was given in 0.75 ml/kg of 0.25% bupivacaine by an observer not related to the study. All blocks were performed in the left lateral position, using a 23G hypodermic needle, under strict aseptic precautions. A small elastoplast dressing was placed over the site of injection. Patients with an anal wink reflex were presumed to have incorrect drug placement and were not to be included in the study, but no patient had a failed caudal block in our study. After surgery residual neuromuscular blockade was reversed, and all patients were transferred to postoperative room and observed for 24 h.

Intraoperatively, heart rate, pulse oximetry, and electrocardiogram were monitored continuously, and blood pressure was measured every 5 min. Any increase in heart rate or blood pressure of >20% of its baseline value was defined as inadequate analgesia and was treated with intravenous fentanyl (1 μg/kg). Postoperatively, heart rate, respiratory rate, and blood pressure were measured every 15 min. Objective pain assessment was made by using a 5-point scale, a modification of the pain/discomfort scale[8] [Table 1].

Patients with a pain score of 4 or 5 were given supplemental analgesia in the form of intravenous fentanyl (1 μg/kg) and time of analgesia (if required) was noted. Patient sedation score was used to quantify sedation[9] [Table 2]. Side effects, if any, were recorded. Respiratory depression was defined as a decrease of oxygen saturation (SpO_2) <93% and patients were given supplemental oxygen.[7]

Statistical analysis

Sample size was determined using Altman's normogram with power of study 80% and deducing a standardized difference equaling the ratio between the smallest clinically worthwhile difference and standard deviation. A commercially available software package SPSS version 12.0 (SPSS for Windows Version 12, Released 2003, SPSS Inc., Chicago) was used to analyze the data. Comparisons were made between the three groups using ANOVA test and within the group using Student's *t*-test. $P < 0.05$ was considered as statistically significant. Null hypothesis formed was that there will be no significant difference in the duration of analgesia among the three doses of morphine. An intention to treat analysis was always kept in mind.

Results

The three groups were comparable with respect to "age and gender distribution" and "types and duration of surgeries" [Table 3]. All patients were "hemodynamically stable" throughout the perioperative period [Table 4]. Three patients in group III had respiratory depression with respiratory rates falling to 8/min associated with a fall in SpO_2 to 90% [Table 4].

By 12 h, 92% of patients in group I and 56% patients in group II had received rescue analgesia [Table 4]. At 16 h, most of the patients in groups I and II had experienced pain whereas

Table 1: Pain score

Facial expressions	Score
Laughing	1
Happy, contended, and playful	2
Calm or asleep	3
Mild-moderate pain — crying, grimacing restless, can be distracted with toy, food or parent	4
Severe pain - crying, screaming, inconsolable	5

Table 2: Modified Wilson sedation score[9]

Sedation level	Sedation score
Asleep, not arousable by verbal contact	4
Asleep, arousable by verbal contact	3
Drowsy/not sleeping	2
Alert/awake	1

Table 3: Patient characteristics

Patient characteristics	Group I	Group II	Group III
Age (years)	5.2 (2.5-11)	5.3 (2-12)	4.9 (2-10.5)
ASA grading (%)			
I	22 (88)	24 (96)	24 (96)
II*	3 (12)	1 (4)	1 (4)
Sex (%)			
Males	23 (92)	23 (92)	22 (88)
Females	2 (8)	2 (8)	3 (12)
Type of surgeries (%)			
Hernioplasty	8 (32)	7 (28)	8 (32)
Urethroplasty	8 (32)	6 (24)	7 (28)
Others	9 (36)	12 (48)	10 (40)
Duration of surgery (h)	1.21±0.35	1.28±0.42	1.19±0.18

**Children with mild anemia. ASA = American Society of Anesthesiologists*

Table 4: Comparison of the three groups

Patient characteristics	Group I (%)	Group II (%)	Group III (%)
Duration of analgesia (h)	8.63±3.91*	13.36±2.47*	19.19±3.02*
Need for rescue analgesia			
At 8 h	17	5	0
At 12 h	23	14	2
At 16 h	24#	25#	7#
Number of patients sedated			
At 8 h	1	10	12
At 12 h	0	0	11
At 16 h	0#	0#	7#
Nausea/vomiting	1 (4)	1 (4)	1 (4)
Bradycardia	None	None	None
Hypotension	None	None	None
Urinary retention	None	None	1 (4)
Pruritis	1 (4)	None	None
Respiratory depression	None	None	3 patients

**P < 0.001 — (between groups I and II, groups I and III, and groups II and III),*
#P < 0.05 — (between groups I and III and groups II and III)

88% of patients in group III were still pain free [Table 4].

Sedation was prolonged in group III. By 16 h, almost all patients in groups I and II were alert and awake whereas 11 out of 25 patients in group III were sedated, though easily arousable [Table 4].

The mean duration of analgesia in group I was 8.63 ± 3.91 h, in group II was 13.36 ± 2.47 h and in group III was 19.19 ± 3.02 h [Table 4].

One patient in group I had itching. One patient each in the three groups had nausea/vomiting. The incidence of urinary retention could not be assessed accurately as most of our patients were catheterized intraoperatively [Table 4].

Discussion

Caudal epidural block is the most common neuraxial block administered in children. To decrease the dose of bupivacaine for avoiding local anesthetic toxicity, and to prolong the duration of analgesia, various adjuncts are added.[1-4,10] Morphine was one of the first additives used in 1981. Since then, many studies have been conducted to prove its efficacy.

We compared the efficacy of 30, 50, and 70 μg/kg of CEM in ASA grades I and II children undergoing lower abdominal and urogenital surgeries. Even low dose of 30 μg/kg provided analgesia lasting up to 12 h with minimal side-effects. Higher dose of 70 μg/kg was associated with respiratory depression.

Krane *et al.* compared different doses of CEM (33, 67, and 100 μg/kg) in children and reported that the mean duration of analgesia was significantly prolonged with 100 μg/kg (13.3 ± 4.7 h) than with 33 μg/kg (10.33 ± 3.3 h) or 67 μg/kg (10.4 ± 4.2 h).[7] We also observed a linear relationship between the dose of CEM and the duration of analgesia.

Stuth *et al.* conducted a randomized control trial to compare the effect of high-dose caudal morphine and intravenous morphine on early extubation and postoperative analgesic requirements for stages 2 and 3 single-ventricle palliation. They concluded that CEM not only delayed the need for rescue analgesia in stage 3 patients but also made early extubation feasible.[11]

Morphine placed in the epidural space may undergo uptake into epidural fat, systemic circulation, or may diffuse across the dura into cerebrospinal fluid (CSF). It produces analgesia by acting on mu, kappa, and delta receptors. Out of these, action on delta receptors can also produce delayed respiratory depression, whereas action on mu1 can lead to bradycardia, hypotension and urinary retention. Cephalad migration of morphine in CSF and subsequent interaction with opioid receptors in trigeminal nucleus leads to pruritis.[12]

Respiratory depression, the most notorious side effect of CEM was first reported by Krane *et al.*[7] We also observed respiratory depression in three patients who had received 70 μg/kg of morphine, but they all responded to supplemental oxygen supplementation only and no naloxone was required. Though a high incidence of other side effects has been reported by various workers, it was much lower in our study [Table 4]. The reason behind this can be lesser reporting of side effects as most of our patients were very young, between 2 and 4 years [Table 3].

Over the last 10 years, there has been a marked increase in the use of other caudal additives.[13] These include midazolam, clonidine, tramadol, and ketamine. Pradhan and Bajracharya used caudal midazolam (50 μg/kg) in addition to bupivacaine and found no significant increase in the duration of analgesia.[2]

Vetter *et al.* have compared single-dose caudal morphine 50 μg/kg, clonidine 2 μg/kg, and hydromorphone 10 μg/kg and have found that morphine provides more sustained initial analgesia, though with a higher incidence of postoperative nausea/vomiting.[6] Fernandez *et al.* compared the efficacy of caudal morphine 20 μg/kg with caudal clonidine 1 μg/kg in children undergoing infraumblical surgeries and concluded that morphine decreased the requirement of analgesics in the postoperative period, although it was associated with an

increased incidence of nausea/vomiting.[5] Another alpha-2 agonist dexmedetomidine is increasingly being used for analgesia and sedation, but still there are many concerns about its use, especially in the pediatric age group.[14-16]

We managed to compare a dose higher and a dose lower than the standard dose of morphine, to achieve a dose with maximum duration of analgesia with minimal side-effects. All patients were kept under observation for 24 h, so that assessment of analgesia and side-effects was done by trained professionals. Limitations to the study include the inability to assess urinary retention as many of our patients were catheterized. Moreover, to prove the efficacy of caudal morphine, we could have compared it with other new additives.

Conclusion

Though the popularity of caudal morphine is decreasing, more so with the advent of newer drugs, the prolonged duration and the intensity of analgesia provided by it, still remains un-paralleled. In doses of 30 and 50 μg/kg also it provides analgesia up to 12 h with minimal side-effects. For analgesia longer than this, 70 μg/kg can also be given, but under close monitoring for respiratory depression.

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Conflicts of interest
There are no conflicts of interest.

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