

## Original Research Article

# Study of morphine with ropivacaine and ropivacaine alone for caudal epidural analgesia in children

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### ABSTRACT

**Background:** Caudal epidural analgesia is one of the most popular and commonly performed regional blocks in pediatric anesthesia. It is reliable and safe technique that can be used with general anesthesia for intraoperative and postoperative analgesia. The aim of this research is to study the effect of morphine (15 µg/kg) with ropivacaine (0.2%) and ropivacaine (0.2%) alone through caudal epidural route on duration of analgesia in children.

**Methods:** The study was performed on 60 ASA grade I and II patients, aged 1 to 7 years scheduled for elective infraumbilical surgeries. After induction of general anesthesia, caudal epidural block was performed. Each group consisted of 30 pediatric patients: group I-caudal epidural 0.2% ropivacaine (1 ml/kg) and group II- caudal epidural 0.2% ropivacaine (1 ml/kg) with morphine 15 µg/kg. Intra-operatively heart rate, blood pressure was recorded at pre-induction, immediately after induction, 5 minutes after administration of caudal block and thereafter every 10 minutes till the completion of surgery. Postoperative heart rate, blood pressure, pain score was assessed periodically till 24th hour.

**Results:** The duration of analgesia was more in group II (7.30±1.78 hour) in comparison to group I (3.93±0.83 hour). The fall in mean arterial pressure and heart rate were not significant in group II as compared to group I.

**Conclusions:** Addition of low dose morphine to ropivacaine resulted in prolonging the duration of analgesia by almost double the duration as compared to ropivacaine alone.

**Keywords:** Caudal epidural analgesia, Ropivacaine, Morphine, Adjuvants

### INTRODUCTION

First described in 1933, caudal epidural analgesia is reliable and safe technique that can be used with general anesthesia for intraoperative and postoperative analgesia in pediatric patients undergoing lower abdominal and lower limb surgery. The main disadvantage of caudal anesthesia is the short duration of action after a single injection of local anesthetic solution.<sup>1</sup> The use of caudal catheters to administer repeated doses or infusion of local anesthetic solutions is not popular, partly because of concerns about infection. So prolongation of caudal analgesia using a 'single shot' technique has been

achieved by the addition of various adjuvants (epinephrine, opioids, ketamine, midazolam, tramadol, neostigmine, dexmedetomidine). Adjuvant drugs are agents that when co-administered with local anesthetic agents improve the speed of onset, the quality and/or the duration of analgesia.

Ropivacaine is the N-propyl homologue of bupivacaine, supplied as the pure S-enantiomer with a high pKa and relatively low lipid solubility. It is long acting aminoamide local anesthetic and introduced in the market in 1996, FDA approved in 2000 and DCGI approved in 2009. The greater sensory-motor separation is

advantageous for prolonged intraoperative and postoperative analgesia.<sup>2</sup> Compared to bupivacaine, ropivacaine has lower incidence of cardiac toxicity and neurotoxicity.<sup>3</sup> Recent studies on different concentrations of ropivacaine have shown that ropivacaine 0.2% appears to be optimum concentration for pediatric caudal block.<sup>4-6</sup> The synergistic effect of epidural opioid and local anesthetic solution on analgesia is well recognized and the combination of these drugs is used commonly than either of the drugs alone. The addition of morphine as an adjuvant helps in achieving effective and prolonged analgesia with the advantage of using a lower dose of local anesthetic which increases the margin of safety and reduces the incidence of unwanted motor blockade.<sup>7,8</sup> Recent studies show that the combination of morphine and ropivacaine improves the quality of postoperative analgesia compared to plain ropivacaine alone when given caudally in small children without causing any side effects.<sup>9</sup>

### Aim of the study

The aim was to study the effect of morphine (15 µg/kg) with ropivacaine (0.2%) and ropivacaine (0.2%) alone through caudal epidural route on duration of analgesia in children and to know the hemodynamic changes of ropivacaine with morphine and ropivacaine alone in caudal epidural analgesia in children.

### METHODS

This randomised double blind study was conducted in the Department of Anesthesiology, Lady Hardinge Medical College, New Delhi after approval from the Institutional Ethical Committee from November 2013 to March 2015.

### Inclusion criteria

60 pediatric patients of ASA I-II, 1 to 7-year age group (upto 20 kg) of both sexes undergoing elective infraumbilical surgeries.

### Exclusion criteria

Patients with history of allergic reaction to local anesthetic agents, pre-existing systemic illness or obvious spinal disease, deranged coagulation profile.

Careful pre-anesthetic examination was performed on all patients and written informed consent from their parents was taken. Patients were kept fasting for appropriate period prior to surgery. All procedures were conducted under general anesthesia. All patients received

midazolam (0.02 mg/kg) intravenously as premedication prior to surgery. Induction was carried out using thiopentone sodium and the inhalation of oxygen, nitrous oxide and isoflurane. Endotracheal intubation was performed using rocuronium at the dose of 0.6 mg/kg. After induction of general anesthesia, caudal epidural block was performed in left lateral position using 23 G hypodermic needle under all aseptic precautions. Patients received study drugs according to the group allotted. Each group consisted of 30 pediatric patients.

*Group I:* Caudal epidural 0.2% ropivacaine (1 ml/kg).

*Group II:* Caudal epidural 0.2% ropivacaine (1 ml/kg) with morphine 15 µg/kg.

At the completion of surgery, residual neuromuscular blockade was reversed and trachea extubated. Patients were transferred to postoperative recovery room and observed for 24 hours. Duration of effective postoperative analgesia i.e., time from caudal block to the time for requirement of first rescue analgesia was noted. Pain assessment was made using FLACC scale.<sup>10</sup>

Intra-operatively heart rate, blood pressure were recorded at pre-induction, immediately after induction, 5 minutes after administration of caudal block and thereafter every 10 minutes till the completion of surgery. Postoperative heart rate, blood pressure, respiratory rate, pain score was assessed at 30 minutes interval for 1<sup>st</sup> hour, 1 hourly interval for next 6 hours, and at 8<sup>th</sup>, 12<sup>th</sup> and 24<sup>th</sup> hour.

The statistical significance of categorical variables was carried out by using qualitative analysis Chi-Square test or Fisher's exact test. P value less than 0.05 was considered statistically significant. The observations were compiled, tabulated and analyzed by using SPSS statistical software version 20.0.

### RESULTS

On comparison, in Table 1, the intraoperative mean heart rate in group I and group II did not show any significant difference.

In the postoperative period, on comparison in Table 2, group I vs group II did not show any significance in mean heart rate.

On comparison, in Table 3, the intraoperative mean arterial pressure (MAP) in group I and group II did not show any significant difference from pre induction time till the end of surgery.

**Table 1: Intraoperative mean heart rate (BPM).**

Time	Group I	Group II	P value (I vs II)
Pre induction	119.33±16.28	124.20±13.97	0.109
After induction	120.43±16.10	125.43±12.41	0.092
5 min after caudal	117.30±15.44	120.97±12.46	0.158
10 min	113.17±13.88	115.00±12.07	0.294

Continued.

Time	Group I	Group II	P value (I vs II)
20 min	108.80±13.76	111.23±12.08	0.245
30 min	105.07±12.00	106.53±11.84	0.318
40 min	102.76±10.18	104.35±10.56	0.303
50 min	98.06±8.55	103.33±11.33	0.602
1 hr	99.87±8.29	103.06±11.78	0.196
1 hr 10 min	101.00±10.95	100.29±9.68	0.446
1 hr 20 min	96.60±7.73	101.50±11.26	0.207
1 hr 30 min	97.00±8.12	102.00±10.65	0.214
1 hr 40 min	96.33±5.51	98.67±6.11	0.324
1 hr 50 min	100.00±1.73	100.00±8.00	0.500
2 hr	104.60±5.66	108.00±0.00	

Table 2: Postoperative mean heart rate (BPM).

Time	Group I	Group II	P value (I vs II)
30 min	104.60±8.88	105.93±12.08	0.314
1 <sup>st</sup> hr	120.40±9.13	106.53±11.55	0.065
2 <sup>nd</sup> hr	102.59±8.03	105.47±11.90	0.141
3 <sup>rd</sup> hr	102.62±10.35	104.30±11.76	0.300
4 <sup>th</sup> hr	99.50±7.37	104.00±12.22	0.165
5 <sup>th</sup> hr	99.00±0.00	102.96±12.01	
6 <sup>th</sup> hr		104.05±12.09	
8 <sup>th</sup> hr		103.86±13.96	
12 <sup>th</sup> hr		112.00±0.80	

Table 3: Intraoperative mean arterial pressure (mmHg).

Time	Group I	Group II	P value (I vs II)
Pre induction	67.93±3.31	68.00±5.21	0.477
After induction	67.70±3.62	67.37±4.86	0.275
5 min after caudal	65.73±3.29	65.27±3.81	0.307
10 min	63.67±3.07	63.30±3.43	0.332
20 min	63.00±3.23	61.97±2.76	0.094
30 min	62.57±2.73	61.67±2.26	0.085
40 min	59.45±13.48	61.65±2.74	0.210
50 min	62.06±2.07	61.11±1.71	0.073
1 hr	58.50±15.83	61.69±2.70	0.217
1 hr 10 min	61.40±1.14	61.38±2.33	0.495
1 hr 20 min	62.20±1.30	61.38±1.41	0.157
1 hr 30 min	62.80±2.68	60.60±1.67	0.079
1 hr 40 min	62.33±3.21	61.33±1.15	0.319
1 hr 50 min	62.67±3.06	60.67±1.53	0.184
2 hr	62.00±1.41	61.00±0.00	

Table 4: Postoperative mean arterial pressure (mmHg).

Time	Group I	Group II	P value (I vs II)
30 min	63.40±3.74	61.07±1.93	0.002
1 <sup>st</sup> hr	63.00±2.98	61.20±2.55	0.007
2 <sup>nd</sup> hr	62.62±3.17	60.90±1.92	0.007
3 <sup>rd</sup> hr	62.45±3.42	60.83±1.39	0.010
4 <sup>th</sup> hr	57.75±11.31	60.50±1.33	0.093
5 <sup>th</sup> hr		61.08±0.97	
6 <sup>th</sup> hr		60.47±1.47	
8 <sup>th</sup> hr		60.40±1.67	
12 <sup>th</sup> hr		63.00±0.00	

**Table 5: Duration of analgesia.**

Duration of analgesia	Group I	Group II	P value (I vs II)
<b>Hours</b>	3.93±0.83	7.30±1.78	0.001

Table 4 shows in postoperative period, group I vs group II showed significant fall in MAP from 30 min till 3<sup>rd</sup> hr postoperatively. Though this fall was statistically significant ( $p < 0.05$ ) it was not significant clinically and no intervention was done for this.

The objective assessment of the duration of analgesia was done using FLACC scale.<sup>10</sup> Rescue analgesia with paracetamol suppository (20 mg/kg) was given when pain score  $\geq 4$  was recorded. The mean duration of analgesia was 3.93±0.83 hour in group I, 7.30±1.78 hour in group II. The duration of analgesia was more in group II compared to group I which was statistically significant, shown in Table 5. Addition of 15 µg/kg caudal morphine resulted in prolongation of postoperative analgesia by approximately double when compared with caudal ropivacaine 0.2 % alone.

**Table 6: Side effects among study groups.**

Side effects	Group I	Group II
<b>PONV</b>	0	1
<b>Pruritis</b>	0	0
<b>Respiratory depression</b>	0	0
<b>Urinary retention</b>	0	0

PONV: postoperative nausea and vomiting.

As seen in the Table 6, no side effects were observed in group I and group II, except 1 patient in group II had PONV.

## DISCUSSION

The study had been conducted on 60 children ASA I and II aged 1 to 7 years undergoing elective infraumbilical surgeries. Morphine 15 µg/kg was used as an additive to 0.2% ropivacaine through caudal epidural route and were compared with ropivacaine 0.2% alone in terms of hemodynamic parameters, quality, duration of analgesia and side effects if any. During intraoperative and postoperative period, the mean heart rate between group I vs group II did not show any significance (Table 1 and 2). During intraoperative period, the change in MAP between group I vs II was not significant from pre induction time till the end of surgery (Table 3). In postoperative period, intergroup comparison of group I vs II showed significant fall in MAP from 30 min till 3<sup>rd</sup> hour postoperatively. This fall was statistically significant (Table 4). Vetter et al found no significant change in hemodynamic parameters in pediatric patients undergoing ureteral reimplantation using single dose of caudal clonidine, morphine 50 µg/kg and hydromorphone each combined with ropivacaine 0.2% (1 ml/kg) with epinephrine 1:200000.<sup>9</sup> Zamora et al observed no change

in hemodynamic parameters in all the three groups of patients who received single dose of caudal epidural bupivacaine 0.50% mixed with morphine in three different doses (11.2 µg, 15 µg and 20 µg/kg respectively) in pediatric patients aged 1 to 15 years who underwent hip surgery for postoperative analgesia.<sup>8</sup> Dostbil et al observed no changes in hemodynamic parameters when caudal levobupivacaine 0.125% mixed with morphine in three different doses (7.5 µg, 10 µg and 15 µg/kg) was used for analgesia in children after circumcision surgery.<sup>11</sup> Kawaragushi et al observed no change in hemodynamic parameters with 0.2% ropivacaine (1 ml/kg) mixed with saline (0.02 ml/kg) and 0.2% ropivacaine (1 ml/kg) mixed with fentanyl (1 µg/kg) were given caudally to pediatric patients undergoing infraumbilical surgery for postoperative analgesia.<sup>12</sup> The results of our study show that the fall in heart rate and MAP were not significant in group II (morphine 15 µg/kg) as compared to group I (ropivacaine alone). Hence patients were stable and these results are in concordance with the studies of Vetter et al, Castillo Zamora et al, Kawaragushi et al and Dostbil et al who also reported hemodynamic stability using different doses of caudal morphine with local anesthetic agents.<sup>8,9,11,12</sup>

The objective assessment of the duration of analgesia was done using FLACC scale.<sup>10</sup> The mean duration of analgesia was 3.93±0.83 hour in group I, 7.30±1.78 hour in group II. The duration of analgesia was more in group II compared to group I which was statistically significant (Table 5). Addition of 15 µg/kg caudal morphine resulted in prolongation of postoperative analgesia by approximately double when compared with caudal ropivacaine 0.2 % alone. De Beer et al compared caudal ropivacaine 0.2% (1 ml/kg) and bupivacaine 0.25% (1 ml/kg) and observed that the duration of analgesia was 4.5 and 3.9 hours respectively in his double blind multicentre study of 245 children aged 1 to 10 years undergoing elective minor surgery.<sup>3</sup> Ivani et al observed a mean duration of analgesia of 4.51±2.01 hours when ropivacaine 0.2% (1 ml/kg) was compared with bupivacaine 0.2% (1 ml/kg) via caudal epidural route in children aged 1 to 10 years undergoing elective minor surgery.<sup>13</sup> Pandya et al compared 0.2% ropivacaine (1 ml/kg) with normal saline 0.04 ml/kg and received 0.2% ropivacaine with tramadol 2 mg/kg by caudal route and observed a mean duration of analgesia of 6.38±0.897 hours with 0.2% ropivacaine alone in pediatric patients aged 1 to 6 years undergoing elective lower umbilical surgery.<sup>14</sup> Kawaragushi et al observed mean duration of analgesia of 12.23 hrs with 0.2% ropivacaine (1ml/kg) mixed with saline (0.02 ml/kg) when compared to 0.2% ropivacaine (1 ml/kg) mixed with fentanyl (1µg/kg) given caudally to pediatric patients undergoing infraumbilical



surgery for postoperative analgesia.<sup>12</sup> Our study results with 0.2% ropivacaine are comparable to the studies of de Beer and Ivani et al whereas Pandya et al and Kawaraguchi et al observed a much longer duration of analgesia with 0.2% ropivacaine alone.<sup>3,12-14</sup>

Cesur et al studied the effects of reduction in the dose of caudal morphine in pediatric circumcision on quality of postoperative analgesia and morphine related side effects and observed analgesia of  $20.71 \pm 5.63$ ,  $22.68 \pm 3.2$  and  $23.76 \pm 0.8$  hours when morphine 7.5 µg, 10 µg and 15 µg/kg of morphine respectively was added to 0.125% levobupivacaine (0.5 ml/kg).<sup>15</sup> Dostbil et al compared the effects of different doses of caudal levobupivacaine 0.125% (0.5 ml/kg) mixed with morphine in three different doses (7.5 µg, 10 µg and 15 µg/kg) for analgesia in children after circumcision surgery. He observed a mean duration of analgesia of  $21.21 \pm 5.5$ ,  $22.68 \pm 3.2$  and  $23.76 \pm 0.8$  hours respectively when levobupivacaine 0.125% was combined with 7.5 µg, 10 µg and 15 µg/kg morphine respectively.<sup>11</sup> Duration of analgesia with addition of morphine in caudal block was much lesser in our study compared to studies done by Cesur et al and Dostbil et al (Table 5).<sup>11,15</sup>

Zamora et al compared three groups with caudal bupivacaine 0.5% (0.4 ml/kg) mixed with morphine in three different doses (11.2 µg, 15 µg and 20 µg/kg respectively). He observed vomiting with the incidence of 46.7%, 60% and 86.7%, pruritis and urinary retention in one patient each (6.66%) in pediatric patients aged 1-15 years who underwent hip surgery for postoperative analgesia.<sup>8</sup> Cesur et al studied the effects of reduction in the dose of caudal morphine in pediatric circumcision on quality of postoperative analgesia and morphine related side effects when 0.125% levobupivacaine (0.5 ml/kg) caudally was mixed with morphine and found out that postoperative incidence of vomiting was 5%, 12.5% and 17.5% with 7.5 µg, 10 µg and 15 µg/kg morphine respectively.<sup>15</sup> In our study, the incidence of PONV was 1 in group II (morphine 15 µg/kg) and nil in group I (ropivacaine alone). These incidences are much less as compared to the studies of Cesur et al and Zamora et al (Table 6).<sup>8,15</sup>

## CONCLUSION

Satisfactory postoperative analgesia was found after caudal ropivacaine and ropivacaine with morphine 15 µg/kg as adjuvant. Addition of morphine 15 µg/kg to caudal ropivacaine is an adequate dose for prolonging postoperative analgesia without significant change in hemodynamic parameters, with no side effects.

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