Caudal Block in Children

Ropivacaine Compared with Bupivacaine

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**Background:** Bupivacaine provides reliable, long-lasting anesthesia and analgesia when given *via* the caudal route. Ropivacaine is a newer, long-acting local anesthetic that (at a concentration providing similar pain relief) has less motor nerve blockade and may have less cardiotoxicity than bupivacaine.

**Methods:** In a double-blind trial, 81 healthy children, undergoing ambulatory surgical procedures, were randomly allocated to receive caudal analgesia with either bupivacaine or ropivacaine, 0.25%, 1 ml/kg. All blocks were placed by an attending anesthesiologist or an anesthesia fellow after induction of general anesthesia.

**Results:** Data were available for 75 children. There were no significant differences between the two groups in baseline characteristics or in anesthesia, surgery, recovery room, or day surgery unit durations. The quality and duration of postoperative pain relief did not differ. Motor and sensory effects were similar. Time to first micturition did not differ.

**Conclusion:** Ropivacaine (0.25%, 1 ml/kg) provided adequate postoperative analgesia with no difference from bupivacaine (0.25%, 1 ml/kg) in quality and duration of pain relief, motor and sensory effects, or time to first micturition in our study children. (Key words: Aminoamide local anesthetic; postoperative analgesia; R- and S-enantiomers.)

BUPIVACAINE (an amide local anesthetic) has provided reliable anesthesia and analgesia. Ropivacaine is also an amide local anesthetic, and in adults it produces pain relief similar to that of bupivacaine with a motor block that is slower in onset, less intense, and shorter in duration. Moreover, animal studies have shown that ropivacaine appears to be less cardiotoxic than bupivacaine.2,3

Although bupivacaine is a racemic mixture of *R* and *S*-enantiomers, ropivacaine is the first local anesthetic to be prepared as a pure *S*-enantiomer.4 It has been shown that block of the inactivated state of the cardiac sodium and potassium (hKvl.5) channels is stereoselective, with *R*-bupivacaine being more potent than *S*-bupivacaine.4 In clinical practice, *S*-bupivacaine, which exhibits a lower affinity for sodium and potassium (hKvl.5) cardiac channels, may be a less cardiotoxic alternative to racemic bupivacaine.4 Also, results of animal research have demonstrated that *R*-bupivacaine is more toxic than the *S*-enantiomer.5-7

By 1996, more than 2,500 adults had received ropivacaine in controlled clinical trials.1 The objective of this double-blind study was to compare the quality and duration of analgesia, motor and sensory effects, and time to first micturition after a single, presurgical caudal block with either ropivacaine or bupivacaine in anesthetized children.

**Methods**

After institutional approval and parental written informed consent were obtained, healthy boys and girls, aged 1-10 yr, American Society of Anesthesiologists (ASA) physical status I or II, scheduled for elective, outpatient urologic, lower abdominal, or lower extremity operations were allocated by random number table to receive caudal anesthesia with either bupivacaine or ropivacaine after induction of a general anesthetic. Children with neuromuscular disease, back problems, skin infection of the caudal area, mental retardation, or delayed development were excluded.
**Anesthetic Procedure**

Patients were fasted and 15–20 min before induction were premedicated in the day surgery unit (DSU) with oral midazolam, 0.5 mg/kg. After applying standard monitors, general anesthesia was induced with halothane and nitrous oxide 60% in oxygen via mask. An intravenous cannula was placed, and glycopyrrolate, 5 mg/kg, was given. Lactated Ringer’s solution was used to correct fluid deficit and for maintenance. The airway was maintained with a mask, laryngeal mask, or endotracheal tube. Intravenous rocuronium, 0.5 mg/kg, was administered to facilitate orotracheal intubation.

The study solutions were provided by the hospital pharmacy and were administered in a double-blind manner. While the child was lying in the left lateral position, a caudal injection of ropivacaine or bupivacaine, 0.25%, 1 ml/kg, was administered, using a short B-bevel, 22-gauge needle. All blocks were accomplished by an attending anesthesiologist or an anesthesia fellow. To detect and avoid an intravenous or subarachnoid injection, the anesthesiologist repeatedly aspirated the needle and injected the local anesthetic in increments while watching vital signs and the electrocardiographic (ECG) monitor. End-tidal halothane was adjusted to 1.2% before surgical incision.

An independent, blinded observer recorded blood pressure and heart rate just before and after surgical incision and every 5 min thereafter until anesthesia was discontinued. If there were no changes in vital signs in response to the initial incision, end-tidal halothane concentration was decreased gradually to 0.6%. If a child responded to the incision with an increase in blood pressure or heart rate, intravenous fentanyl, 1 pg/kg, was administered. At the end of surgery, muscle paralysis was reversed with glycopyrrolate and neostigmine. The child was extubated when awake.

**Observations and Statistical Analysis**

Postoperatively, the independent observer recorded (1) the quality of pain relief using a modified pain score as described by Hannallah,8 (2) the duration of pain relief (defined as the time from caudal placement until the first dose of postoperative analgesia), (3) motor power and reflexes (table 1), (4) sensory level and sensory recovery (time from caudal placement until the child regained complete sensory recovery), and (5) time to first micturition. Sensory level and recovery were evaluated by pinprick test every 15 min. Pain relief, motor power recovery, reflexes, and micturition were evaluated every 15 min until hospital discharge; sensation was evaluated until complete sensory recovery. In the post-anesthesia care unit (PACU), intravenous morphine, 0.05–0.1 mg/kg, was given when a patient scored 4 or higher on the pain scale. Nurses in the PACU decided when morphine was needed and administered it. After hospital discharge, children were given acetaminophen-codeine elixir (10 mg/kg with codeine, 1 mg/kg) by parental determination.

Anesthesia duration, surgery duration, and awakening time (period from end of anesthesia to opening of eyes) were recorded. Children were not discharged until they were awake and pain was controlled. They were not required to drink, pass urine, have complete sensory recovery, or regain complete muscle power before discharge.

Sample size calculation—to compare the effect of bupivacaine with ropivacaine on pain score, motor power, reflexes, and sensation, power analysis was performed. This analysis was based on the two-sample t test with a P < 0.05, 80% power, and the following assumptions: a detection of a mean difference in pain score of 1.5 with an SD 1.5, a mean difference in motor power of 1.0 with an SD of 1.5, and a mean difference in reflex score of 1.0 with an SD of 1.0. It was also assumed that the time from caudal placement to sensory recovery will differ by 30 min and SD will be 20 min in both groups. Power analysis indicated that the minimal number of patients in each group should be 36.

Student t test and Wilcoxon test were used for continuous variables, including baseline characteristics; vital signs; durations of surgery, anesthesia, PACU stay, DSU...
stay, caudal analgesia; and time to first micturition. Fisher exact test was used for categorical data such as gender; type of surgery; and use of fentanyl in operating room, morphine in PACU, or acetaminophen-codeine elixir at home. A P value < 0.05 was considered statistically significant. All statistical comparisons were accomplished with SAS for NT (version 6.12; SAS Institute, Cary, NC).

Results

Although 81 children were randomly allocated to medication, the anesthesiologist was unable to place the caudal block in two older children, and four children (two younger than 1 yr and two older than 10 yr) were eliminated to decrease the age range. Therefore, 75 children, aged 1-10 yr, comprised the study population, and all were included in the analysis. They had urologic, lower abdominal, or lower extremity operations, and the type of surgery did not differ between the two groups (table 2). Thirty-six children received bupivacaine and 39 received ropivacaine. There were no differences between the two groups in age; weight; gender; ASA physical status; baseline blood pressure or heart rate; or durations of anesthesia, surgery, awakening time, PACU, or DSU (table 3). After surgical incision, the two groups did not differ in intraoperative vital signs (table 4). None of the children developed a hemodynamic problem, respiratory difficulty, or any other adverse effect.

Pain Relief

The quality and duration of postoperative pain relief did not differ between the two groups. Thirty-six percent of children in the bupivacaine group and 33% in the ropivacaine group required no additional pain medication during the 24-h study period. Six children (one given bupivacaine; five given ropivacaine) were given fentanyl, 1 μg/kg, at the start of surgery because they responded to the initial incision (P = 0.2). Three of 36 patients receiving bupivacaine and two of 39 receiving ropivacaine required morphine in the recovery room. Acetaminophen-codeine elixir was given at home to 23 and 26 children in the bupivacaine and ropivacaine groups, respectively. The median time from caudal placement to the first administration of pain medication (either morphine or acetaminophen-codeine) was 680 min for both treatment groups. The 25th percentile was 375 min for bupivacaine and 465 min for ropivacaine. The 75th percentile was 1,440 min (24 h) for both groups. There was no correlation between pain score (or need for analgesia) and regression of sensory or motor blockade.

Motor Power and Reflex Recovery

None of our study children had complete motor power recovery (score 10) within 3 h after placement of the caudal block; the highest observed score within 3 h was 8 for both groups (fig. 1). Most patients were discharged with a score of 8. Some children with residual muscle weakness walked with assistance (holding a parent’s hand), whereas others were carried to the car. Reflex scores did not differ between the two groups (fig. 2).

Sensory Effects

Sensory level and sensory block did not differ between the treatment groups. The median sensory level was T10 for both groups. The 25th percentile was T10 for the bupivacaine group and T11 for the ropivacaine group. The 75th percentile was T10 for both groups. Sensory block resolved completely by 80 ± 27 min in the bupivacaine group and by 83 ± 23 min in the ropivacaine group (fig. 3).

There was no difference between the two groups in

Table 3. Patient Characteristics and Clinical Parameters

<table>
<thead>
<tr>
<th>Variable</th>
<th>Bupivacaine (n = 36)</th>
<th>Ropivacaine (n = 39)</th>
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</thead>
<tbody>
<tr>
<td>Age (mo)</td>
<td>44 ± 29</td>
<td>38 ± 27</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>17 ± 6</td>
<td>15 ± 7</td>
</tr>
<tr>
<td>Gender, male (%)</td>
<td>35 (97)</td>
<td>37 (95)</td>
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<tr>
<td>Caudal placement to surgery</td>
<td></td>
<td></td>
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<tr>
<td>start (min)</td>
<td>9 ± 4</td>
<td>10 ± 5</td>
</tr>
<tr>
<td>Anesthesia duration (min)</td>
<td>57 ± 24</td>
<td>66 ± 39</td>
</tr>
<tr>
<td>Surgery duration (min)</td>
<td>39 ± 22</td>
<td>43 ± 39</td>
</tr>
<tr>
<td>End of anesthesia to awakening (min)</td>
<td>34 ± 21</td>
<td>34 ± 21</td>
</tr>
<tr>
<td>PACU duration (min)</td>
<td>80 ± 30</td>
<td>89 ± 39</td>
</tr>
<tr>
<td>DSU duration (min)</td>
<td>33 ± 25</td>
<td>35 ± 35</td>
</tr>
</tbody>
</table>

Values are mean ± SD.

PACU = postanesthesia care unit; DSU = day surgery unit.
Table 4. Intraoperative Vital Signs

<table>
<thead>
<tr>
<th>Time</th>
<th>Bupivacaine</th>
<th>Ropivacaine</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>MBP</td>
</tr>
<tr>
<td>Baseline</td>
<td>37</td>
<td>61 ± 14</td>
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<tr>
<td>Incision</td>
<td>26</td>
<td>56 ± 7</td>
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<tr>
<td>5 min</td>
<td>20</td>
<td>56 ± 9</td>
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<tr>
<td>10 min</td>
<td>17</td>
<td>54 ± 8</td>
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<tr>
<td>15 min</td>
<td>15</td>
<td>54 ± 9</td>
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<tr>
<td>20 min</td>
<td>11</td>
<td>57 ± 9</td>
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<tr>
<td>25 min</td>
<td>8</td>
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<tr>
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<td>5</td>
<td>50 ± 6</td>
</tr>
<tr>
<td>60 min</td>
<td>0</td>
<td>N/A</td>
</tr>
</tbody>
</table>

Values are mean ± SD. No differences were found between bupivacaine group and ropivacaine group.

MBP = mean blood pressure = diastolic BP + (systolic BP - diastolic BP)/3; HR = heart rate; N/A = not applicable.

* Significant change from baseline value.

mean time to first micturition (254 ± 140 min for bupivacaine and 321 ± 164 min for ropivacaine; no child required catheterization.

Discussion

Our study substantiates recent reports that a single, caudal injection of ropivacaine after induction of anesthesia provides reliable and long-lasting analgesia in children having ambulatory surgery. It resembles bupivacaine. Similar to early adult studies with ropivacaine, we used 0.25% solution for both anesthetics. In 1998, it was reported that 2 mg/kg of 0.2% ropivacaine is sufficient to obtain a sensory block for lower abdominal or genital surgery in children aged 1-9 yr. Placing the block before the surgical incision provides intraoperative pain relief, reduces the general anesthetic requirement, affords earlier recovery of airway reflexes, and contributes to a comfortable awakening.

In our study, children receiving fentanyl were not equally divided between the two treatment groups, which may have caused us to overestimate the effectiveness and duration of analgesia in the ropivacaine group.

Fig. 1. Mean ± SD for motor power recovery score from time of caudal placement up to 3 h in two treatment groups. None of our study children had complete motor power recovery (score 10) within 3 h after placement of the caudal block; the highest observed score within 3 h was 8 for both groups.

Fig. 2. Mean ± SD for reflex recovery score from time of caudal placement up to 3 h in two treatment groups. Reflex scores did not differ between the two groups.
ROPIVACAINE COMPARED WITH BUPIVACAINE

Fig. 3. Percentage of patients having complete sensory recovery from time of caudal placement up to 3 h in two treatment groups. Sensory recovery did not differ between the two treatment groups.

However, we expect fentanyl, 1 µg/kg, to "wear off" within 30 - 45 min (mean surgery duration, 41 min), and the mean period from surgery start time to awakening was not longer in the ropivacaine group. None of these six children receiving fentanyl required additional intraoperative fentanyl, and halothane concentration was reduced from end tidal 1.2% to 0.6%. In the recovery room, all children demonstrated signs of motor block, and all had adequate sensory levels.

Our median time from caudal placement to first dose of pain medication was 11 h for both treatment groups. A similar pediatric trial using 0.375% bupivacaine or ropivacaine, 1 ml/kg, showed that postoperative analgesia was required at a mean time of 5 h for both drugs. In contrast, Ivani et al.9 reported a significant difference between the two drugs in the mean time to requirement of additional analgesia (253 min for bupivacaine and 520 min for ropivacaine, P < 0.05).

Similar to previous studies, we included children scheduled for genital operations having lumbosacral innervation (low procedures) or operations in locations having lower thoracic innervation (high procedures); the number of low or high procedures did not differ between our two treatment groups. Previously, Wolf et al.13 demonstrated that 0.75 ml/kg of 0.25% or 0.125% bupivacaine was adequate for high procedures in children. We administered 1 ml/kg for both drugs.

In the PACU, all of our study children demonstrated signs of motor block (fig. 1), and there was early resolution of sensory block when compared with the recovery pattern for motor block. Ivani et al.9 using caudal injection of bupivacaine, 0.25%, or ropivacaine, 0.2%, 2 mg/kg, found no motor block on awakening in either group. Da Conceicao and Coelho,10 who used a higher concentration (0.375%), reported that their ropivacaine group (receiving 1 ml/kg) showed a significantly shorter duration of motor block.

Most adult clinical trials to date, and our pediatric trial, have shown no significant differences in the quality or duration of sensory blockade between equal doses and concentrations of bupivacaine and ropivacaine.14-16 However, other studies have reported differences in the duration of sensory block.17-19

An infant rat model to study local anesthetic effects in percutaneous sciatic nerve blockade was recently reported.20 Blockade with bupivacaine and ropivacaine lasted much longer in the infant than in the adolescent or adult rats when the same volume and concentrations of drug were given. Neither drug appeared to be more sensory selective than the other in young and older rats.21 Infant rats were much more resistant to the toxicity of bupivacaine and ropivacaine than older rats, and ropivacaine was invariably (and at all ages) less toxic than bupivacaine.21 However, it has been reported that human infants are at a greater risk of bupivacaine toxicity compared with older age groups.22-25

Few pharmacokinetic studies of ropivacaine in children have been published. Habre et al.24 reported that 1 ml/kg of ropivacaine, 2.5 mg/ml, by caudal block produced a maximal venous plasma concentration of 0.72 ± 0.24 mg/l at 2 h, which is much later than that reported for bupivacaine in children (29 ± 3.1 min)25 and considerably lower than the maximal tolerated venous plasma concentration of ropivacaine in 12 adult volunteers (2.2 ± 0.8 mg/l).20

In conclusion, caudal ropivacaine provided reliable postoperative analgesia similar to bupivacaine in quality and duration of pain relief, motor and sensory effects, and time to first micturition in our study children. Because it is less cardiotoxic, it may be safer.

References

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