Clinical Effects and Maternal and Fetal Plasma Concentrations of Epidural Ropivacaine Versus Bupivacaine for Cesarean Section

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Background: Ropivacaine is a new amide local anesthetic structurally similar to bupivacaine and mevipacaine. Previous studies showed that ropivacaine has a similar clinical effect as bupivacaine with regard to sensory anesthesia and slightly less motor blockade than bupivacaine. Ropivacaine appears to be less cardiotoxic and arrhythmogenic than bupivacaine. The clinical and pharmacokinetic effects of 0.5% ropivacaine (5 mg/ml) versus 0.5% bupivacaine (5 mg/ml) when used epidurally for elective cesarean section were investigated.

Methods: Using a randomized, double-blind study design, 60 ASA physical status 1 or 2 term parturients presenting for elective cesarean section received either 0.5% bupivacaine (150 mg) or 0.5% ropivacaine (150 mg) epidurally in appropriate fractionated doses over a 10-min period. Onset, duration, and regression of sensory and motor blockade were noted until complete resolution was observed. Quality of intraoperative anesthesia and abdominal wall muscle relaxation were noted. Maternal plasma concentrations of local anesthetic were determined before anesthetic administration and 5, 10, 20, 30, and 60 min and 2, 3, 6, 8, 12, and 24 h after drug injection in 20 subjects. Umbilical cord blood was obtained at time of delivery for acid-base values and determination of the free and total plasma concentration of local anesthetic. Neonates also were examined for neurobehavioral assessments by Scanlon’s and Neurologic and Adaptive Capacity Scores at 2 and 24 h after delivery.

Results: All patients received satisfactory anesthesia for operation. The onset, duration, and regression of sensory blockade were similar for both groups. Onset of degree 1 and 2 motor blockade was faster, and duration of degree 1 motor blockade was longer in the group receiving bupivacaine. Hemodynamic sequelae were similar between groups. All neonates had 5-min Apgar scores of 7 or greater and normal acid-base values and neurobehavioral assessments. Pharmacokinetic analysis showed that the \( t_{1/2} \), was similar for both drugs (1.3 ± 0.09 for ropivacaine and 1.1 ± 0.09 µg/ml for bupivacaine). The \( t_{1/2} \) of ropivacaine versus bupivacaine (5.2 ± 0.60 versus 10.9 ± 1.08 h, respectively; \( P < 0.01 \)). The free (i.e., unbound) concentrations of ropivacaine were approximately twice those of bupivacaine in both maternal and neonatal blood at the time of delivery. The ratio of umbilical vein to maternal vein concentration of unbound drug was 0.72 for ropivacaine and 0.69 for bupivacaine.

Conclusions: Ropivacaine, 0.5%, epidurally provided satisfactory and similar sensory anesthesia compared to 0.5% bupivacaine for elective cesarean section. The \( t_{1/2} \) was similar for both drugs; although the terminal half-life of ropivacaine was significantly shorter, and the blood concentrations of ropivacaine were significantly greater than that for bupivacaine. These values were less than concentrations shown to be toxic in animals. (Key words: Anesthesia; epidural; obstetric. Local anesthetics: bupivacaine; ropivacaine.)

ROPIVACAINE (1-propyl-2,6-piperidinoxyethylid hydrochloride monohydrate) is a new, long-acting amide local anesthetic with a structure closely related to bupivacaine and mevipacaine. Whereas both bupivacaine and mevipacaine are available as a racemic mixture, ropivacaine is available only as the pure 5-enantiomer.

Reports of animal studies show that ropivacaine has less central nervous and cardiovascular system toxicity than does bupivacaine.† In human volunteers, ropivacaine has been shown to be less toxic than bupivacaine with regard to central nervous system and cardiovascular changes after intravenous infusion.‡ Clinically, during the use of epidural anesthesia in nonpregnant human subjects, ropivacaine and bupivacaine in equipotent doses are associated with similar onset time, duration of sensory blockade, and overall

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clinical effects, ropivacaine is considered to be preferable to bupivacaine. Ropivacaine is not associated with arterial blood pressure changes.

Although ropivacaine and bupivacaine are structurally similar, ropivacaine is metabolized by the liver and excreted in the bile. This characteristic may contribute to the more rapid metabolism of ropivacaine compared to bupivacaine.

Methodology

The protocol was approved by the institutional review board. All patients were informed of the potential complications of surgery and consented to participate in the study. The institutional review board approved the study protocol and the study was conducted in accordance with the Declaration of Helsinki. All patients were monitored with a cardiac monitor and pulse oximeter. Intravenous access was obtained with a 22-gauge needle. Patients were placed in a blanket position on the operating table in the L2–L3 or L3–L4 interspace. The epidural catheter was threaded through a 19-gauge Tuohy needle. The epidural space was confirmed by the loss of Ringer’s lactate on the injection of 1 cc of saline. The epidural needle was removed, and the epidural catheter was secured to the patient’s skin with tape. The catheter was then used for continuous infusion of ropivacaine every 8 h. The study was performed with a 2 × 2 factorial design for the following variables: Ropivacaine versus Bupivacaine and 0.5% versus 0.75% concentration. The number of patients in each group was determined based on the number of Astra Pharma representatives who agreed to participate in the study. The study began at 5, 10, 15, and 20 min after the study began.
Epidural Ropivacaine and Bupivacaine

Clinical efficacy. However, the intensity of motor block appears to be reduced with ropivacaine compared to bupivacaine. In pregnant sheep, ropivacaine is not associated with any adverse effects on uterine artery blood flow or fetal well-being.

Although ropivacaine has been investigated in non-pregnant humans for a variety of surgical and anesthetic procedures, this agent has not been described in the pregnant patient. We conducted a randomized, double-blind trial comparing a fixed dose (150 mg) of 0.5% ropivacaine and 0.5% bupivacaine for elective cesarean section. The purpose of this trial was to assess the clinical effects and pharmacokinetics of ropivacaine, in humans, when used in obstetric anesthesia.

Methods

The protocol was approved by our hospital institutional review board, and informed consent was obtained from all patients. Inclusion criteria were uncomplicated singleton pregnancy between 37 and 42 weeks, age 16–40 yr; weight less than 110 kg; scheduled, elective cesarean section; no concomitant maternal or fetal medical complications; and planned epidural anesthesia. Before induction of epidural anesthesia, each patient received 10 mg metoclopramide intravenously and 30 ml Nutricel (sodium citrate solution; N.E. Pharmaceuticals, Peabody, MA) orally, and acute volume expansion with 1,500–2,000 ml of Ringer’s lactate solution intravenously. The epidural space was identified using a 17-G Weiss needle at the L2–L3 or L3–L4 interspace using loss-of-resistance to air technique, and 2–5 cm of the epidural catheter was threaded through the needle. After placement of the epidural catheters, all patients were placed in the supine position with uterine displacement achieved by a blanket roll under the right hip. Three milliliters of study solution was injected as a test dose, and the patient was observed for signs of subarachnoid or intravascular injection. Thirty milliliters of either 0.5% bupivacaine or 0.5% ropivacaine was injected epidurally in divided doses over 10 min. Randomization was performed using a computer-generated random-number scheme and all drugs were supplied in sequentially numbered, identical-appearing ampules provided by Astra Pharmaceutical (Södertälje, Sweden). All study personnel were blinded to the drug administered. Assessment of sensory block to pinprick was determined at 5, 10, 15, 20, 25, and 30 min after the injection of the study drug. Thereafter, assessments were made every 30 min up to 5 h and then every hour until the return of normal sensation. The degree of motor blockade was assessed bilaterally at the same times using a modified Bromage scale: 0 = ability to move hips, knees, and ankles; 1 = inability to raise extended leg (just able to flex knee); 2 = inability to flex knee (able to flex foot only); and 3 = inability to flex knee (unable to flex foot or knee).

Maternal heart rate, systolic, and diastolic blood pressure were followed intermittently during induction of anesthesia, surgery, and the postoperative period by using an automatic blood pressure recorder. Values were recorded at 5, 10, 20, 30, 60, 90, 120, 150, and 180 min after the injection of epidural solution. Hypotension was defined as the systolic blood pressure of ≤90 mmHg or 30 mmHg below the baseline systolic pressure. Hypotension was corrected with 5–10 mg intravenous ephedrine and infusion of Ringer’s lactate. Fetal heart rate was recorded continuously during induction of epidural anesthesia. Quality of anesthesia and abdominal wall muscle relaxation were judged by one of the investigators and surgeons after the end of the surgery as satisfactory or unsatisfactory. Patients were asked to rate their perceived pain on a 100 mm visual analog scale with ‘0’ as no pain and ‘100’ as ‘worst pain ever.’ Visual analog scale assessments were observed at the following times: (1) at skin incision, (2) at uterine incision, (3) at uterine exteriorization, and (4) on arrival in recovery room.

Neonatal assessments were done by measuring umbilical vein and umbilical artery blood gas measurements at the time of delivery from a double-clamped segment of umbilical cord. A sample of maternal blood was drawn from the antecubital vein at the time of delivery. Apgar scores at 1 and 5 min were determined by a pediatrician. All infants were examined using both neurologic and adaptive capacity scores and Scanlon’s early neonatal neurobehavior scores at 2 and 24 h after birth.

Pharmacokinetic Assessments

Peripheral maternal venous blood samples were collected from 20 subjects via an indwelling large bore intravenous catheter with a stopcock connected, located in a large vein in the arm contralateral to that used for intravenous infusions. Blood samples of 5 ml were collected for determination of total drug concentration at the following times: before epidural drug administration (baseline); O (end of local anesthetic injection); 5, 10, 20, 30, and 60 min and 2, 4, 6, 8,
12, and 24 h after completion of the injection, and at the time of delivery. An additional 5 ml of blood was taken for determination of free drug concentration and concentration of α 1 acid glycoprotein at baseline, 30 min, and delivery. Maternal venous blood gas measurements were determined at time of delivery. Umbilical artery and vein blood samples were obtained from a double-clamped segment of cord for determination of total and free local anesthetic concentration and α 1 acid glycoprotein. Blood samples were centrifuged at room temperature within 60 min of collection, and the plasma was transferred to fresh tubes (5 ml, Cryotube, Nunc, Denmark). All plasma was immediately frozen and maintained at −20°C. The total concentrations of local anesthetics were determined by using gas chromatography. The detection limit of the method was 0.008 mg/l (0.03 μmol/l), the interassay precision about 5%, and the recovery close to 100%.

The free concentration of ropivacaine and bupivacaine was determined by coupled-column liquid chromatography after ultrafiltration of the plasma samples. Ropivacaine and bupivacaine were detected by ultraviolet at 210 nm, and the limit of detection was set at 0.003–0.008 mg/l (0.01–0.03 μmol/l). The interassay precision was about 3% for the two drugs, determined from aqueous standards. The recovery was close to 100% for both drugs. The analysis of α 1 acid glycoprotein was performed by using a radioimmunoassay procedure, using a commercially available kit (NOR-Patien, Behringwerke, Marburg, Germany). The limit of determination was set at 2 μmol/l. The precision was 5%.

The peak plasma concentration (Cmax) of ropivacaine was estimated from the observed concentration-time points using log linear regression. Epipodal clearance was calculated as dose (mg base)/total area under the plasma concentration-time curve, assuming 100% bioavailability from the epidural space.

### Table 1. Patient Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Ropivacaine (n = 31)</th>
<th>Bupivacaine (n = 29)</th>
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</thead>
<tbody>
<tr>
<td>Maternal age (yr)</td>
<td>31.5 ± 0.92</td>
<td>33.0 ± 0.86</td>
</tr>
<tr>
<td>Maternal height (cm)</td>
<td>160 ± 0.56</td>
<td>161 ± 0.47</td>
</tr>
<tr>
<td>Maternal weight (kg)</td>
<td>75.2 ± 5.37</td>
<td>73.0 ± 4.62</td>
</tr>
<tr>
<td>Infant birth weight (kg)</td>
<td>3.6 ± 0.14</td>
<td>3.4 ± 0.18</td>
</tr>
</tbody>
</table>

No significant differences between groups. Values are mean ± SE.

Statistical analysis was performed using analysis of variance, Wilcoxon's rank-sum test, chi-square test, and Fisher's exact test, where appropriate. Wilcoxon's rank-sum test was used to compare the treatments with regard to onset and duration of sensory and motor block. Onset and duration were compared at each segment for sensory block and at each degree of motor block. Results are expressed as mean ± SE. A P value of <0.05 was considered statistically significant.

### Results

Sixty-nine subjects were enrolled in the protocol. Nine patients were excluded because of technical failures (5), lost data (1), prolonged delay due to inability to schedule an operating room (1), protocol deviation due to obesity (1), and necessity of administration of chloroprocaine to achieve T1 block (1). Thus, 60 subjects remained for evaluation: 31 received ropivacaine, and 29 received bupivacaine. A comparison of the two groups of patients (table 1) revealed no significant differences in maternal demographic characteristics.

**Sensory Block**

Figures 1 and 2 present the mean onset and offset of sensory block by segment. Mean onset of sensory anesthesia was similar between groups for all segmental levels. It varied between 2.7 min (L1) to 14.1 min (S3) for ropivacaine and 2.8 min (L1) to 13.3 min (S3) for bupivacaine. T4 block occurred in a mean of 14 ± 8 min in ropivacaine group and 14 ± 3 min in bupivacaine group; however, this was not statistically significant. No patient had a prolonged onset of sensory block (5 min or more). The mean duration of sensory block was 7.3 ± 1.0 h in ropivacaine group and 7.0 ± 1.2 h in bupivacaine group; this difference was not statistically significant.

**Motor Block**

Motor block occurred in 11 patients in ropivacaine group and in 13 patients in bupivacaine group. Motor block occurred in 83%, 74%, 68%, and 67% of patients in ropivacaine versus bupivacaine groups. Mean time to achieve 2 to 3 motor block was 2 to 3 h in ropivacaine group and 2 to 3 h in bupivacaine group. There were no significant differences between motor block times (table 2).

### Table 2. Motor Block Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Ropivacaine (n = 31)</th>
<th>Bupivacaine (n = 29)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset of block (min)</td>
<td>2.7 ± 0.5</td>
<td>2.8 ± 0.6</td>
</tr>
<tr>
<td>Mean duration (h)</td>
<td>7.3 ± 1.0</td>
<td>7.0 ± 1.2</td>
</tr>
</tbody>
</table>

No significant differences between groups. Values are mean ± SE.

The incidence of both groups was high. The incidence of side effects was similar in both groups (table 3). No other side effects for the two groups were observed.
EPIDURAL ROPIVACAINE AND BUPIVACAINE

Fig. 2. Levels of offset of sensory epidural anesthesia as a function of time for ropivacaine and bupivacaine.

14 ± 8 min for ropivacaine and 17 ± 10 min for bupivacaine, which was not statistically different. The maximum upper level of sensory block observed in any patient for ropivacaine was C8 versus T1 for bupivacaine. Mean duration of sensory block at the T4 dermatome was 2.4 ± 0.9 h (ropivacaine) versus 2.4 ± 1.0 h (bupivacaine) and 6.5 ± 1.5 h (ropivacaine) versus 6.3 ± 2.2 h (bupivacaine) at the T12 dermatome (P = NS).

Motor Block

Frequency of motor blockade did not differ between groups. In the bupivacaine group, 97%, 77%, and 40% achieved degrees 1, 2, and 3, respectively, compared to 83%, 59%, and 21% for the patients in the ropivacaine group (P = NS). It required a significantly longer mean time for onset of motor blockade degrees 1 and 2 to occur in patients receiving ropivacaine (table 2). There was also significantly shorter duration of degree 1 motor blockade for patients in the ropivacaine group (table 2).

Maternal Blood Pressure

The incidence of maternal hypotension was 90% in both groups; 28 patients in ropivacaine needed ephedrine versus 26 patients in bupivacaine group (P = NS; table 3). A similar dose of ephedrine was used in both groups of patients: 17.4 ± 5.1 mg and 18.2 ± 3.2 mg for the ropivacaine and bupivacaine groups, respectively.

Table 2. Motor Blockade

<table>
<thead>
<tr>
<th>Degree</th>
<th>Onset (min)</th>
<th>Duration (h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>10.3 ± 0.89*</td>
<td>3.1 ± 0.19*</td>
</tr>
<tr>
<td>2</td>
<td>16.0 ± 0.95*</td>
<td>2.6 ± 0.25</td>
</tr>
<tr>
<td>3</td>
<td>28.0 ± 3.36</td>
<td>3.0 ± 0.45</td>
</tr>
</tbody>
</table>

Values are mean ± SE.

* P < 0.05, ropivacaine versus bupivacaine, Wilcoxon's rank-sum test.

Quality of Sensory Anesthesia and Muscular Relaxation

Satisfactory anesthesia and muscle relaxation were observed in both groups. None of the patients perceived any pain during skin incision. One patient in the ropivacaine group experienced mild pain (visual analog scale score <3) during uterine incision. Three patients in each group experienced pain during uterine exteriorization. One patient in the bupivacaine group and one in the ropivacaine group experienced mild to moderate pain (visual analog scale score 3–6) on arrival in the recovery room. None of the patients needed intravenous analgesia or sedation during surgery.

Neonatal Data

No abnormalities in fetal heart rate were noted during induction of epidural anesthesia. Apgar scores were 7 or greater at 5 min in all neonates in both groups, and normal pH values in the cord blood were observed. There were no significant differences between either Scanlon’s early neonatal neurobehavior scores or neurologistic and adaptive capacity scores between the two groups.

Pharmacokinetic Analysis

Plasma concentration-time profiles of ropivacaine and bupivacaine are shown in figures 3 and 4. A similar

Table 3. Mean (±SE) Value for Maternal Heart Rate and Blood Pressure

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Heart Rate</th>
<th>Systolic Blood Pressure</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>87 ± 2.7</td>
<td>117 ± 2.1</td>
</tr>
<tr>
<td>5</td>
<td>95 ± 3.8</td>
<td>111 ± 2.9</td>
</tr>
<tr>
<td>10</td>
<td>90 ± 2.9</td>
<td>115 ± 3.0</td>
</tr>
<tr>
<td>15</td>
<td>91 ± 3.6</td>
<td>112 ± 2.0</td>
</tr>
<tr>
<td>30</td>
<td>88 ± 3.6</td>
<td>116 ± 1.8</td>
</tr>
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</table>

No significant differences between groups.

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Cmax was obtained: 1.3 ± 0.09 for ropivacaine and 1.1 ± 0.10 μg/ml for bupivacaine (table 4). The half-life of the terminal decline in plasma concentration was 5.2 ± 0.60 h for ropivacaine and 10.9 ± 1.07 h for bupivacaine (P < 0.01). The clearance, however, was the same for both agents (0.25 ± 0.02 l/min for ropivacaine, and 0.29 ± 0.02 l/min for bupivacaine). The free plasma maternal concentrations of ropivacaine at time of delivery were much higher than those of bupivacaine (4.2 ± 0.5 vs. 0.5 ± 0.1 μg/ml). The plasma concentrations of ropivacaine were 0.008 μg/ml (95% CI 0.001–0.019 μg/ml) and of bupivacaine were 0.004 μg/ml (95% CI 0.001–0.012 μg/ml). The peak umbilical vein concentration was 0.003 μg/ml for ropivacaine and 0.006 μg/ml for bupivacaine.

Discussion

Pharmacokinetics of drugs administered to attempt to achieve local anesthetic block, that is epidural anesthesia, during labor, is the most common type of anesthesia used in the United States. The sensory motor block is achieved by placing a catheter in the subarachnoid space, and when adequate anesthesia is achieved, the toxicity is minimal. However, during pregnancy, the fetus is sensitive to the effects of local anesthetics and may possess a greater susceptibility to bupivacaine due to its capacity to cross the placenta. This may cause a greater risk of fetal bradycardia and arrest during fetal development. 

The results of ropivacaine were better than those of bupivacaine.

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Table 4. Pharmacokinetic Parameters

<table>
<thead>
<tr>
<th></th>
<th>Ropivacaine</th>
<th>Bupivacaine</th>
</tr>
</thead>
<tbody>
<tr>
<td>C_{max} (µg/ml)</td>
<td>1.3 ± 0.09</td>
<td>1.1 ± 0.00</td>
</tr>
<tr>
<td>T_{1/2} (h)</td>
<td>5.2 ± 0.6*</td>
<td>10.9 ± 1.08</td>
</tr>
<tr>
<td>Free plasma concentrations (µg/ml)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maternal vein</td>
<td>0.099 ± 0.008*</td>
<td>0.055 ± 0.004</td>
</tr>
<tr>
<td>Umbilical vein</td>
<td>0.072 ± 0.008*</td>
<td>0.041 ± 0.002</td>
</tr>
<tr>
<td>Umbilical artery</td>
<td>0.075 ± 0.005*</td>
<td>0.038 ± 0.003</td>
</tr>
<tr>
<td>UV/MV ratio</td>
<td>0.72</td>
<td>0.69</td>
</tr>
<tr>
<td>CL (l/min)</td>
<td>0.25 ± 0.02</td>
<td>0.29 ± 0.02</td>
</tr>
</tbody>
</table>

C_{max} = peak plasma concentrations; T_{1/2} = terminal half-life; UV/MV ratio = umbilical vein to maternal vein concentration; CL = clearance.

*P < 0.01, ropivacaine versus bupivacaine.

At time of delivery were about twice as high as the free concentrations of bupivacaine (0.099 ± 0.008 µg/ml vs. 0.055 ± 0.004 µg/ml, P < 0.01). The neonatal free plasma concentrations (from umbilical vein) of ropivacaine was greater than for bupivacaine, 0.072 ± 0.008 µg/ml compared to 0.041 ± 0.002 µg/ml, respectively (P < 0.01). At the time of delivery, free plasma concentrations of both drugs (from umbilical vein) were greater in the neonate compared to the mother. Umbilical artery concentrations were twice as great in the ropivacaine group compared to bupivacaine group (0.075 µg/ml ± 0.005 mg/l vs. 0.038 ± 0.003 µg/ml, P < 0.01).

Discussion

Pharmacologic and laboratory investigations continue to attempt to develop a new long-acting local anesthetic that is efficacious and safe. Bupivacaine has become the most popular agent for obstetric analgesia and anesthesia during labor, because of its favorable sensory-motor differentiation. However, bupivacaine has been associated with severe cardiovascular toxicity when accidentally injected intravascularly, and this toxicity has been observed to be significantly greater during pregnancy.\(^\text{14-16}\) Intact animal studies and in vitro nerve preparations demonstrated ropivacaine to possess sensory anesthetic effects similar to those of bupivacaine.\(^\text{17}\) However, ropivacaine appears to have a greater margin of safety with regard to cardiovascular and arrhythmogenic toxicity compared to bupivacaine.\(^\text{1-6}\)

The results of the current study demonstrated that ropivacaine and bupivacaine provided similar sensory anesthesia, which was adequate for the surgical procedure. Motor blockade occurred with slower onset and shorter duration in patients who received ropivacaine. These findings may be of clinical significance with regard to postoperative recovery room stay and use of these agents during labor, although these parameters were not assessed in this study. A previous study in volunteers also observed satisfactory sensory anesthesia with minimal blockade of motor function using ropivacaine at a concentration of 0.5%; however, an increase in concentration to 0.75% or 1.0% resulted in a more profound motor blockade.\(^\text{11}\)

The incidence of hypotension was greater in the current study in both groups (90%) than that previously reported using bupivacaine.\(^\text{11}\) This was most probably related to faster onset of sympathetic block due to the short time (10 min) over which this 30 ml was injected. The hypotension was corrected promptly and maternal and neonatal pH values were normal. Neonatal Apgar scores and neurobehavioral examination results were within normal limits.

The maternal and neonatal free plasma concentrations of ropivacaine were greater at the time of delivery than were the corresponding values for bupivacaine (maternal 0.09 ± 0.008 mg/l vs. 0.06 ± 0.006 mg/l and neonatal 0.09 ± 0.008 mg/l vs. 0.06 ± 0.006 mg/l, ropivacaine vs. bupivacaine, respectively). This may be explained, in part, by the lesser degree of protein binding capacity of ropivacaine compared to bupivacaine. The lipid solubility of ropivacaine is much less than that of bupivacaine (relative n-heptane/buffer partitioning of bupivacaine versus ropivacaine is 10:2.9).\(^\text{19}\) Thus, the epidural fat may act as a depot for bupivacaine more so than for ropivacaine, facilitating systemic absorption of ropivacaine from this tissue compartment. This might explain the shorter half-life of the terminal decline in plasma concentration in the case of ropivacaine. The other mechanism that may be involved is rapid hepatic clearance.\(^\text{20}\) The shorter half-life of ropivacaine compared to bupivacaine has also been observed by others.\(^\text{21,22}\)

The clinical implications of this difference in plasma concentrations is probably of little significance, because both ropivacaine and bupivacaine concentrations (including C_{max}) in our study were less than the reported concentrations causing convulsions in an animal study (11.4 and 18.0 mg/l, respectively)\(^\text{7}\) and were apparently well tolerated by the mothers and fetuses. Unlike that for bupivacaine, ropivacaine’s cardiotoxicity has been shown, in some animal models, not to
be enhanced by pregnancy.\(^{15,16}\) A study in sheep appeared to challenge this conclusion, when toxic manifestations occurred at similar blood concentrations for ropivacaine and bupivacaine after intravenous infusions, and pregnancy did not appear to enhance the toxicity of either drug.\(^{23}\) However, these authors found that greater doses of ropivacaine were needed to produce signs of central nervous system or cardiovascular toxicity compared to bupivacaine.

In conclusion, 0.5% epidural ropivacaine and 0.5% bupivacaine each produced adequate and equivalent sensory anesthesia for cesarean section, with ropivacaine resulting in slower onset and shorter duration of degree 1 motor blockade.

The authors thank Eva Bredberg, Ph.D., Astra Pain Control AB, Södertälje, Sweden, for performance of the pharmacokinetic evaluation, and Torbjörn Arvidsson, Ph.D., Astra Pain Control, for the biochemical analyses.

References