Comparison of ropivacaine 0.1%-fentanyl and bupivacaine 0.125% - fentanyl infusions for epidural labour analgesia

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Purpose: To compare analgesic efficacies of ropivacaine-fentanyl and bupivacaine-fentanyl infusions for labour epidural analgesia.

Methods: In this double-blind, randomized study 100, term, nulliparous women were enrolled. Lumbar epidural analgesia (LEA) was started at cervical dilatation < 5 cm using either bupivacaine 0.25% followed by bupivacaine 0.125% + 2 µg·ml⁻¹ fentanyl infusion (n=50) or ropivacaine 0.2% followed by ropivacaine 0.1% + 2 µg·ml⁻¹ fentanyl infusion (n=50). Every hour maternal vital signs, visual analog scale (VAS) pain score, sensory levels, and motor block (Bromage score) were assessed. Data were expressed as mean ± 1 SD and analyzed using Chi-Squared and Mann-Whitney U tests at < 0.05.

Results: The onset times were 10.62 ± 4.9 and 11.3 ± 4.7 min for the bupivacaine and ropivacaine groups respectively (P = NS). The median VAS scores were not different between the groups at any of the evaluation periods. However, at least 80% of patients in the ropivacaine group had no demonstrable motor block after the first hour compared with only 55% of patients given bupivacaine (P = 0.01).

Conclusions: Both bupivacaine and ropivacaine produce satisfactory labour analgesia. However, ropivacaine infusion is associated with less motor block throughout the first stage of labour and at 10 cm dilatation.

Objectif : Comparer l'efficacité analgésique des perfusions de ropivacaine-fentanyl et de bupivacaine-fentanyl pour l'analgésie péridurale pendant le travail obstétrical.

Méthode : Cent femmes nullipares et à terme ont été recrutées pour participer à une étude randomisée et à double insu. L'analgésie péridurale lombaire (APL) a été amorcée quand la dilatation cervicale était < 5 cm en utilisant soit de la bupivacaine à 0,25 % suivie de bupivacaine à 0,125 % + une perfusion à 2 µg·ml⁻¹ de fentanyl (n=50), soit de la ropivacaine à 0,2 % suivie de ropivacaine à 0,1 % + une perfusion à 2 µg·ml⁻¹ de fentanyl (n=50). On a noté à toutes les heures : les signes vitaux de la mère, les scores de douleur à l'échelle visuelle analogique (EVA), les niveaux sensitifs et le bloc moteur (score de Bromage). Les données ont été exprimées en termes de moyenne ± un écart type et analysées d'après le test Chi² et le test U de Mann-Whitney à <0,05.

Résultats : Les délais d'installation ont été de 10,62 ± 4,9 et de 11,3 ± 4,7 min pour la bupivacaine et la ropivacaine respectivement (P = NS). Les scores moyens de l'EVA n'ont pas affiché de différence intergroupe. Cependant, au moins 80 % des patientes qui ont reçu de la ropivacaine n'avaient pas de bloc moteur vérifiable après la première heure contrairement à 55 % seulement des patientes à qui on a donné de la bupivacaine (P = 0,01).

Conclusion : La bupivacaine et la ropivacaine produisent une analgésie satisfaisante pendant le travail obstétrical. La perfusion de ropivacaine est toutefois associée à un bloc moteur moins intense pendant la première phase du travail et à 10 cm de dilatation.

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Accepted for publication April 8, 2000.

EFFECTIVE pain relief and minimal motor block are the necessary ingredients of an ideal epidural block for labour analgesia. Rosenberg and Heinonen¹ have shown, on isolated vagus nerve preparations, that ropivacaine at low concentrations was more effective in blocking A δ and C-fibres than similar concentrations of bupivacaine but 16% less effective in blocking motor fibres.² Wildsmith *et al.*³ have shown, in *in vitro* experiments, at comparable concentrations ropivacaine is a more effective frequency-dependent blocker than bupivacaine. Thus, the ability to block the pain fibres with relative sparing of the motor fibres makes ropivacaine a suitable agent for labour epidural analgesia. In this study we report our experience with the efficacy of ropivacaine and bupivacaine with reference to onset time, pain relief and lower extremity motor block in a tertiary care maternity hospital. With each local anesthetic, we used a common commercially available concentration of the drug for the initiation of the block and one-half of that concentration with opioid for the maintenance of analgesia.

Methods

One hundred and three ASA physical status I or II nulliparous patients with term, singleton pregnancy with the vertex as the presenting part were enrolled in this randomized double-blind study. The following were exclusion criteria for the study: severe medical or obstetrical conditions, drug, medication or alcohol abuse, neurological disease, psychiatric disease, lack of sufficient mastery of the English language, the administration of parenteral analgesics < one hour before the block. Following written informed consent, parturients in active labour (cervical dilatation $\leq$ 5 cm) were randomized using a computer generated list to either bupivacaine or ropivacaine group. An independent anesthesiologist was responsible for dispensing the study drug. All labels on 20 ml syringes containing the study drug as well as labels on the infusion bags were hidden with masking tape. Neither the patient nor the investigator knew what drug was being used in a given patient.

With the patient in the sitting position, the epidural space was identified at the L₂₋₃ or L₃₋₄ interspace and a 3 ml test dose of lidocaine 1.5% with 1:200,000 epinephrine was administered through the catheter. Bupivacaine 0.25% and ropivacaine 0.2% were chosen for initiation of epidural analgesia because those two concentrations are commercially available in standard single-dose vials in the United States and there is no need for further dilution. In the bupivacaine group, 10 ml bolus of bupivacaine 0.25% was injected. If the patient was still uncomfortable after 10 min, an addi-

tional 5 ml of the local anesthetic was given. In the ropivacaine group, the protocol was similar except that 0.2% ropivacaine was used for the induction of the block. The patients were asked to rate their pain intensity on a VAS (0-100 mm) during two consecutive contractions 5 – 10 min before the test dose was given.

After the patient reported at least a 70% reduction in her visual analog scale (VAS) score for pain, she was connected to a local anesthetic infusion containing fentanyl at 2 $\mu\text{g}\cdot\text{ml}^{-1}$ at a fixed rate of 12 $\text{ml}\cdot\text{hr}^{-1}$ in both groups. The patients in the bupivacaine group received bupivacaine 0.125% and those in the ropivacaine group ropivacaine 0.1%. If the pain relief was inadequate at any time throughout labour (VAS score > 40), the investigator gave an additional 5 ml bolus of the study drug.

The onset time for analgesia was noted. The sensory level was assessed by noting alteration in temperature sensation to an alcohol swab. The intensity of motor block was graded using a Bromage (Br) score 1-4: Br 1 indicated a complete motor block with the patient unable to flex both hips and knees, Br 2 indicated flexion only at the ankle, Br 3 indicated flexion only at the knee and ankle, Br 4 indicated flexion at the hips, ankles and knees. Bromage scores for each lower extremity was assessed separately. Only those patients with bilateral Br 4 scores were considered to have no demonstrable motor block.

The patients were assessed every hour until they reached 10 cm dilatation and the following data were recorded: cervical dilatation, fetal heart rate (FHR), maternal blood pressure and heart rate (HR), VAS pain scores, motor block and sensory level. In addition, the time interval from induction of epidural block to 10 cm dilatation, total amount of drug used, the amount and frequency of rescue doses, mode of delivery, duration of second stage, neonatal Apgar score at one minute and five minutes and neonatal birth weight were recorded. The study was terminated if the block failed, if the patient refused participation or if there were protocol violations.

Data are presented as mean $\pm$ SD. All data were entered into computerized database (Corel Paradox 8, Corel Corp, Ottawa, Ontario, Canada K1Z8R7). For statistical analysis, a commercial computer program (Statistica, Statsoft Inc., Tulsa, OK, USA, 74104) was used. The interval data were compared using unpaired t test. The VAS pain scores were compared longitudinally in the same group using Friedman statistic.⁴ A Mann-Whitney U-test was used to compare VAS data between the groups at corresponding time intervals. All nominal data were analyzed using Chi-squared analysis. A *P* value $\leq$ 0.05 was considered statistically significant.

Results

One hundred and three, nulliparous women were enrolled. Two patients did not complete the study because of failure to achieve analgesia and one patient chose to discontinue her participation. Of the remaining 100 patients, 50 were in the bupivacaine group and the remaining 50 in the ropivacaine group.

No differences existed between the two groups in maternal height, weight, and age, gestational age, the number of patients receiving oxytocin either for induction or augmentation of labour, systolic blood pressure (SBP) and HR and FHR (Table I). Although we col-

TABLE I Demographics, gestational age, birth weight, baseline maternal and fetal hemodynamic data and oxytocin use

	<i>Bupivacaine</i> <i>n = 50</i>	<i>Ropivacaine</i> <i>n = 50</i>
Height (cm)	164.3 ± 5.8	163.2 ± 5.1
Weight (kg)	79.9 ± 9.8	81.8 ± 12.9
Maternal age	27.4 ± 3.2	28.1 ± 2.8
Gestational age (wk)	39.6 ± 1.5	39.5 ± 1.3
Birth weight (kg)	3.4 ± 0.49	3.4 ± 0.45
Oxytocin (induction, n)	17	14
Oxytocin (stimulation, n)	15	17
Maternal SBP (mm Hg)	125.9 ± 16.8	127.3 ± 20.4
Maternal HR/min	83.6 ± 16.5	85.9 ± 12.1
Maternal temp (°C)	37.8 ± 12.9	35.8 ± 18.0
Fetal heart rate (bpm)	132.6 ± 16.0	131.0 ± 21.0

The data are mean ± 1 SD. No differences existed between the groups in any of the parameters. Abbreviations used: HR = heart rate; SBP = systolic blood pressure.

TABLE II Local anesthetic usage and duration of labour

	<i>Bupivacaine</i>	<i>Ropivacaine</i>
Onset of analgesia (min)	10.62 ± 4.9	11.3 ± 4.7
Initial bolus volume (ml)	11.3 ± 2.9	11.1 ± 2.2
Infusion volume: ml	69.0 ± 49.7	66.8 ± 81.0
Epidural – 10 cm duration (min)	276.7 ± 181.4	278.1 ± 153.7
Patients requiring reboluses	7	7
Rebolus “top up” volume(ml)	2.9 ± 6.45	3.1 ± 5.4
Stage II duration (min)	126.7 ± 76.9	98.1 ± 74.8

The data are mean ± 1 SD. No differences existed between the groups in any of the parameters

TABLE III Labour Outcome

	<i>Bupivacaine</i>	<i>Ropivacaine</i>
Mode of Delivery		
NSVD	28	30
Forceps	7	5
Vacuum extraction	7	4
Cesarean section	8	11

Abbreviations used: NSVD = normal spontaneous vaginal delivery. No differences existed in any of the categories between the groups.

lected data for 10 hr, the data presented here represent only the first six hours because many patients delivered in the first six hours leaving an inadequate number of patients for statistical analysis. The numbers used for analysis are: n=50 for baseline and after block measurements and n = 43,36,27,21,21, and 15 from the first to sixth hour respectively and n= 45 for measurements at 10 cm dilatation. Three patients in the bupivacaine group and six patients in the ropivacaine group were delivered by Cesarean section before they reached complete dilatation and were, therefore, not included for data collection at 10 cm dilatation.

After the block, the SBP decreased to 104 ± 20 mmHg in the bupivacaine group and to 113 ± 14 mmHg in the ropivacaine group ($P = 0.04$). No other subsequent SBP measurements differed between the two groups at any of the measurement points. The maternal HR ranged from 79 ± 12 to 98 ± 13 bpm in the bupivacaine group and in the ropivacaine group it ranged from 76 ± 10 to 83 ± 10 bpm in the ropivacaine group with no intergroup differences at any of the measurement periods reported. The FHR varied between 122 ± 24 and 145 ± 13 in the bupivacaine group and between 130 ± 26 and 136 ± 11 beats/min in the ropivacaine group with no differences between the groups.

The onset time, initial bolus volume, total infusion volume, epidural analgesia to 10 cm dilatation, and the duration of second stage were not different between the two groups. (Table II). The number of patients requiring additional “top-up doses” for break-through pain as well as the volumes of local anesthetic used for this purpose was similar in the two groups (Table II). The number of spontaneous deliveries, Cesarean sections and instrumental deliveries did not differ between the two groups. (Table III). No baby from either group had an Apgar score of <7 at one minute or <9 at five minutes.

The median VAS scores did not differ between the groups before analgesia (Figure 1). The VAS scores did not differ between the groups soon after onset of action or at any of the subsequent evaluation periods (Figure 1). In both groups, most patients had little motor block after induction (Figure 1). However, in the subsequent evaluation periods, up to 80-100% of patients had a grade 4 motor block in the ropivacaine group and only 20-55% of patients had a grade 4 motor block in the bupivacaine group (Figure 2, $P = 0.01$).

Discussion

Commonly, bupivacaine 0.25% is used to induce epidural labor analgesia, and one half of that concentration with 2 µ·mL⁻¹ fentanyl for continuous infusion. Ropivacaine 0.2% is also effective for this purpose.^{5,6}

FIGURE 1 Percentage of patients with motor blocks in the ropivacaine and bupivacaine groups. Abbreviations used: BL = Baseline, before epidural insertion; Post bl. = after epidural insertion; 1 HR = one hour after epidural insertion; 10 cm = 10 centimeters cervical dilatation

* significantly different from the corresponding value from the other group. $n=50$ for baseline and post block measurements and $n=43, 36, 27, 21, 21$, and 15 from the first to sixth hour respectively and $n=45$ for measurements at 10 cm dilatation.

FIGURE 2 Median VAS scores for pain during labour. All post block values are lower than the respective baseline value. No differences existed between groups at any of the corresponding measurement periods. For abbreviations as well the number of cases at each measurement point, please see the legend for Figure 1.

In this study, we used one half of the initial concentration of ropivacaine for maintenance with fentanyl. The doses used for initiation of the epidural were chosen for convenience as bupivacaine is commercially available in the single dose vial at 0.25% and ropivacaine is available at 0.2%. Our data show that both

drugs produce satisfactory analgesia from initiation of anesthesia and throughout labour but, in most patients, ropivacaine is associated with less motor block. The inclusion of only nulliparous women who are more likely to have longer labours than multiparous women enabled us to assess sensory and motor effects of local anesthetics over extended periods of time. In addition, nulliparous women have more intense labour pain than do multiparous women.⁷ Our study addressed the sensory and motor effects of the two anesthetics only during first stage of labour and no data were collected during "active pushing" during second stage.

Polley *et al.*⁸ suggested that ropivacaine is less potent and that bupivacaine has a better toxic/therapeutic ratio. They measured the minimum local anesthetic concentration (MLAC) of ropivacaine and bupivacaine during first stage of labour using the approach suggested by Columb *et al.*⁹ The measured MLAC in Polley's⁸ and Columb's⁹ studies for bupivacaine respectively were 0.067%, and 0.064%, although Polley *et al.*¹⁰ in a previous study had determined the MLAC of bupivacaine to be 0.104%. The MLAC of ropivacaine was 0.111% in the study by Polley *et al.*⁸ and Columb *et al.*⁹ did not study ropivacaine.

Polley *et al.*⁸ further suggested that only at equipotent analgesic concentrations should the relative motor and sensory effects of these two agents be compared. However, in their study, 35-45% of women were multiparous women at 3-7 cm dilatation and the MLAC was measured following a single 20 ml injection of either ropivacaine or bupivacaine. It has been shown that multiparous patients have less pain than primiparous patients; therefore, it is important to separate these groups when comparing pain scores.⁷

The MLAC required to produce analgesia increases with increasing cervical dilatation¹¹ and a snapshot observation done at one point may not be representative of the rest of the labour. In addition, in most institutions, a test dose of local anesthetic is used before the definitive dose is injected and the local anesthetics are used with opioids, thus making it difficult to choose the anesthetic concentration of a particular agent by the measured MLAC value alone. In the study by Gautier *et al.*¹² the patients given bupivacaine 0.1% with sufentanil rated their analgesia to be unsatisfactory and this concentration of bupivacaine is higher than its recently reported⁸ MLAC. On the contrary, our study evaluated the sensory and motor effects of local anesthetic infusions administered during the course of first stage in primiparous women and, therefore, more likely represents the clinical efficacy of the agents studied.

Owen *et al.*¹³ in a smaller study concluded that 0.125% concentrations of bupivacaine and ropivacaine were clinically indistinguishable when used for labour analgesia. In this study, the local anesthetics were administered by the patient controlled analgesia mode (PCA) combined with a basal infusion rate. No opioids were added to the local anesthetic solution. The study also used a 7 ml lidocaine 2% test dose solution which can lead to considerable analgesia and motor block in its own right. It is also to be noted that the number of on-demand injections was almost identical in both groups in this study. Eddleston *et al.*¹⁴ demonstrated no differences in sensory or motor effects between ropivacaine 0.25% and bupivacaine 0.25% in parturients receiving labour analgesia. However, in this study, intermittent injection rather than infusions were used for analgesia and the bupivacaine group needed more top-up injections than did the ropivacaine group. Both these studies showed^{13,14} that ropivacaine, despite its lower potency, provided similar degree of analgesia as bupivacaine at comparable concentration.

It is possible that bupivacaine 0.125% used in our study may represent a supramaximal concentration of the drug for producing analgesia. However, we doubt that such was the case because both groups had comparable VAS scores throughout labour. The number of patients requiring top-up injection, the doses of induction and top-up doses, and the total volumes of drug solution used did not differ between the two groups. Although the two agents were clinically indistinguishable in terms of their sensory effects, they were distinguishable on the basis of their motor effects. One may argue that the increased incidence of motor block in the bupivacaine group was due to the higher concentration bolus (0.25%) used to initiate epidural analgesia. However, we do not think that the initial bolus contributed to a more profound block because 1) no difference in motor block was noted between the two groups soon after the block was initiated, and 2) it is unlikely that the motor effects of the initial bolus persisted beyond two hours after injection. Thus, more intense motor block in the bupivacaine group was the result of the infusion and not of the initial bolus. There was no difference in labour outcome between the groups in our study 100 of patients. We believe that this sample size is too small to make conclusions on the association between motor sparing and improved labour outcome. It is interesting to note, in this context, that in the study by Eddleston *et al.*¹⁴ parturients given ropivacaine 0.25% had more spontaneous vaginal deliveries than those given bupivacaine 0.25%.

In conclusion, epidural infusions of ropivacaine 0.1% + fentanyl 2 µg·mL⁻¹ or bupivacaine 0.125% + fentanyl 2

µg·mL⁻¹ mixtures provided comparable degrees of labour analgesia. There was less motor block over entire the course of labour with ropivacaine-fentanyl infusion.

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