

A Comparison of Median Effective Doses of Intrathecal Levobupivacaine and Ropivacaine for Labor Analgesia

Alex T. Sia, M.Med.,* Raymond W. Goy, F.A.N.Z.C.A.,† Yvonne Lim, M.Med.,† Cecilia E. Ocampo, M.D.‡

Background: The study was designed to determine and compare the median effective doses (MEDs) of intrathecal ropivacaine with levobupivacaine for labor analgesia.

Methods: In this double-blind study, 100 parturients in early labor were randomized to receive either intrathecal ropivacaine or levobupivacaine. For each drug, the patients were assigned to receive one of the five doses studied, namely 1, 1.5, 2, 2.5, or 3 mg. Effective analgesia was defined as a pain score (0–100 visual analog scale) of less than 10 within 15 min of injection, lasting for 45 min or more after the induction of analgesia. MEDs were derived from probit analysis. The duration of analgesia rendered by the two drugs at 2.5 and 3 mg was also compared.

Results: The MED for levobupivacaine was 1.07 mg (95% confidence interval, 0.88–1.25 mg), and the MED for ropivacaine was 1.40 mg (95% confidence interval, 1.20–1.61 mg). Levobupivacaine was found to be 1.31 (95% confidence interval, 1.04–2.01) times more potent than ropivacaine. At doses of 2.5 mg or greater, there was no significant difference in duration of analgesia between levobupivacaine (median, 63.5 min; range, 46–123 min) and ropivacaine (median, 59.0 min; range, 47–93 min; $P = 0.18$). We detected no difference in the incidence of hypotension, nausea and vomiting, motor block, or abnormal fetal heart tracing between the two drugs.

Conclusions: The MED of intrathecal ropivacaine for labor analgesia was significantly greater than levobupivacaine experimentally, but this significance was reduced when the comparison was based on molar potency. There was no difference in the duration of analgesia or adverse effects between the two drugs at higher doses (2.5 mg or greater).

LEVOBUPIVACAINE and ropivacaine are the two most recently introduced amide local anesthetics that, at equivalent doses, possess a lower risk of causing cardiotoxicity than bupivacaine. Although experimental evidence suggests that ropivacaine administered neuraxially for labor pain relief could be less potent than bupivacaine,¹ this impact on clinically relevant doses is debatable.² Recent evidence also infers that ropivacaine and levobupivacaine are indistinguishable in their effects when these agents were used epidurally to effect labor analgesia.^{3,4} Apart from this, a previous study with intrathecal levobupivacaine and ropivacaine also suggested

that 2.5 mg of either drug was uniformly effective for labor analgesia, with no demonstrable difference in the duration of action.⁵ However, there is a lack of traditional dose-response data for these two agents when used intrathecally for labor analgesia.

In this study, we compared the dose-effect relation of intrathecal levobupivacaine and ropivacaine when used in early labor analgesia. A difference in the median effective dose (MED), derived from probit analysis, between the two drugs would suggest a possible difference in their potencies. The MED could be assumed to be the dose that would be necessary to provide effective analgesia for 50% of the patients treated. However, clinicians would usually institute a clinically effective dose (usually a combination of local anesthetic and lipophilic opioid), to provide adequate analgesia for a majority, if not all the patients. In this study, we also analyzed the potential difference in the duration of analgesia between levobupivacaine and ropivacaine for patients who received more clinically relevant doses of the local anesthetics. A lack of difference between ropivacaine and levobupivacaine at these "clinical" doses (≥ 2.5 mg) would suggest a lack of clinical difference in this respect between the two drugs, even if their MEDs were significantly different.

Materials and Methods

This study was conducted with the approval of the hospital ethics committee (KK Women's and Children's Hospital, Singapore) and written consent from the patients. Only healthy (American Society of Anesthesiologists physical status I) nulliparous patients who were in early spontaneous labor (cervical dilatation < 5 cm in the previous half hour before the block) and had a pain score of greater than 50 on a 0–100 visual analog scale (VAS) at the time of request for intrapartum neuraxial block were recruited. The exclusion criteria included the use of parenteral opioids (intramuscular meperidine) 2 h before block, the use of preblock oxytocin, maternal height less than 150 cm or greater than 170 cm, maternal weight less than 60 kg but greater than 90 kg, maternal age younger than 20 yr or older than 45 yr, multiple pregnancies, fetal malposition (breech, occipital-posterior), and a history of maternal drug abuse.

A recruitment of 100 parturients was planned. With the help of a computer-generated random numerical table, the parturients were assigned by using opaque, sealed envelopes to receive one of the following doses: 1, 1.5, 2, 2.5, or 3 mg of either intrathecal ropivacaine (Naropin; AstraZeneca, Mölndal, Sweden) or levobupi-

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* Director of Obstetric Anesthesia, † Registrar, ‡ Clinical Fellow.

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Address reprint requests to Dr. Sia: Department of Anesthesia, KK Women's and Children's Hospital, 100 Bukit Timah Road, Singapore 229 899. Address electronic mail to: athsia@kkh.com.sg. Individual article reprints may be purchased through the Journal Web site, www.anesthesiology.org.

vacaine (Chirocaine; Abbott, Kent, United Kingdom). Hence, the patients were divided into 10 groups, *i.e.*, R1, R1.5, R2, R2.5, R3, L1, L1.5, L2, L2.5, and L3, of equal numbers. No placebo was used in the study because a deliberate dural puncture performed for this purpose was deemed unjustifiable by the committee.

The cervical dilatation, preblock VAS score, and systolic blood pressure (SBP) (measured noninvasively on the right brachial artery with a 15% left lateral tilt while lying supine) were recorded. After establishing venous access and prehydration with 500 ml lactated Ringer's solution, combined spinal-epidural analgesia was instituted in the right lateral position. All the blocks were performed at the L3-L4 intervertebral level by only one operator (R.W.G.) to eliminate interoperator variability. After accessing the epidural space by using the loss of resistance to air technique (< 2 ml air was injected), a 27-gauge atraumatic spinal needle was passed through the 18-gauge epidural needle (Espocan; B. Braun, Melsungen, Germany) to effect dural puncture. A free flow of cerebrospinal fluid from the spinal needle was established before the test drug (diluted to a total of 2 ml with normal saline solution) was administered intrathecally. The test solutions were prepared by another investigator (A.T.S., Y.L., or C.O.), and their contents were not revealed to the investigator who performed the block. This injection was undertaken in approximately 15 s, and the time of its completion was denoted as T0.

An epidural catheter (20 gauge) was then inserted 3 cm into the epidural space. No further injections were given *via* the epidural catheter. The presence of blood when the catheter was aspirated with a 2-ml syringe resulted in replacing the epidural catheter in another intervertebral space. The patient was excluded from the study and the envelope was reassigned to the next patient without revealing its content to the operator.

The following parameters were assessed:

1. VAS score at 15, 30, and 45 min after block
2. SBP at 5, 10, 15, 20, 25, and 30 min after block
3. Highest sensory block to ice cubes in the midline at 5, 15, and 30 min after block
4. Motor block as assessed by the modified Bromage scale (0 = able to lift extended leg at hip, 1 = able to flex knee but unable to lift extended leg, 2 = able to move foot only, 3 = unable to move even foot) at 5, 15, and 30 min after block
5. Fetal heart rate was monitored continuously by either an external or scalp electrode by an attending obstetrician who was blinded to the drugs received by the parturients and not involved in the study in the first 30 min after block. The cardiocogram was classified as normal (reactive) based on the following criteria: at least two accelerations (> 15 beats for > 15 s) in 20 min, baseline heart rate 110-150 beats/min, baseline variability of 5-25 beats/min, and early decelerations.

Any deviation from the above was classified as abnormal (nonreassuring). All fetal heart tracings were assessed to be normal before block.

6. The incidence of adverse effects: nausea and/or vomiting (0 = no, 1 = yes) and shivering (0 = no, 1 = yes) based on direct questioning at 5, 15, and 30 min after block

The block was deemed successful if the VAS score was less than 10 at 15 min after block and if the VAS score remained at this level 45 min after T0 without further request for supplemental analgesia. The duration of analgesia, which was taken as the time difference between T0 and the time when the patient requested analgesia (T END), was documented. Only parturients who had experienced successful blocks were followed up to determine the duration of analgesia.

If the VAS score was 10 or greater at 15 min or 45 min after T0, it was considered a failure. If the VAS score was greater than 10 at 30 min after T0, epidural analgesia was instituted by injections of 5-ml aliquots of 0.2% ropivacaine every 5 min up to a total of 15 ml. No further data was collected from these cases.

If the SBP was reduced by more than 20% of the baseline value, 5-mg intravenous ephedrine boluses were given. Patients with nausea and/or vomiting had their SBP checked to exclude hypotension; otherwise, it would be treated with metoclopramide at the patient's request. New changes suggestive of an abnormal (nonreassuring) fetal heart pattern in the 30 min after T0 resulted in appropriate obstetric intervention. These included left uterine displacement, supplemental oxygen *via* facemask, and tocolytic drugs (0.4 mg terbutaline) if uterine hyperactivity was suspected.

The patients were divided *a priori* into those who received a high dose (≥ 2.5 mg ropivacaine or levobupivacaine) or a low dose (< 2.5 mg ropivacaine or levobupivacaine). Our previous study demonstrated that 2.5 mg of either intrathecal ropivacaine or levobupivacaine was effective for a population of women in early labor.⁵ By analyzing the patients who received 2.5 mg or more intrathecal ropivacaine or levobupivacaine, we planned to investigate the relation between the duration of analgesia and the drug used in this cohort of patients.

Statistical Analysis

Maternal age, height, weight, preblock cervical dilatation, and preblock VAS score were compared between patients in the levobupivacaine and ropivacaine groups, using the Student *t* test for parametric data and the Mann-Whitney U test for nonparametric data. Probit analysis was computed to compare the dose-effect relation between levobupivacaine and ropivacaine. As a backup, univariate logistic regression analyses were performed by computing the success of combined spinal-epidural analgesia as the dependent variable and drug

Table 1. Anthropometric and Preblock Data for All Patients

	Levobupivacaine (n = 50)	Ropivacaine (n = 50)	P Value
Maternal age, yr	27.4 (5.7)	26.8 (4.8)	0.56
Maternal height, cm	159.0 (5.5)	159.2 (5.0)	0.79
Maternal weight, kg	66.8 (9.8)	69.8 (11.5)	0.17
Cervical dilatation, cm	3 (2-4)	3 (2-4)	0.72
Pain score, 0-100 VAS	80 (55-100)	80 (50-100)	0.95
Systolic blood pressure, mmHg	123 (13)	121 (14)	0.59

All values are expressed as mean (SD) except for preblock cervical dilatation and preblock pain score, which are expressed as median (minimum-maximum). No significant difference was found between the two groups.

VAS = visual analog scale.

(levobupivacaine or ropivacaine), doses (1, 1.5, 2, 2.5, or 3 mg), age, maternal weight, maternal height, cervical dilatation (1-4 cm), and preblock VAS score (0-100) as independent variables. Variables with $P < 0.1^6$ were entered into a stepwise multiple logistic regression procedure with forward elimination to identify significant independent predictors for success of the induction of analgesia.

For the analysis of the duration of analgesia, data from patients who had received 2.5 and 3 mg were combined, and a comparison between ropivacaine and levobupivacaine was made. A sample size of 20 per drug was computed to detect a 30-min difference, with an SD of 25 min in the duration of analgesia between ropivacaine and levobupivacaine based on the results of our previous study,⁵ with a power greater than 80%, and $\alpha = 0.05$.⁷ Two-way analysis of variance was also performed as a back-up test, using the type of local anesthetic and dose as the independent variables and the duration of analgesia as the dependent variable in patients within the clinical dose category. The greatest percentage of SBP reduction [(preblock SBP - lowest postblock SBP) \times 100/preblock SBP], highest sensory block, and lower limb motor between levobupivacaine and ropivacaine in patients who received a clinical dose in the first 30 min after T0 were also compared. SPSS version 9.0 (SPSS Inc., Chicago, IL) was used for computation and analyses of data. $P < 0.05$ was considered statistically significant.

Results

A total of 105 patients were recruited, but 5 were excluded before collection of data because of accidental intravascular catheterization. Their envelopes were resealed and reassigned, with their contents unknown to the operator. There were no cases of accidental dural puncture by the epidural needle. None of the patients gave birth during the first 45 min after block. None of the patients in the high-dose group (n = 40) gave birth before loss of analgesia. There was no difference in the preblock characteristics between parturients in the ropivacaine and levobupivacaine groups (table 1).

Table 2. Data on the Distribution of "Successful" Blocks

Drug	Dose, mg	Number of "Successful" Blocks	Total Number of Patients
Levobupivacaine	1	4	10
	1.5	9	10
	2	10	10
	2.5	10	10
Ropivacaine	3	10	10
	1	1	10
	1.5	6	10
	2	9	10
	2.5	10	10
	3	10	10

Probit Analysis

Spinal analgesia was effective in 40, 90, and 100% of the L1, L1.5, and L2 groups, respectively. The corresponding success rates for R1, R1.5, and R2 were 10, 60, and 90%, respectively. There were no failures reported in doses greater than 2 mg with either drug. (table 2) The MED for levobupivacaine was 1.07 mg (95% confidence interval [CI], 0.88-1.25 mg), and the MED for ropivacaine was 1.40 mg (95% CI, 1.20-1.61 mg). With the aid of logarithmic transformations, the MED for levobupivacaine was found to be significantly lower, and the potency ratio of MED of levobupivacaine to ropivacaine was found to be 0.76 (95% CI, 0.50-0.96). Levobupivacaine was thus 1.31 (95% CI, 1.04-2.01) times more potent than ropivacaine (fig. 1). This was supported by multiple logistic regression that showed a larger dose (odds ratio, 23.4; 95% CI, 4.56-120.6) and the use of levobupivacaine (odds ratio, 7.46; 95% CI, 1.16-47.8) were significant predictors of a successful block apart from the degree of cervical dilatation (table 3).

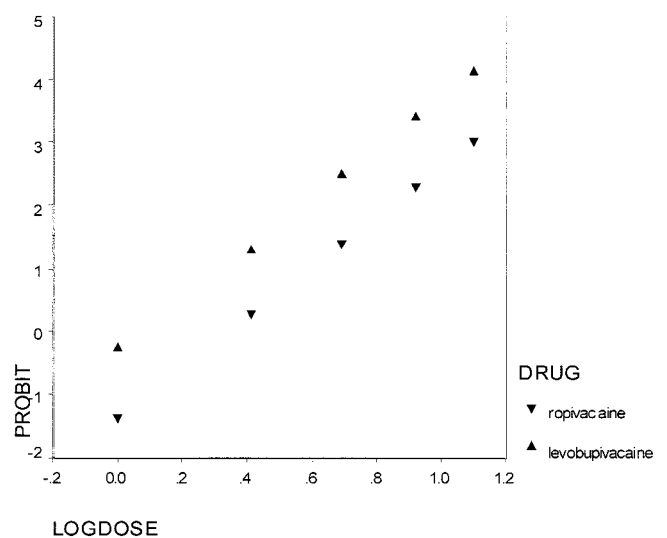


Fig. 1. Probit values against log (dose) for ropivacaine* and levobupivacaine#. * $\beta = 3.98$ (95% confidence interval, 3.98-4.00); β constant = -1.35. # $\beta = 4.012$ (95% confidence interval, 3.86-4.15); β constant = -0.289.

Table 3. Predictors of "Success" of CSE: Results of Multiple Logistic Regression*

Variable	B	SE	Significance (P Value)	R	Odds Ratio	95% CI for Odds Ratio	
						Upper	Lower
Drug (1)	2.01	0.95	0.03	0.16	7.46†	1.16	47.8
Dose	3.15	0.84	0.00	0.35	23.4†	4.56	120.6
Cervix	-2.83	1.14	0.01	-0.20	0.06†	0.01	0.55

* Variables that did not show a trend toward achieving statistical significance as predictors ($P > 0.1$) of success of combined spinal-epidural analgesia (CSE) in the *a priori* univariate logistic regression and hence were not included in the final multiple logistic regression were the following: maternal age (Exp(B) = 1.07, 95% confidence interval [CI] for Exp(B) = 0.97-1.18, $P = 0.26$); maternal height (Exp(B) = 0.99, 95% CI for Exp(B) = 0.90-1.09, $P = 0.85$); maternal weight (Exp(B) = 0.99, 95% CI for Exp(B) = 0.95-1.04, $P = 0.73$); and preblock pain score (Exp(B) = 0.97, 95% CI for Exp(B) = 0.93-1.02, $P = 0.26$). † Significant differences were detected.

For levobupivacaine, a higher dose and lesser preblock cervical dilatation were significant ($P < 0.05$) predictors of success of the blocks. No interaction terms were examined as the drug and dose were randomly assigned. Bold type indicates P values less than 0.05.

B = Beta; Cervix = preblock cervical dilatation in centimeters; dose = intrathecal dosage of ropivacaine or levobupivacaine used (1, 1.5, 2, 2.5, or 3 mg); drug(1) = levobupivacaine.

Adverse Effects

In this study, there was a low incidence of nausea and/or vomiting and shivering (*i.e.*, $< 5\%$ in either group). The incidence of new fetal heart trace abnormality was approximately 10%, but all of the parturients responded to conservative treatment *vide ante*, including the use of tocolytics in two patients. A higher sensory block to cold in the first 30 min after block was found in patients who had received levobupivacaine. We did not detect any significant difference in the profile of adverse effects between levobupivacaine and ropivacaine, although our study was not powered in this respect (table 4). The incidence of motor block was in excess of 10% with either drug, and this was predomi-

Table 4. Highest Sensory Block and the Profile of Side Effects for Patients Receiving Levobupivacaine versus Ropivacaine*

	Levobupivacaine (n = 50)	Ropivacaine (n = 50)	P Value
Highest thoracic sensory block to cold in the first 30 min after block	T7 (T4-T12)	T8 (T4-T12)	0.02†
Highest % of SBP reduction in the first 30 min after block‡	8.7 (6.7)	8.0 (6.8)	0.67
Hypotension (SBP reduction > 20%)	6	5	1.0
Shivering	3	1	0.61
Nausea ± vomiting	3	1	0.61
Motor block (Bromage score > 0)§	7	9	0.9
Abnormal fetal heart rate	4	5	1.0

The highest sensory block to cold is expressed as median (minimum-maximum), the highest percent of systolic blood pressure (SBP) reduction is expressed as mean (SD), and the actual numbers of patients are reported for hypotension, shivering, nausea ± vomiting, lower limb motor block, and abnormal fetal heart rate.

* 1, 1.5, 2, 2.5, and 3 mg levobupivacaine vs. 1, 1.5, 2, 2.5, and 3 mg ropivacaine.

† Significant difference was found between the two groups. ‡ (Preblock SBP - lowest postblock SBP) × 100/preblock SBP. § None of the patients had had a Bromage score greater than 1.

nantly contributed by the use of the higher clinical doses (table 5).

Characteristics of Block from a "Clinical" Dose

The corresponding estimated ED₉₅s (95% CIs) from probit analysis were 2.12 mg (1.81-2.81 mg) for ropivacaine versus 1.61 mg (1.37-2.14 mg) for levobupiva-

Table 5. Preblock and Postblock Data of Patients Who Had Received a "Clinical" Dose*

	Levobupivacaine (n = 20)	Ropivacaine (n = 20)	P Value
Maternal age, yr	29.1 (5.7)	27.3 (6.3)	0.35
Maternal height, cm	159 (4.8)	160 (4.4)	0.52
Maternal weight, kg	69.7 (11.0)	72.3 (11.8)	0.47
Preblock SBP, mmHg	121 (14.5)	126 (15.0)	0.66
Preblock cervical dilatation, cm	3 (2-3)	3 (2-4)	0.80
Preblock pain score, 0-100 VAS	80 (55-100)	80 (60-90)	0.86
Duration of analgesia, min	63.5 (46-123)	59.0 (47-93)	0.18
Highest sensory block to cold in the first 30 min after block	T5 (T4-T8)	T7 (T4-T10)	0.03†
Highest % of SBP reduction in the first 30 min after block‡	11.1 (7.0)	13.1 (8.8)	0.40
Hypotension (SBP reduction > 20%)	3	4	1.0
Shivering	1	1	1.0
Nausea ± vomiting	3	1	0.60
Motor block (Bromage score > 0)§	5	6	0.9
Abnormal fetal heart rate	2	3	1.0

All values are expressed as mean (SD) except for preblock cervical dilatation, preblock pain score, highest sensory block, duration of analgesia, and highest percent reduction of systolic blood pressure (SBP), which are expressed as median (minimum-maximum). Actual numbers of patients are reported for hypotension, shivering, nausea ± vomiting, lower limb motor block, and abnormal fetal heart rate.

* 2.5 and 3 mg levobupivacaine vs. 2.5 and 3 mg ropivacaine. † Significant difference was found between the two groups. ‡ (Preblock SBP - lowest postblock SBP) × 100/preblock SBP. § None of the patients had had a Bromage score greater than 1.

VAS = visual analog scale.

caine. The duration of analgesia rendered by levobupivacaine and ropivacaine in doses greater than 2 mg was indistinguishable. (table 5) We have categorized the two doses, *i.e.*, 2.5 and 3 mg collectively, *a priori*, as a clinical dose and powered the analysis of the comparison between the two drugs according to the results of our previous study.⁵ In fact, the *post hoc* analysis confirmed that, based on the SD (18 min), our sample size ($n = 20/\text{group}$) was adequate to detect a mean difference of 18 min with $\alpha = 0.05$ and $\beta = 0.2$.⁷ Also, in the two-way analysis of variance, neither the local anesthetic ($F = 0.348$, $P = 0.35$) nor the dose ($F = 2.80$, $P = 0.103$) used was found to be a significant independent variable for the duration of analgesia, even though our study was not powered for this analysis. There were no other differences detected in the preblock and postblock characteristics of patients receiving a clinical dose of levobupivacaine compared with ropivacaine, apart from a higher sensory block to cold in the first 30 min after block (table 5). It is unclear whether the latter finding was attributed to the higher potency of levobupivacaine compared with ropivacaine.

Discussion

Our study demonstrated that the MED of intrathecal levobupivacaine was significantly lower than that of ropivacaine to achieve a similar labor analgesic target. In quantifying the magnitude of difference from the ratio of the MEDs, intrathecal levobupivacaine was approximately 31% more potent than ropivacaine for labor analgesia. In contrast, previous studies investigating the minimum local anesthetic concentrations from randomized sequential allocation did not show a significant difference between epidurally administered levobupivacaine and ropivacaine in labor analgesia.^{3,4} Apart from the difference in the route of drug administration, the discrepancy between the findings of these studies and ours could have been contributed by the difference in the setting of analgesic targets. In both studies of the minimum local anesthetic concentrations, success was defined singularly as a VAS score reduction to less than 10 (on a scale of 0–100) within 30 min after injection. However, we had used a reduction of VAS score of less than 10 in the time from 15 min to 45 min after block to define success due to its clinical relevance. Therefore, a successful block was, categorically, one that conferred at least 30 min of analgesia. In practice, apart from the onset, the duration of analgesia would also be an important consideration in justifying combined spinal-epidural analgesia during early labor.⁸ Therefore, our study suggests that by this definition of success, we were able to unmask the potential difference in the MEDs of these agents when used intrathecally to provide labor analgesia. As a corollary, the findings of our study regarding the

ratio of MEDs of the two agents may not be extrapolated to other clinical situations, as exemplified by neuraxial block for cesarean delivery, due to the differences in anesthetic goals.

The increased likelihood of levobupivacaine (instead of ropivacaine) and a higher dose in predicting the success of the block were also supported by logistic regression analysis. None of the patients who had received a clinical dose of intrathecal analgesics (R2.5, R3, L2.5, and L3) had block failures. These clinically effective doses would be relevant to anesthesiologists who should be endeavoring to provide adequate analgesia for a majority if not all of the patients. We did not use doses greater than 3 mg because our previous study suggested that this was probably superfluous, because we had encountered uniformly effective analgesia with 2.5 mg intrathecal levobupivacaine and ropivacaine.⁵ This was also supported by another previous study that demonstrated the adequacy of 3 mg intrathecal ropivacaine as the sole intrathecal analgesic during early labor.⁹ Besides, we were unwilling to expose our patients to higher doses of these intrathecal analgesics because we were uncertain whether this would result in more unnecessary adverse effects, such as hypotension and increased lower limb motor block.

In the absence of failed blocks, the duration of analgesia was a primary parameter that was used in our study to compare the effectiveness of the two agents in the clinical dose category. This was deemed clinically significant because a more prolonged block could potentially obviate the need for and the frequency of supplemental analgesia, hence reducing anesthesiologists' workload. The lack of difference in the duration analgesia between the two drugs at clinically relevant doses in this study was consistent with our previous study.⁵ Similarly, the lack of difference in the duration of post-cesarean delivery analgesia between these two drugs when given intrathecally has also been documented in another study.¹⁰

Our study found a higher sensory block rendered by levobupivacaine compared to ropivacaine. The maximum level of sensory block has been found to be directly related to the dose of a local anesthetic administered intrathecally.¹¹ However, we are uncertain whether the disparity of the maximum levels of sensory block represents a relative "overdose" of patients in the levobupivacaine group (hence suggestive of a greater potency) compared with the ropivacaine group. Moreover, other factors, such as the relative densities of spinal injectates that could have influenced their spread in the subarachnoid space,¹² were not assessed in our study.

Apart from the difference in the maximum level of sensory block, our study found that these two agents were indistinguishable at clinically relevant doses. We could therefore infer that although the MEDs of the two agents seem disparate experimentally, extending this

relation to clinical doses may not be justifiable. This may also help to explain the fact that despite the difference in the minimum local anesthetic concentrations of ropivacaine and racemic bupivacaine in epidural labor analgesia, most authors were unable to find clinically relevant differences between the two drugs.¹³⁻¹⁵

In the comparison of the MEDs of levobupivacaine and ropivacaine, other considerations must be borne in mind. First, the concentration of levobupivacaine is expressed as milligrams per milliliter of base (molecular weight, 288), whereas ropivacaine, like racemic bupivacaine, is expressed as milligrams per milliliter of hydrochloric salt.^{16,17} Therefore, at the same mass, levobupivacaine would be expected to have more active molecules than ropivacaine if their molecular weights were similar. However, the molecular weight of ropivacaine is only 95% that of bupivacaine when their bases are compared. Therefore, for the same mass, levobupivacaine would have some 7.5% more active molecules than ropivacaine. When probit analysis was computed based on the number of molecules (micromoles), the MED for levobupivacaine was 3.71 μmol (95% CI, 3.04–4.20 μmol) versus 4.50 μmol (95% CI, 3.92–5.17 μmol) for ropivacaine. With the aid of logarithmic transformations, the ratio of MED of ropivacaine to levobupivacaine in this case was found to be 1.21 (95% CI, 1.00–1.76). Even though the disparity in the MEDs was decreased, levobupivacaine still demonstrated a trend toward being approximately 20% more potent than ropivacaine. However, based on the results of our study, the potentially greater local anesthetic activity of the levobupivacaine molecule compared with ropivacaine is unlikely to have a strong impact clinically.

A previous study had shown that the duration of analgesia induced by combined spinal-epidural analgesia was shortened for patients who had had a greater degree of preblock cervical dilatation.¹⁸ The direct relation between cervical dilatation and analgesic requirements was also expounded by another study.¹⁹ Even though we limited our study to nulliparous women in early spontaneous labor, we still found the degree of preblock cervical dilatation to be a significant predictor of a successful block. A greater degree of cervical dilatation (probably indicative of a more advanced stage of labor) was associated with a lower rate of success. However, this potential confounding factor was addressed by randomization, and we did not detect a difference in the degree of preblock cervical dilatation between subjects who had received either drug.

In conclusion, our study showed that the MED of

intrathecal ropivacaine was significantly higher than that of levobupivacaine to achieve a similar labor analgesic target. Levobupivacaine exhibited a trend toward being 20% more potent than ropivacaine even when the comparison was based on the mass of active molecules. This discrepancy in potencies was not apparent when higher (clinical) doses were used. We also could not establish any other significant difference between the block characteristics rendered by these two agents at clinical doses (2.5 and 3 mg) apart from a higher degree of sensory block rendered by levobupivacaine.

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