Obstetrical and Pediatric Anesthesia

Low dose intrathecal ropivacaine with or without sufentanil provides effective analgesia and does not impair motor strength during labour: a pilot study

[Une faible dose de ropivacaine intrathécale, avec ou sans sufentanil, fournit une analgésie efficace et n'affecte pas la force motrice pendant le travail : une étude pilote]

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Purpose: Although ropivacaine has been used to provide spinal anesthesia in the surgical population, its intrathecal administration for labour analgesia has only recently been described. We evaluated the effects of low dose intrathecal ropivacaine with or without sufentanil for labour analgesia.

Methods: Thirty-six term parturients in active labour were randomly assigned to receive 3 mg of intrathecal ropivacaine (group R) or 3 mg ropivacaine with 10 µg of sufentanil (group RS). Patients were evaluated by a blinded observer for hypotension, linear analogue score (VAS 0–100) for labour pain, motor power in the lower limbs, onset of analgesia, sensation to cold and pin prick, duration of analgesia, and neonatal Apgar scores. The following day patients were assessed for satisfaction, headache and neurologic deficit.

Results: The mean duration of analgesia in the R group was 41.4 ± 4.9 min and 95.0 ± 6.1 min in the RS group (mean $\pm$ SEM, $P=0.0001$). All subjects had satisfactory analgesia at five minutes, although analgesia from the ropivacaine-sufentanil combination was superior to that provided by ropivacaine alone. Total duration of labour was no different between the groups (R- 306 ± 34 , RS- 384 ± 44 min, $P=0.17$). No patient showed evidence of motor block. All patients were satisfied with the labour analgesia. No neurological complications were observed.

Conclusions : Low dose ropivacaine provides effective analgesia during labour via the intrathecal route. It can be mixed with sufentanil in the above-mentioned concentrations to improve both the quality and duration of analgesia. Fetal outcome remains favourable.

It may provide minimal or no motor block, to facilitate ambulation.

Objectif : Même si la ropivacaine a été utilisée pour la rachianesthésie chirurgicale, son administration intrathécale comme analgésie pendant le travail n'a été étudiée que récemment. Nous avons évalué les effets d'une faible dose de ropivacaine intrathécale avec ou sans sufentanil comme analgésie pendant le travail.

Méthode : Trente-six parturientes à terme, en travail actif, ont été réparties au hasard et ont reçu 3 mg de ropivacaine intrathécale (groupe R) ou 3 mg de ropivacaine avec 10 mg de sufentanil (groupe RS). Un observateur objectif a évalué l'hypotension, la douleur du travail selon une échelle visuelle analogique (EVA, 0–100), la force motrice des membres inférieurs, le début de l'analgésie, la sensation de froid, la sensibilité à la piqure, la durée de l'analgésie chez la mère et l'indice d'Apgar chez le nouveau-né. Le jour suivant l'accouchement, on a noté la satisfaction des patientes, la présence de céphalées et de déficit neurologique.

Résultats : La durée moyenne de l'analgésie a été, dans le groupe R, de $41,4 \pm 4,9$ min et, dans le groupe RS, de $95,0 \pm 6,1$ min (moyenne $\pm$ erreur type), $P = 0,0001$). Toutes les patientes étaient satisfaites de l'analgésie à cinq minutes, quoique l'analgésie fournie par la combinaison de ropivacaine-sufentanil ait été supérieure à l'analgésie fournie par la ropivacaine seule. La durée totale du travail n'a pas présenté de différence intergroupe (R- 306 ± 34 , RS- 384 ± 44 min, $P = 0,17$). Aucune patiente n'a présenté d'évidence de bloc

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moteur. Toutes les patientes ont été satisfaites de l'analgésie pendant le travail. Aucune complication neurologique n'est survenue.

Conclusion : L'administration intrathécale d'une faible dose de ropivacaine fournit une analgésie efficace pendant le travail. Elle peut être combinée au sufentanil selon les concentrations susmentionnées afin d'améliorer la qualité et la durée de l'analgésie. L'évolution du bébé demeure favorable. La ropivacaine peut entraîner un blocage moteur minimal, ou l'absence de bloc, ce qui permet à la patiente de déambuler.

INTRATHECAL labour analgesia using lipid soluble opioids has gained popularity. The addition of low doses of local anesthetic agents provides superior quality analgesia with minimal side effects.¹ Camann *et al.*² reported the efficacy of intrathecal sufentanil to provide labour analgesia and Campbell and his colleagues³ showed benefits of adding bupivacaine. The addition of local anesthetics to intrathecal opioids has the potential disadvantages of augmenting sympathetic and motor block. This may be of concern especially in an era where more and more anesthesiologists are using low dose labour analgesic regimens or the so called "walking epidural labour analgesia".⁴ Doses as low as 2.5 mg of bupivacaine have been shown to impair motor function.¹ Ropivacaine is an amino amide local anesthetic recently introduced into clinical practice. The specific gravity of ropivacaine ranges from 1.002 to 1.005 at 25°C and its pKa is similar to bupivacaine (8.1).

Although ropivacaine has been used to provide spinal anesthesia in the surgical population⁵ its intrathecal administration for labour analgesia has not been adequately studied. Levin *et al.* studied ropivacaine combined with sufentanil and compared it to bupivacaine with sufentanil.⁶ Available clinical data indicate that it may produce a lesser degree and shorter duration of motor block compared to bupivacaine.^{7,8} We have evaluated the analgesic profile of low dose intrathecal ropivacaine alone and when combined with sufentanil during labour.

Methods

After IRB approval and written informed consent, 36 term parturients in active labour, who requested analgesia, were enrolled in the study. They were randomly assigned to one of two groups using computer generated randomization table (Microsoft Excel, version 5/95). The person who recruited patients was not aware of the group assignment and was the blind-

ed independent assessor as well. The person who administered the analgesia knew what was being administered but the patient was blinded. Patients in group R received 3 mg of intrathecal ropivacaine (Naropin 0.2%; Astra, Westboro, MA, USA, 1.5 mL) while patients in group RS were given 3 mg ropivacaine (0.2%, 1.5 mL) mixed with 10 µg (diluted with preservative free saline to 1 mL) of sufentanil (Sufenta; Janssen, Piscataway, NJ, USA). Patients who had a previous history of backache and evidence of neurological disease were excluded.

The chosen doses of ropivacaine were tested and found to be physically compatible with sufentanil and did not precipitate either *in vitro* or with CSF when aspirated into the syringe. The dose of intrathecal ropivacaine was decided after a pilot study on 15 patients involving a range of doses from 2 to 4 mg. Two milligrams seemed to have a very short lasting effect where as 4 mg consistently provided a high level of sensory block reaching up to the 5th thoracic dermatome. A combined spinal epidural, needle through needle technique was utilized. A 17G Tuohy needle was used to locate the epidural space using loss of resistance to saline. A 24G pencil point Sprotte® spinal needle was used for injecting intrathecal medication. No epidural test dose was given after initiating spinal analgesia. Epidural analgesia using 15 mL of bupivacaine 0.04% along with fentanyl 1.66 µg·mL⁻¹ was initiated at the first request for further analgesia. Patients were evaluated by a blinded observer for any hypotension (20% drop in systolic blood pressure from the base line), labour pain (before and after the block) with a linear analogue score (VAS 0–100), motor power in the lower limbs using a modified Bromage scale [grade 1- complete block; grade 2- moves feet only; grade 3- moves feet and knees; grade 4- weakness of hip flexion; grade 5- no weakness of hip flexion when supine; grade 6- can do partial knee bend on standing],⁴ onset of analgesia, sensation to cold and pin prick, duration of analgesia (end point defined as the first request for analgesia), and neonatal Apgar scores. The following day patients were assessed for satisfaction from analgesia (using a yes/no format), headache and any neurologic complication.

Statistical analysis was performed using ANOVA and student's t test for parametric variables and data are presented as mean ± SEM. Fisher exact test was used for analysing dichotomous variables; pruritus, oxytocin augmentation, low blood pressure. Power analysis using our patient population mean and standard deviation suggested that 15 patients in each group would be sufficient to find a difference in 30 min duration of analgesia.

Results

There were no differences between the two groups in terms of age, height, weight, parity, cervical dilatation and use of oxytocin at the time of providing analgesia, initial pain scores, and Apgar scores at one and five minutes (Table I). There were no significant changes in fetal heart rate within 30 min of the onset of analgesia in any patient. The duration of analgesia with ropivacaine was 41.4 ± 4.9 min (mean $\pm$ SEM) with a range of 15–85 min. When combined with sufentanil it increased to 95.0 ± 6.1 min, range 45–132 min ($P=0.0001$). All subjects had satisfactory analgesia five minutes after the block, but analgesia from the ropivacaine-sufentanil combination was superior to that provided by ropivacaine alone (Table II). Total duration of labour after the onset of analgesia was no different between the groups (R- 306 ± 34 , RS- 384 ± 44 min, $P=0.17$). One patient in group RS developed hypotension, and the sensory level to pin prick was found to be T4. No patient showed any evidence of motor block (all grade 6). Fifty percent of the patients (11 in group R and seven in group RS) had no discernible sensory block to pin prick while 30.5% had no block to cold sensation (Table II). In the remaining 69.5% the sensory level to cold sensation ranged from T12 to T4. When asked about sensation in the lower extremities, 44% of patients in group R and 55% in the RS group felt a warm tingling sensation; in this subset a sensory level to pin prick could not be demonstrated in eight patients (four in each group). A sensory level was demonstrated in 50% of those patients whose legs felt normal. No patient felt sedated and 9/18 patients in the RS group experienced pruritus compared to 3/18 in group R ($P < 0.05$). None of the

patients reported any unpleasant side effects during or after the injection. There was no difference in the birth weights of the neonates born among the two groups (group R- 3585 ± 110 g; group RS- 3331 ± 169 g; $P=0.22$). All patients were satisfied with the analgesia provided during labour and no neurological complications including headaches were observed in any of the patients.

Discussion

We have compared a mixture of intrathecal ropivacaine and sufentanil with ropivacaine alone. The solubility of ropivacaine decreases with increases in pH above six. We did not observe any precipitation in the syringe upon aspiration of CSF during the administration of 3 mg of ropivacaine with or without sufentanil. It was also physically compatible with diluted sufentanil when the mixture was freshly prepared. When used alone, intrathecal ropivacaine provided shorter duration of analgesia as compared to the similar dose mixed with sufentanil. At this dose maternal hemodynamic instability was minimal and adverse fetal effects were absent.

Ropivacaine is a local anesthetic with lower cardiotoxic potential than racemic bupivacaine.⁹ The majority of published data on ropivacaine are on its use in the epidural space.^{10,11} There is little data available for its intrathecal use. Animal studies in dogs¹² and mice¹³ show that, at equal drug concentrations, intrathecal ropivacaine is less potent and produces a shorter duration of motor block. Iida *et al.*¹⁴ using an *in vivo* closed spinal window technique in a canine model showed that ropivacaine vasoconstricts, in a dose dependent fashion, pial arterioles and venules as compared to bupivacaine

TABLE I Demographic data

Group(n)	Age (yr)	Height (cm)	Weight (kg)	Gravida (median & range)	Para (median & range)	Oxytocin before block
R (18)	30.7 ± 1.4	164.1 ± 1.5	75.8 ± 2.5	2 (1–3)	1 (0–2)	8/18
RS (18)	29.9 ± 1.4	162.1 ± 1.3	74.0 ± 2.5	1 (1–4)	0 (0–2)	8/18
P value	NS	NS	NS	NS	NS	NS

R=Ropivacaine group; RS=Ropivacaine with sufentanil group; NS= Not significant.

TABLE II Analgesic profile and sensory changes (mean $\pm$ SEM)

Groups (n)	Post-spinal VAS	Pre-post spinal VAS difference	Duration of analgesia (min)	No sensory level to cold (n)	No sensory level to pin prick (n)
R (18)	37.4 ± 7.0	32.9 ± 6.7	41.4 ± 4.9	9	11
RS (18)	6.6 ± 1.2	67 ± 2.8	95 ± 6.1	2	7
P value	0.0005	0.0001	0.0001	<0.025	NS

SEM=standard error of the mean; VAS=visual analogue score for pain; R=ropivacaine group; RS=ropivacaine with sufentanil group; NS=not significant. $P < 0.05$ considered significant.

which dilates them. Kristensen *et al.*¹⁵ recently reported its relative safety when using ropivacaine in a rat model. Using clinically relevant doses they suggested it can be administered in the intrathecal space without significantly reducing spinal cord blood flow. van Kleef *et al.* first reported its intrathecal use in patients undergoing lower abdominal surgery by comparing 3 mL of 0.5% ropivacaine with 0.75% ropivacaine.⁵ They found less intense motor block and lesser duration of block with 0.5% ropivacaine and equated the anesthetic properties of 0.75% ropivacaine with those of 0.5% bupivacaine. Levin *et al.*⁶ described the use of a small dose of intrathecal ropivacaine mixed with sufentanil for labour. Comparing it with a bupivacaine sufentanil mixture they found no difference in the duration of analgesia, side effects and motor block.

In our study, low dose intrathecal ropivacaine alone provided a short duration of action, clinically insignificant sensory deficit during the period of analgesia and no loss in lower extremity motor function. When pooling data from both groups, fifty percent of patients had no discernible block to pin prick. It did strike us as strange that more patients in group R had no sensory level to pin prick, but this difference was lesser when sensory level was tested with ice. This may suggest an additive effect of sufentanil on sensory level. The different volumes in the two groups may have influenced the results but this seems unlikely. Using equidose hyperbaric and isobaric intrathecal bupivacaine, Malinovsky *et al.* reported that volume had no significant influence on either cephalad spread or duration of sensory blockade.¹⁶

With these potentially beneficial properties, ropivacaine may find a place in providing neuraxial analgesia and anesthesia, especially in settings where ambulation should be retained, such as analgesia during labour or outpatient anesthesia. Although this study is small, we did not find any clinical evidence for residual neuronal deficit or transient radiculopathy.

We have shown that low dose intrathecal ropivacaine provides effective analgesia during labour. Mixed with sufentanil in the above-mentioned concentrations it improves both the quality and duration of analgesia. Fetal outcome remains favourable. It is associated with minimal or no motor block, which should facilitate ambulation during labour.

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