

Low-dose combined spinal-epidural anesthesia for Cesarean delivery : a comparison of three plain local anesthetics

H. C. COPPEJANS and M. P. VERCAUTEREN

Abstract : The new local anesthetics have been poorly studied for intrathecal use during Cesarean section surely in low doses and in combination with an opioid substance. The purpose of the present study was to compare bupivacaine and the newer local anesthetics in equipotent doses.

During the induction of combined spinal-epidural anesthesia, 91 elective Cesarean section patients were randomly assigned to receive a spinal injection of either 10 mg ropivacaine or 6.6 mg bupivacaine or levobupivacaine both combined with sufentanil 3.3 µg. After securing the epidural catheter patients were turned to the supine position respecting a 15° left lateral tilt. The three local anesthetics were compared with respect to sensory and motor block, the need for epidural supplementation, the severity of hypotension and neonatal outcome.

More patients in bupivacaine had a Bromage-3 motor block at incision. The ropivacaine group required additional local anesthetics by the epidural route in 23% of the cases versus 10% in the bupivacaine group and 9% with levobupivacaine. This caused the interval between the spinal injection and the end of surgery to be longer in the ropivacaine group. Hemodynamic values were comparable between the three groups although a trend towards better systolic blood pressures and a lower incidence of severe hypotension were noticed in favor of levobupivacaine. Apgar scores and umbilical pH values did not differ.

When performing a low-dose combined spinal-epidural technique for Cesarean section, the present study confirms that the new local anesthetics can be used successfully, induce less motor block but that ropivacaine requires at least a 50% larger dose than bupivacaine or levobupivacaine.

Key words : Anesthesia ; combined spinal-epidural ; cesarean ; bupivacaine ; ropivacaine ; levobupivacaine.

There are only few studies evaluating the spinal use of the new local anesthetics for Cesarean section, at least not in low doses and combined with an opioid.

The intrathecal ED95 doses for ropivacaine and levobupivacaine, when used alone for Cesarean section were calculated to be 27 mg and 13.5 mg (1, 2). Especially for ropivacaine this dose is rather

high as compared to racemic bupivacaine. For the epidural route the potency difference between bupivacaine and ropivacaine during labor was found to be less i.e. 40% (3, 4). However this was contested in most clinical studies as such a difference could not be evidenced. When using levobupivacaine in labouring parturients the epidural potency difference in comparison with racemic bupivacaine has been found to be minimal (5).

While potency differences between the ropivacaine and racemic bupivacaine when administered epidurally are discussed for almost one decade, for the spinal route several studies showed that a 50% higher dose of ropivacaine as compared to racemic bupivacaine is mandatory to offer a similar quality of sensory and motor block (6-8). In a previous study we were able to demonstrate that the intrathecal injection of 15 mg ropivacaine corresponded fairly well with 10 mg levobupivacaine in terms of quality and duration of the block (9).

Also for Cesarean section a similar dose difference has been proven to be clinically correct (10-12). Despite the use of a 50% larger dose, ropivacaine still seems to induce a faster regression of motor block (13).

Another benefit in favor of ropivacaine was shown in a comparison with bupivacaine administered in equal intrathecal doses and finding less hypotension and/or less ephedrine requirements during Cesarean section anesthesia (14, 15).

Since one decade we use for Cesarean delivery a mixture of bupivacaine 0.5% (2 mL) and sufentanil 5 µg (1 mL) of which 2 mL are injected intrathecally corresponding with bupivacaine 6.6 mg and sufentanil 3.3 µg.

H. C. COPPEJANS, M.D. ; M. P. VERCAUTEREN, M.D., Ph.D., Dept of Anesthesia, University Hospital Antwerp, Wilrijkstraat 10, B-2650 Edegem, Belgium.

Correspondence to : Marcel P. Vercauteren, Associate Professor, Dept of Anesthesia, University Hospital Antwerp, Wilrijkstraat 10, B-2650 Edegem, Belgium.
Tel. : 0032 3 821 3044. Fax : 0032 3 825 0594. E-mail : marcel.vercauteren@uza.be.

The purpose of the present study was to evaluate whether there was a difference in anesthetic quality and side-effects during spinal anesthesia with low-dose equipotent mixtures of bupivacaine 6.6 mg, levobupivacaine 6.6 mg or ropivacaine 10 mg all in combination with sufentanil 3.3 µg.

METHODS

After approval by the Hospital Ethics committee and written informed consent, 91 term parturients with a duration of pregnancy exceeding 37 weeks and presenting for elective Cesarean delivery were enclosed in a prospective randomised double-blind study. Excluded were those females suffering from preeclampsia, hypertension, diabetes, obesity i.e. a body weight exceeding 110 kgs or multiple pregnancies.

Patients were positioned in the right lateral decubitus position to perform a combined spinal-epidural anesthetic technique. Before initiating the technique they received 1000 ml of Ringer's Lactate and 500 ml of Hetastarch 6% (Voluven®, Fresenius, France).

At the L3-L4 or L4-L5 interspace a skin wheel was raised with lidocaine 1% (Linisol®, B. Braun, Germany) and using the Durasafe Adjustable BD needle combination the epidural space was identified with the loss-of-resistance technique to air. Subsequently the 27G spinal Whitacre needle was introduced. Following appearance of CSF, bupivacaine 6.6 mg, levobupivacaine 6.6mg or ropivacaine 10 mg, all in combination with sufentanil 3.3 µg were slowly injected. The epidural catheter was introduced and withdrawn leaving 3 cm in the epidural space. After securing the catheter and prophylactic administration of ephedrine 5 mg patients were placed in a supine position respecting a moderate 15° left lateral tilt position.

The progress of sensory block was tested every two minutes with ether swabs and motor impairment was assessed using the modified Bromage scale. Surgery was allowed to start when at least the T5 dermatomal level was obtained. The extent and degree of sensory and motor block obtained at incision were considered as the maximal score as further follow-up was considered to be unpractical.

In case of insufficient cephalad spread or when pain sensations reappeared, incremental epidural supplements were injected consisting of 4 mL of lidocaine 2% and when necessary additional 2 ml boluses were given.

During the complete surgical procedure hemodynamics were registered every 2 minutes. Ephedrine increments of 5mg were given in case of hypotension i.e. when the systolic blood pressure decreased 20% below base-line values or was less than 95 mmHg. Also when patients felt nauseous the same treatment was initiated regardless of the blood pressure values obtained at that particular moment. Other side-effects such as nausea, vomiting and pruritus were registered throughout the intra-operative period.

At birth neonates were evaluated by Apgar score (at 1 and 5 minutes), umbilical venous (UV) and arterial (UA) pH values.

The degree of motor block was scored at the end of surgery. Patients were discharged to the ward when bilaterally the motor block had regressed to a degree of Bromage-1 or less.

Statistical evaluation was performed using the ANOVA-test, unpaired two-tailed Student-t test and the Fisher's exact test as appropriate. A $p < 0.05$ value was considered to be significant.

RESULTS

There were no differences in patient demographics with respect to age, weight, height, parity and the duration of pregnancy (Table 1).

All patients had a sensory block reaching at least T5 except for two females in the bupivacaine group (Table 2). More patients in the bupivacaine group had a complete motor block at incision whereas the majority of patients receiving the new local anesthetics was still able at that moment to flex ankles or knees. This was also reflected at the end of surgery when 22% of the levobupivacaine and 29% of the ropivacaine treated patients had a Bromage motor block of 1 or zero as opposed to 66% of those receiving bupivacaine ($p < 0.01$). Seven patients (23%) in the ropivacaine group required supplementation or extension of the block by the epidural route versus three in the other groups (NS). Nevertheless, due to this, the interval between the spinal injection and termination of surgery was significantly prolonged in the ropivacaine group.

The total ephedrine requirements and incidence of ephedrine supplementation were identical. There was a trend towards a higher systolic blood pressures and less profound hypotension in the levobupivacaine as in this group only 2 patients (6%) had systolic values lower than 90 mmHg as compared to 20% for bupivacaine and ropivacaine

Table 1

Patient demographics. Data are expressed as mean \pm (SD) or as number of patients. There are no significant differences

	Bupivacaine N = 30	Ropivacaine N = 30	Levobupivacaine N = 31
Age – yrs-	31 (4)	32 (4)	32 (5)
Weight – Kgs- range	75 (10) (51-100)	77 (9) (59-109)	75 (11) (65-110)
Height – cm-	166 (6)	167 (6)	166 (6)
Parity -nulli/multi-	10/20	11/19	11/20
Duration of pregnancy – wks-	38 (1)	38 (1)	39 (1)

Table 2

Block characteristics. Data are expressed as N (%) or mean (SD). CSE (Combined Spinal Epidural)

	Bupivacaine n = 30	Ropivacaine n = 30	Levobupivacaine n = 31	p value
Sensory block Range	T3-T4 C5-T7	T3-T4 C4-T5	T3-T4 T1-T4	NS
Motor block Bromage-3 (<i>incision</i>)	21 (70)	11 (36)*	8 (26)*	< 0.01
Motor block > Bromage-1 (<i>end of surgery</i>)	20 (66)	9 (30)*	7 (22)*	< 0.01
Epidural supplementation	3 (10)	7 (23)	3 (9)	NS
CSE-end of surgery -min.-	55 (10)	67 (13)	59 (13)	< 0.05

Table 3

Hemodynamic effects. Data are expressed as mean (SD) or number of patients (%). There were no significant differences

	Bupivacaine n = 30	Ropivacaine n = 30	Levobupivacaine n = 31
Lowest SBP (mmHg)	104 (18)	108 (19)	114 (20)
Ephedrine (mg)	8.5 (7)	9.7 (7.6)	8.3 (6.8)
Ephedrine suppl (%)	50	36	35
SBP < 100mmHg	9 (30)	11 (36)	9 (29)
SBP < 90mmHg	6 (20)	6 (20)	2 (6)
Nausea / vomiting	14/1 (47/3)	12/3 (40/10)	8/1 (25/3)

but the difference did not reach statistical significance (Table 3).

At the end of surgery no differences were noticed in the incidence of pruritus (12 patients in each group). Neonates had similar Apgar scores being 9 or more at 5 minutes (Table 4). Umbilical venous and arterial pH values were equal in the three groups.

DISCUSSION

The present study found that ropivacaine and levobupivacaine provide good anesthetic quality during CSE anesthesia for elective Cesarean section as compared to bupivacaine. When used in equipotent doses but significantly less than the reported ED95 doses and combined with sufentanil

no epidural supplementation was required in the majority of patients.

The advantage of a CSE procedure is that low-dose anesthesia can be produced and adjusted or prolonged by the epidural route when the duration of surgery exceeds the duration of analgesia or when the spread or density of the block are insufficient. Nevertheless, several centers will find a supplementation incidence of 23%, as required in our ropivacaine group too much because it will prolong the stay in the operating room while motor block may be reinstalled or enhanced which may delay discharge times.

There may have been several problems in the ropivacaine group (epidural supplements, nausea/vomiting) being responsible for longer intraoperative times. The economical implications of this are probably more important than the clinical relevance.

Table 4

Neonatal outcome : Apgar scores and UV(umbilical vein) and UA (umbilical artery) pH.
There were no statistically significant differences

	Bupivacaine	Ropivacaine	Levobupivacaine
Apgar at 1 min. (range)	8 6-9	8 6-9	9 8-10
Apgar at 5 min. (range)	9 7-10	9 9-10	9 8-10
UV pH (SD)	7.35 (0.04)	7.36 (0.04)	7.36 (0.03)
UA pH (SD)	7.30 (0.03)	7.30 (0.03)	7.31 (0.03)

The relative potencies of local anaesthetics by the neuraxial route will remain subject of debate. Although a 40% difference in epidural ED50 doses has been found in parturients between racemic bupivacaine and ropivacaine, it seems difficult to confirm this in routine clinical use (3, 4). This may be explained by the lack of clinical relevance of ED50 values or the addition of adjuvant substances. For levobupivacaine the potency difference calculated also during labour analgesia in comparison with racemic bupivacaine seems to be as low as 2% (5).

Despite discussions with respect to potency differences for the epidural route, it seems to be beyond any discussion that intrathecal ropivacaine requires at least a 50% larger dose than

racemic bupivacaine or levobupivacaine (6-9). Although levobupivacaine seems to allow equal doses as used previously for racemic bupivacaine (16), GAUTIER *et al.* found that intrathecal levobupivacaine 8 mg with sufentanil required more epidural supplementation than the same dose of bupivacaine (11). This may correspond with the higher ED95 values for levobupivacaine as compared to bupivacaine i.e. 13.5 mg and 9.9 mg resp. (2). As the same authors found that for ropivacaine this dose was 27 mg, this would suggest that ropivacaine requires a dose at least twice that of bupivacaine or levobupivacaine to offer a comparable anesthetic quality (1, 2). These values were based upon the need for epidural supplementation without any details regarding the moment during the procedure when this additional dose was required. An epidural supplement required during skin closure is more related to duration of effect than to potency. In a subsequent study KHAW *et al.* still had a large amount of failures when using 25 mg of plain ropivacaine while a hyperbaric solution appeared to be more effective but caused more hypotension (17).

With respect to motor block potency both local anesthetics seem to have higher ED50 values

than bupivacaine while even a 15% difference was noticed between ropivacaine and levobupivacaine (18, 19). CHUNG *et al.* found that spinal anaesthesia with 18mg ropivacaine still offered a faster recovery of motor block than 12 mg racemic bupivacaine (9). This was confirmed in the study by GAUTIER *et al.* comparing levobupivacaine (8 mg), racemic bupivacaine (8 mg) and ropivacaine (12 mg) for Cesarean section, all in combination with sufentanil (11). The authors found shorterlasting motor block with the new local anesthetics without any difference between levobupivacaine and ropivacaine. Other studies have found less profound, rather than shorterlasting motor block with intrathecal and epidural levobupivacaine in both laboring and C-section patients (20, 21).

The difference in maximal motor block degree is remarkable and the incidences for bupivacaine correspond with our previous experience (22). Bupivacaine caused a complete motor block in 70% of the patients while none of all patients was able to flex the knee. In the present study 30% of the patients receiving either levobupivacaine or ropivacaine was able to do this. Motor block at the end of surgery still differed in favor of the new local anesthetics which allowed earlier discharge from the recovery room to the ward. Based upon a few studies in the literature some evidence is growing that ropivacaine might cause less hypotension than racemic bupivacaine. Two intrathecal studies using 15 mg of bupivacaine and ropivacaine found better hemodynamics with the latter (13, 14). However, the most important question which arises is about the 'equipotency' of the doses used. In addition, in the study of WHITESIDE *et al.*, ropivacaine appeared to induce a more limited cephalad spread while it was also less hyperbaric than bupivacaine (14).

BADER *et al.* showed that levobupivacaine when used epidurally for Cesarean section also tends to cause less hypotension and ephedrine requirements but statistical significance was

borderline (23). Despite the existence of few abstracts, up to now no reports have been published in peer reviewed journals showing hemodynamic benefit with the intrathecal use of levobupivacaine. We believe that the low doses used in combination with colloid prehydration and ephedrine prophylaxis, as in the present study, will make it less likely to find significant hemodynamic differences. The only suggestive finding in our study was a 10mm higher systolic blood pressure value in the levobupivacaine group as compared to bupivacaine while values < 90 mmHg were registered in only 6% for levobupivacaine versus 20% with both other substances.

In conclusion, the new local anesthetics can be used safely for intrathecal anesthesia during Cesarean section. They induce less motor block than racemic bupivacaine. Ropivacaine even in a dose being 50% larger than levobupivacaine seems to induce less reliable anesthesia. Levobupivacaine tends to behave better hemodynamically. To avoid excessive supplementation by the epidural route a larger ropivacaine dose may be suggested although this may have possible consequences upon motor block and hemodynamics.

References

1. Khaw K. S., Ngan Kee W. D., Wong E. L., *et al.*, *Spinal ropivacaine for cesarean section : a dose-finding study*, ANESTHESIOLOGY, **95**, 1346-50, 2001.
2. Khaw K., Ngan Kee W. D., Ng F., Leung P., *Dose-finding comparison of spinal levobupivacaine and bupivacaine for caesarean section*, INT. J. OBSTET. ANESTH., **13** (suppl) : 028, 2004.
3. Polley L. S., Columb M. O., Naughton N. N., *et al.*, *Relative analgesic potencies of ropivacaine and bupivacaine for epidural analgesia in labor*, ANESTHESIOLOGY, **90**, 944-50, 1999.
4. Capogna G., Celleno D., Fusco P., *et al.*, *Relative potencies of bupivacaine and ropivacaine for analgesia in labour*, BR. J. ANAESTH., **82**, 371-3, 1999.
5. Lyons G., Columb M., Wilson R. C., *et al.*, *Epidural pain relief in labour : potencies of levobupivacaine and racemic bupivacaine*, BR. J. ANAESTH., **81**, 899-901, 1998.
6. Gautier E., De Kock M., Van Steenberghe A., *et al.*, *Intrathecal ropivacaine for ambulatory surgery*, ANESTHESIOLOGY, **91**, 1239-45, 1999.
7. McDonald S. B., Liu S. S., Kopacz D. J., Stephenson C. A., *Hyperbaric spinal ropivacaine : a comparison to bupivacaine in volunteers*, ANESTHESIOLOGY, **90**, 971-7, 1999.
8. Malinovsky J. M., Charles F., Kick O., *et al.*, *Intrathecal Anesthesia : Ropivacaine versus Bupivacaine*, ANESTH. ANALG., **91**, 1457-60, 2000.
9. Breebaart M. B., Vercauteren M., Hoffmann V. L., Adriaensen H. A., *Bladder-scanning for evaluation of micriturition after day case arthroscopy : a comparison between intrathecal lignocaine, ropivacaine and levobupivacaine*, BR. J. ANAESTH., **90**, 309-13, 2003.
10. Chung C. J., Choi S. R., Yeo K. H., *et al.*, *Hyperbaric spinal ropivacaine for cesarean delivery : a comparison to hyperbaric bupivacaine*, ANESTH. ANALG., **93**, 157-61, 2001.
11. Gautier P., De Kock M., Huberty L., *et al.*, *Comparison of the effects of intrathecal ropivacaine, levobupivacaine, and bupivacaine for Caesarean section*, BR. J. ANAESTH., **91**, 684-9, 2003.
12. Danelli G., Fanelli G., Berti M., Cornini A., Lacava L., Nuzzi M., Fanelli A., *Spinal ropivacaine or bupivacaine for cesarean delivery : a prospective, randomized, double-blind comparison*, REG. ANESTH. PAIN MED., **29**, 221-6, 2004.
13. Kallio H., Snall E. V., Kero M. P., Rosenberg P. H., *A comparison of intrathecal plain solutions containing ropivacaine 20 or 15 mg versus bupivacaine 10 mg*, ANESTH. ANALG., **99**, 713-7, 2004.
14. Ögün C. Ö., Kirgiz E. N., Duman A., *et al.*, *Comparison of intrathecal isobaric bupivacaine-morphine and ropivacaine-morphine for Caesarean delivery*, BR. J. ANAESTH., **90**, 659-664, 2003.
15. Whiteside J. B., Burke D., Wildsmith J. A., *Comparison of ropivacaine 0.5% (in glucose 5%) with bupivacaine 0.5% (in glucose 8%) for spinal anaesthesia for elective surgery*, BR. J. ANAESTH., **90**, 304-308, 2003.
16. Glaser C., Mayrhofer P., Zimpfer G., *et al.*, *Levobupivacaine versus racemic bupivacaine for spinal anesthesia*, ANESTH. ANALG., **94**, 194-8, 2002.
17. Khaw K. S., Ngan Kee W. D., Wong M., *et al.*, *Spinal ropivacaine for cesarean delivery : a comparison of hyperbaric and plain solutions*, ANESTH. ANALG., **94**, 680-5, 2002.
18. Camorcica M., Capogna G., Lyons G., Columb M., *Epidural test dose with levobupivacaine and ropivacaine : determination of ED50 motor block after spinal administration*, BR. J. ANAESTH., **92**, 850-3, 2004.
19. Lacassie H. J., Columb M. O., *The relative motor blocking potencies of bupivacaine and levobupivacaine in labor*, ANESTH. ANALG., **97**, 1509-13, 2003.
20. Vercauteren M., Hans G., De Decker K., Adriaensen H., *Levobupivacaine combined with sufentanil and epinephrine for intrathecal labor analgesia : a comparison with racemic bupivacaine*, ANESTH. ANALG., **93**, 996-1000, 2001.
21. Faccenda K. A., Simpson A. M., Henderson D. J., Smith D., McGrady E. M., Morrison L. M., *A comparison of levobupivacaine 0.5% and racemic bupivacaine 0.5% for extradural anesthesia for caesarean section*, REG. ANESTH. PAIN MED., **28**, 394-400, 2003.
22. Vercauteren M., Coppejans H., Hoffmann V., Saldien V., Adriaensen H., *Small-dose hyperbaric versus plain bupivacaine during spinal anesthesia for Cesarean section*, ANESTH. ANALG., **86**, 989-93, 1998.
23. Bader A. M., Tsen L. C., Camann W. R., Nephew E., Datta S., *Clinical effects and maternal and fetal plasma concentrations of 0.5% epidural levobupivacaine versus bupivacaine for cesarean delivery*, ANESTHESIOLOGY, **90**, 1596-601, 1999.