

Spinal anesthesia : Comparison of plain ropivacaine, bupivacaine and levobupivacaine for lower abdominal surgery

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Abstract : This study was performed to compare the anesthetic efficacy and safety of three local anesthetic agents : racemic bupivacaine and its two isomers : ropivacaine and levobupivacaine, in patients undergoing lower abdominal surgery. One hundred-twenty patients, ASA I-III, were randomized to receive an intrathecal injection of one of three local anesthetic solutions. Group A (n = 40) received 3 ml of isobaric bupivacaine 5 mg/ml (15 mg). Group B (n = 40) received 3 ml of isobaric ropivacaine 5 mg/ml (15 mg). Group C (n = 40) received 3 ml of isobaric levobupivacaine 5 mg/ml (15 mg). The onset and duration of sensory block at dermatome level T8, maximum upper spread of sensory block, time for 2-segment regression of sensory block as well as the onset, intensity and duration of motor block were recorded, as were any adverse effects, such as bradycardia, hypotension, hypoxia, tremor, nausea and/or vomiting. Time to unassisted standing up and voluntary micturition was also recorded. The onset of motor block was significantly faster in the bupivacaine group compared with that in the ropivacaine group and almost the same of that in the levobupivacaine group ($P < 0.05$). Ropivacaine presented a shorter duration of both motor and sensory block than bupivacaine and levobupivacaine ($P < 0.05$). Bupivacaine required more often the use of a vasoactive drug (ephedrine) compared to both ropivacaine and levobupivacaine and of a sympathomimetic drug (atropine) compared to the ropivacaine group.

Key words : Anesthetic techniques, regional ; anesthetic techniques, subarachnoid ; anesthetics local, bupivacaine ; ropivacaine ; levobupivacaine ; surgery.

INTRODUCTION

Spinal anesthesia is widely used, providing a fast onset and effective sensory and motor blockade. Bupivacaine is available as a racemic mixture of its enantiomers, dextrobupivacaine and levobupivacaine (19). The last few years, its pure S-enantiomers, ropivacaine and levobupivacaine, have been introduced into clinical practice because of their lower toxic effects for heart and central nervous system (5, 12-14, 16). The clinical profile of spinal bupivacaine, ropivacaine and levobupivacaine has been evaluated in volunteers and clinical

studies ; however, to our knowledge, only a few reports are available on the use of these three local anesthetics in patients undergoing lower abdomen surgery (2).

The aim of the present study was to compare the safety and efficacy of either plain ropivacaine 15 mg, plain bupivacaine 15 mg or plain levobupivacaine 15 mg in patients undergoing lower abdominal surgery under spinal anesthesia.

MATERIAL AND METHODS

With the approval of the Institutional Ethical Committee and written informed consent of the patient, 120 ASA physical status I-III patients, scheduled for elective lower abdominal surgery (inguinal hernia repair and varicocele) under spinal anesthesia, were prospectively enrolled. Patients who had contraindications to spinal anesthesia, allergy to amide local anesthetics and a significant history of drug or alcohol abuse were excluded.

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Exclusion criteria also included morbid obesity (Body Mass Index BMI > 29 kg/m²), as well as diabetic, neurological and musculoskeletal diseases that could make our technique difficult.

Following arrival in the anesthetic room, I.V. access was established and an infusion of 500 ml Ringer's lactated (L-R) commenced. Patients were premedicated with 3 mg of midazolam intravenously and placed in the left lateral position. After skin's infiltration with 2% lidocaine, a 20G introducer needle was inserted at the L3/4 interspace in the midline through which a 25G High Flow Whitacre needle (Becston Dickinson and Co, Franklin Lakes, NJ) was passed. Correct needle placement was identified by free flow of cerebrospinal fluid and 3 ml (15 mg) of the study drug was injected over 10 s. Using a sealed envelope technique, patients were randomly allocated to three groups: patients in group A received plain bupivacaine 15 mg (3 ml isobaric 0.5%), in group B received plain ropivacaine 15 mg (2 ml isobaric 0.75% + 1 ml 0.9% NaCl) and in group C received plain levobupivacaine 15 mg (3 ml isobaric 0.5%). All 3-ml solutions were prepared in an adjacent room by a supervisor not involved in the subsequent evaluation of the study-patient. After the injection of the drug the spinal needle was removed and the patient placed supine.

Standard monitoring was used throughout the operation. ECG and pulse – oximetry were monitored continuously while arterial pressure was measured at 5-min intervals (Dinamap, Johnson & Johnson). Heart rate and arterial pressure were recorded before intrathecal injection, 5 minutes after the intrathecal drug administration, and thereafter every 10 minutes till the end of the operation and one hour after the end of the operation, at the ward. Any hypotension (mean arterial pressure lower than 60 mmHg) or bradycardia (heart rate < 50/min) incidents were treated with ephedrine 5 mg or atropine 0.5 mg increments. A decrease in SpO₂ to < 93% was defined as hypoxia and treated with supplemental oxygen via a Venturi - mask 40% at 10 l/min.

The level of sensory block was evaluated by loss of pinprick sensation (20-gauge hypodermic needle). The test was performed every 5 minutes till loss of discrimination to pinprick for the first 60 minutes and then every 10 minutes until its full recovery. We checked bilaterally S1, L3, T12, T10, T8, T6 or higher (T4) dermatomes by needle protrusion 2 mm through a guard and we used C5-6 as baseline point for normal sensation. Sensory block score was determined using the following scale:

1 = hypoalgesia, 2 = analgesia, 3 = analgesia and hypoaesthesia and 4 = anesthesia. Motor blockade was assessed using a modified Bromage scale (0 = no motor block, 1 = hip blocked, 2 = hip and knee blocked, 3 = hip, knee and ankle blocked). The maximum Bromage score reached and duration of the motor block (from spinal injection until Bromage 1 and/or 0 score) were registered every 5 minutes after drug's injection until full recovery.

The onset time of sensory or motor blockade was defined as the interval between intrathecal administration and maximum pinprick score, or a Bromage score of 3, respectively. The duration of sensory or motor blockade was defined as the interval from intrathecal administration to the point of complete resolution of the sensory block, or to the point in which the Bromage score was back to zero. The maximum level of sensory block, the onset time, the duration of sensory and motor blockade, as well as the interval from intrathecal administration to the point of a 2-segment regression of sensory blockade and the eligibility for home discharge was recorded. Most of the patients (115 of 120) had day-case surgery. Criteria for home discharge were stable vital signs, ability to stand up without help and void spontaneously, with no nausea or pain. The occurrence of adverse events, including bradycardia, hypotension, decrease in oxygen saturation SpO₂ < 93%, tremor, as well as nausea and vomiting was also recorded.

STATISTICS

All statistical analyses were performed using the SPSS version 10, 1 for windows (SPSS Inc., Chicago, Illinois®). Quantitative data are presented as means and standard deviation (mean ± sd) and qualitative data as frequency and 95% confidence interval (CI). Age, weight, height and BMI as well as ASA physical status were analyzed using Frequencies test. We analysed systolic, diastolic and mean arterial pressure, as well as heart rate and surgical time, using ANOVA Repeated Measures test with correction according to Bonferroni. Onset time, spread and duration of either motor or sensory blocks as well as use of vasoconstrictive drugs or atropine were analysed with χ^2 or student's t test. Side effects' incidence (nausea, vomiting, tremor, convulsions) was analysed using Fischer's exact test. Time to stand up and void without help (modified PADSS) was analysed using the Mann – Whitney test. Significance was defined as $P < 0.05$.

Table 1

Patient characteristics and duration of surgery for the three groups

	Group A (n = 40) x ± SD	Group B (n = 40) x ± SD	Group C (n = 40) x ± SD
Age (ys)	53 ± 14	55 ± 12	57 ± 10
Weight (kg)	73 ± 13	67 ± 11	70 ± 9
Height (cm)	169 ± 9	166 ± 5.5	165 ± 9.3
ASA I-III	36/3/1	36/4/0	35/5/0
BMI (Kg/m ²)	26 ± 3	24 ± 2.7	26 ± 4.7
Sex (M/F)	26/14	25/15	24/16
Duration of surgery (min)	60 ± 25	62 ± 19	59 ± 30

RESULTS

The characteristics of the three groups were comparable in terms of age, height, weight, gender, body mass index (BMI), and ASA physical status. Time of surgery was comparable also (Table 1). One patient from each group was excluded from the study, due to insufficient height of the sensory block. All statistical analyses were therefore based on 39 patients in each group.

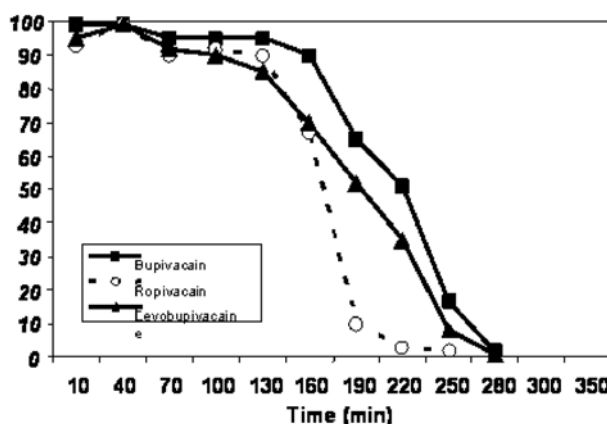
The onset of motor block (time to achieve a Bromage score of 3) was significantly faster in the bupivacaine group (group A) : 8 ± 5 min compared with 12 ± 5 min in the ropivacaine group (group B) and 11 ± 7 min in the levobupivacaine group (group C) (P < 0.05). The mean time of onset to achieve a Bromage score of 1 or of 2 was 2 ± 1 min and 3 ± 1 min in the bupivacaine group, 3 ± 1 min and 5 ± 2 min in the ropivacaine group, and 2 ± 1 min and 4 ± 2 min in the levobupivacaine group, respectively. These differences were not significant. Ropivacaine presented a shorter duration of motor block than bupivacaine and levobupivacaine (269 ± 20 min, 278 ± 70 min and 273 ± 80 min, respectively) (P < 0.05). No difference was observed in the duration of motor block among bupivacaine and levobupivacaine (278 ± 70 min and 273 ± 80 min, respectively). Furthermore, the duration of sensory block was significantly shorter in patients receiving ropivacaine than in those receiving bupivacaine or levobupivacaine (220 ± 30 min, 237 ± 88 min and 230 ± 74 min, respectively). There were no significant differences in the duration of sensory block between bupivacaine and levobupivacaine, as well as in the onset and upper extend of sensory block among the three groups (P > 0.05). Table 2, as well as figure 1, present the characteristics (onset and duration) of motor block in groups A (bupivacaine), B (ropivacaine), and C (levobupivacaine).

Table 2

Time (min) for the transition from Bromage score 0 to Bromage score 1, 2 or 3

Time (min)	Group A x ± SD	Group B x ± SD	Group C x ± SD
Bromage 1	2 ± 1	3 ± 1	2 ± 1
Bromage 2	3 ± 1	5 ± 2	4 ± 2
Bromage 3	8 ± 5*	12 ± 5*	11 ± 7*

* (P < 0.05).



Patients (%)

Fig. 1. — Onset and duration of motor block with time after intrathecal administration of isobaric bupivacaine 5 mg/ml, ropivacaine 5 mg/ml or levobupivacaine 5 mg/ml.

Figure 2 describes the maximum cephalad spread and variation of sensory block in the three groups. One patient from each group was excluded due to insufficient height of sensory block. There were no statistically significant differences among the three groups.

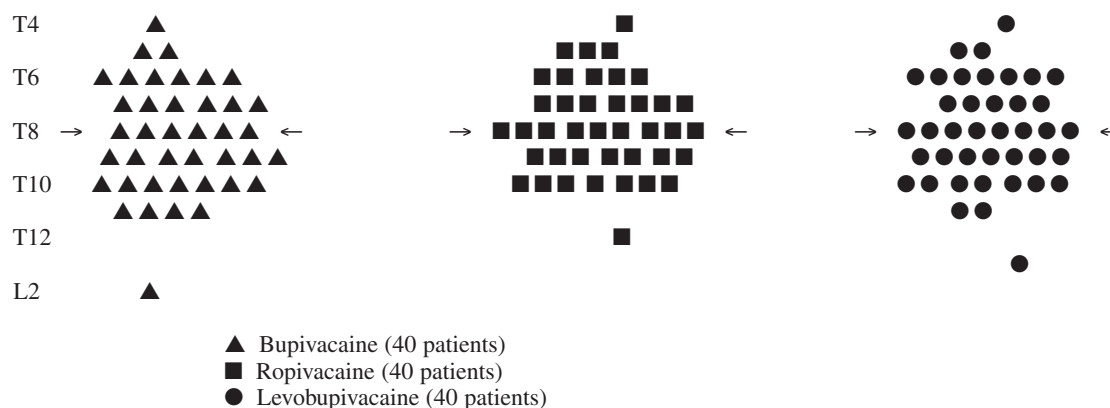


Fig. 2. — Maximum cephalad spread and variation of sensory block in the three groups. Every point represents a patient and the arrows stand for mean values in each group. One patient from each group was excluded from the study, due to insufficient height of sensory block.

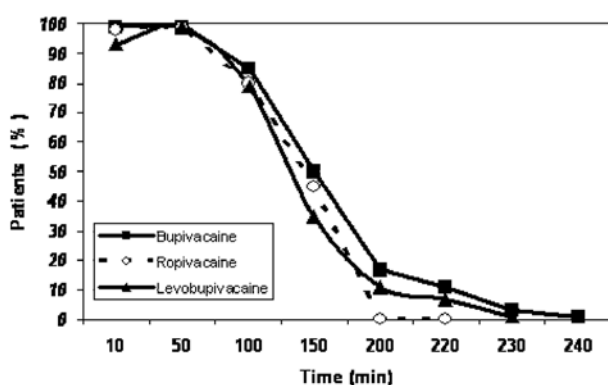


Fig. 3. — Onset, duration and regression of sensory block with time after intrathecal administration of isobaric bupivacaine 5 mg/ml, ropivacaine 5 mg/ml or levobupivacaine 5 mg/ml.

Figure 3 presents the onset, duration and time for regression of sensory block with time after intrathecal administration of isobaric bupivacaine 5 mg/ml, ropivacaine 5 mg/ml or levobupivacaine 5 mg/ml. Statistically significant were only the differences in sensory block onset between the ropivacaine and the bupivacaine and the ropivacaine and the levobupivacaine groups respectively ($P < 0.05$).

Time to achieve surgical analgesia up to T8 dermatome was 13 ± 9 min for the bupivacaine group, 12 ± 7 min for the ropivacaine group and 11 ± 6 min for the levobupivacaine group. Time for regression of motor block from Bromage scale 3 \rightarrow 2 was 85 ± 20 min for group A, 65 ± 15 min for group B and 79 ± 19 min for group C. Regression time from Bromage scale 2 \rightarrow 1 was 102 ± 35 min for group A, 84 ± 18 min for group B and 97 ± 25 min for group C. Finally complete regression of the motor block (Bromage scale 1 \rightarrow 0) took 150 ± 40 min for the bupivacaine, 100 ± 34 min for the ropivacaine and 145 ± 37 for the levobupivacaine group. Time for 2-segment regression of sensory blockade (from T8-T10) was 69 ± 16 for group A,

60 ± 9 for group B and 65 ± 11 for group C. There were no statistically significant differences between groups except for the fact that the regression of motor block from one stage of the Bromage scale to the previous one (from 3 to 2, 2 to 1, or 1 to 0), as well as the 2-segment regression of sensory block (from T8 to T10 dermatome) was significantly faster in the ropivacaine group than in the other two groups.

There was a slight reduction in mean arterial blood pressures after the spinal injection in all groups, which however was significant only in the bupivacaine group. In addition, the decrease in heart rates after local anesthetic agent's injection was significant in all groups. However, there were no significant intergroup differences in heart rates (Table 3). Intraoperative hypotension requiring treatment with I.V. ephedrine occurred more often in the bupivacaine group (42.5% of patients) than in the ropivacaine and levobupivacaine groups (25% and 17.5% of patients, respectively) ($P = 0.02$). Bradycardia was also more common in the bupivacaine group (5 patients) than in the ropivacaine group (2 patients), respectively ($P = 0.04$). The most commonly reported adverse events were nausea, vomiting, tremor, and decrease in oxygen saturation $SpO_2 < 93\%$. These events were equally distributed between groups (Table 4). In no case was urinary retention reported, and time to unassisted standing up and voluntary micturition was 2 ± 1 hours in the bupivacaine group, 2 ± 1 hours in the ropivacaine group, and 2 ± 0.9 hours in the levobupivacaine group ($P = 0.99$).

DISCUSSION

This study shows that the intrathecal administration of either 15 mg ropivacaine, 15 mg bupiva-

Table 3

Mean arterial pressure (MAP in mmHg) and heart rate (HR) before the spinal anesthesia and up to 1 hour after the end of surgery

	Group A (MAP mmHg) (HR) x ± SD	Group B (MAP mmHg) (HR) x ± SD	Group C (MAP mmHg) (HR) x ± SD
0	109 ± 15 100 ± 15	108 ± 15 102 ± 15	106 ± 11 100 ± 18
1	98 ± 17 80 ± 12	104 ± 17 80 ± 12	103 ± 14 78 ± 15
2	88 ± 9 75 ± 14	92 ± 15 75 ± 15	96 ± 11 75 ± 26
3	81 ± 15 72 ± 25	90 ± 15 72 ± 19	91 ± 24 74 ± 11
4	78 ± 11 74 ± 12	89 ± 9 70 ± 21	86 ± 11 74 ± 12
5	79 ± 8 78 ± 14	86 ± 11 75 ± 17	88 ± 12 77 ± 14
6	84 ± 14 79 ± 12	87 ± 7 79 ± 12	86 ± 14 79 ± 11
7	88 ± 10 75 ± 10	94 ± 14 75 ± 9	96 ± 17 75 ± 12

0 = MAP and HR just before spinal injection, 1 = MAP and HR 5 min after spinal injection, 2 = MAP and HR 10 min later, 3 = MAP and HR 20 min later, 4 = MAP and HR 30 min later, 5 = MAP and HR 40 min later, 6 = MAP and HR at the end of the operation and 7 = MAP and HR 1 hour after the end of the operation.

caine or 15 mg levobupivacaine was well tolerated and an adequate block for lower abdominal surgery was achieved in all but one patient in each group. Ropivacaine presented a slower onset and a shorter duration of motor block, as well as a faster resolution of sensory block compared with the other two local anesthetics, even though this was not associated with a significant acceleration of home discharge. Intergroup differences between levobupivacaine and bupivacaine were insignificant both with regard to the onset time of sensory blockade and the duration of sensory and motor blockade. The

cephalic spread of sensory block was similar in all groups. These results are partially in agreement with those of other investigators (2, 3, 6-8, 10, 15). The present study is the first, to our knowledge, to compare the efficacy and safety of these three glucose-free solutions, ropivacaine 5 mg ml⁻¹, bupivacaine 5 mg ml⁻¹ and levobupivacaine 5 mg ml⁻¹ as a sole anesthetic agent in patients undergoing lower abdominal surgery under spinal anesthesia.

McNAMEE *et al.* (15), compared 17.5 mg of plain ropivacaine with 17.5 mg of plain bupivacaine in patients undergoing total hip arthroplasty under spinal anesthesia. There were no significant differences in the upper extent of sensory block, in the onset of motor and sensory block, as well as in the intraoperative efficacy between the two groups. On the other hand, a more rapid postoperative recovery of sensory and motor function was seen in the ropivacaine group compared with the bupivacaine group, which is also in accordance with our findings. Moreover, GAUTIER *et al.* (6), compared the effects of intrathecal administration of either 8 mg isobaric bupivacaine, 8 mg isobaric levobupivacaine, or 12 mg isobaric ropivacaine, all combined with sufentanil 2.5 microg in patients undergoing caesarean section. Once more, bupivacaine provided a longer duration of analgesia and motor block than ropivacaine. It was also associated with a significant superior success rate to that observed in the levobupivacaine group, which contrasts with our results and those reported by GLASER *et al.* (8), and by CHENG *et al.* (3). In addition, the faster complete regression of spinal anesthesia observed in patients receiving ropivacaine in our study approximates the values recently reported by CASATI *et al.* (2). However, in their study, no differences were observed in the onset time both of sensory and motor block between ropivacaine, levobupivacaine or bupivacaine. The reason for the observed

Table 4

Adverse events after spinal injection

	Group A No (%)	Group B No (%)	Group C No (%)
Nausea	3 (7,5%)	2 (5%)	4 (10%)
Vomiting	1 (2,5%)	0 (0%)	0 (0%)
Tremor	11(27,5%)	13 (32,5%)	15 (37,5%)
Ephedrine (5 mg) > 1 bolus	17 (42,5%)*, §	10 (25%)*	7 (17,5%) §
Atropine (0,5 mg)	5 (12,5%)*	2 (5%)*	4 (10%)
SpO ₂ < 93% / Vm	6(15%)	4(10%)	5(12,5%)

No = number of patients, (%) = percentage of patients

*, § statistically significant intergroup differences

P = 0,01 for ephedrine and P = 0,04 for atropine.

differences between our results and those seen in the above-mentioned studies, is not apparent, but it could be attributed to methodological differences, such as a difference in the dosage use, in the population studied, or in the potency.

CAMORCIA *et al.* (1), determined the analgesic potency ratios for these three local anesthetics for intrathecal labor analgesia. The relative analgesic potency ratios were 0.65 (0.56-0.76) for ropivacaine : bupivacaine, 0.80 (0.70-0.92) for ropivacaine : levobupivacaine, and 0.81 (0.69-0.94) for levobupivacaine : bupivacaine. In their study, there were significant trends for greater motor block with bupivacaine and levobupivacaine, which is in keeping with our findings.

The slower onset of motor block in the ropivacaine group compared with that in the bupivacaine and levobupivacaine groups was also noticed by COPPEJANS *et al.* (4), in a low-dose combined spinal-epidural anesthesia for caesarean delivery. That study confirmed that these three local anesthetics can be used successfully, induce less motor block but that ropivacaine requires at least a 50% larger dose than bupivacaine or levobupivacaine. POLLEY *et al.* (17), also ascertained that ropivacaine is approximately 40% less potent than bupivacaine when they were administered epidurally to abolish the pain of the first stage of labour. Furthermore, GAUTIER *et al.* (7), compared 4 ml of intrathecal hyperbaric 0.2% bupivacaine (8 mg) with 4 ml of 0.2, 0.25, 0.3 or 0.35% hyperbaric ropivacaine (8, 10, 12 or 14 mg) in patients undergoing knee arthroscopy. In ropivacaine group, adequate sensory and motor block were achieved only after the intrathecal administration of 12 or 14 mg of ropivacaine. They estimated that the 12 mg dose of ropivacaine was approximately equivalent to bupivacaine 8 mg. Although the duration of both sensory and motor block was significantly shorter in the ropivacaine group in our study, these differences were not as pronounced as those seen in the above-mentioned study. This may reflect a difference in the dosage use, in the baricity of the solution used or in potency.

In another recent study, in patients undergoing transurethral resection of the bladder or prostate, patients were randomized to receive either 5 ml of 0.2% isobaric bupivacaine (10 mg) or 5 ml of 0.3% isobaric ropivacaine (15 mg) for spinal anesthesia. Despite the fact that a lower dose of bupivacaine was used in comparison with ropivacaine, there was a significant increase in the cephalad spread of the sensory block in the bupivacaine group. The degree of motor block was similar which is in accordance

with our study, where a lower intensity of motor block was seen with ropivacaine than with bupivacaine with the same dose (11).

Sensory block in the present study was tested using loss of sensation to pin-prick as used by others (18). The choice of this method, instead of others (such as loss of sensation to ice, pain perception, tetanic twitch or chemical irritation with capsaicin), was based on Hocking's study which proved the reliability and easy application of the pinprick method (9).

In terms of safety, either intrathecal ropivacaine, levobupivacaine or bupivacaine provide a high degree of cardiovascular stability with a higher incidence of hypotension in bupivacaine group. The most commonly reported adverse events, nausea, vomiting, tremor, and decrease in oxygen saturation $SpO_2 < 93\%$, were equally distributed between the three groups. These results correlate well with those reported by other investigators (2, 6-8, 15).

In conclusion, intrathecal administration of either 15 mg bupivacaine, 15 mg ropivacaine, or 15 mg levobupivacaine was well-tolerated and provided similar, effective anesthesia for lower abdominal surgery. In an equal milligram dose, ropivacaine produced a shorter duration of motor and sensory block than bupivacaine or levobupivacaine, even if this was not associated with a shorter home discharge time. So intrathecal ropivacaine may prove useful when surgical anesthesia of a similar quality but of a shorter duration than that of bupivacaine or levobupivacaine is desired.

References

1. Camorcia M., Capogna G., Lyons G., Columb MO., *Epidural test dose with levobupivacaine and ropivacaine determination of ED50 motor block after spinal administration*, BR. J. ANAESTH., **92** (6), 850-3, 2004.
2. Casati A., Moizo E., Marchetti Ch., Vinciguerra F., *A prospective, randomized, double-blind comparison of unilateral spinal anesthesia with hyperbaric bupivacaine, ropivacaine, or levobupivacaine for inguinal herniorrhaphy*, ANESTH. ANALG., **99**, 1387-92, 2004.
3. Cheng C. R., Su T. H., Hung Y. C., Wang P. T., *A comparative study of the safety and efficacy of 0.5% levobupivacaine and 0.5% bupivacaine for epidural anesthesia in subjects undergoing elective caesarean section*, ACTA ANAESTHESIOLOGICA SINICA, **40** (1), 13-20, 2002.
4. Coppejans H. C., Vercauteren M. P., *Low dose combined spinal - epidural anesthesia for caesarean delivery. A comparison of three plain anesthetics*, ACTA ANAESTHESIOLOGICA BELGICA, **57** (1), 39-43, 2006.
5. Foster R. H., Markham A., *Levobupivacaine : a review of its pharmacology and use as a local anaesthetic*, DRUGS, **59** (3), 551-79, 2000.
6. Gautier P. E., De Kock M., Huberty L., Demir T., Izudorczic M., Vanderick B., *Comparison of the effects of*

- intrathecal ropivacaine, levobupivacaine and bupivacaine for caesarean section*, Br. J. ANAESTH., **91** (5), 684-9, 2003.
7. Gautier P. E., De Kock M., Van Steenberge A., Poth N., Lahaye-Goffart B., Fanard L., Hody J. L., *Intrathecal ropivacaine for ambulatory surgery. A comparison between intrathecal bupivacaine and intrathecal ropivacaine for knee arthroscopy*, ANESTHESIOLOGY, **91**, 1239-45, 1999.
 8. Glaser C., Marhofer P., Zimper G., Heinz M. T., Sitzwohl Ch., Kapral St., Schindler I., *Levobupivacaine vs bupivacaine in spinal anesthesia*, ANESTH. ANALG., **94**, 194-224, 2002.
 9. Hocking G., Wildsmith J. A. W., *Intrathecal drug spread*, Br. J. ANAESTH., **93** (4), 568-11, 1993.
 10. Kallio H., Snall E. V., Kero M. P., Rosenberg P. H., *Comparison of intrathecal plain solutions of ropivacaine 20 or 15 mg vs bupivacaine 10 mg*, ANESTH. ANALG., **99** (3), 713-717, 2004.
 11. Malinovsky J. M., Charles F., Kick O., Lepage J. Y., Malinge M., Cozian A., Bouchot O., Pinaud M., *Intrathecal anesthesia : ropivacaine versus bupivacaine*, ANESTH. ANALG., **91**, 1457-60, 2000.
 12. Markham A., Faulds D., *Ropivacaine. A review of its pharmacology and therapeutic use in regional anaesthesia*, DRUGS, **52** (3), 429-49, 1996.
 13. McClellan K. J., Faulds D., *Ropivacaine : an update of its use in regional anaesthesia*, DRUGS, **60** (5), 1065-93, 2000.
 14. McClellan K. J., Spencer C. M. *Levobupivacaine*. DRUGS, **56** (3), 355-62, 1998.
 15. McNamee D. A., McClelland A. M., Scott S., Milligan K. R., Westmann L., Gustafsson U., *Spinal anesthesia : comparison of plain ropivacaine 5 mg/ml with bupivacaine 5 mg/ml for major orthopaedic surgery*, Br. J. ANAESTH., **89** (5), 702-6, 2002.
 16. Milligan K. R., *Recent advances in local anaesthetics for spinal anaesthesia*, Eur. J. ANAESTHESIOLOGY, **21**, 837-847, 2004.
 17. Polley L. S., Columb M. O., Naughton N. N., Wagner D. S., van de Ven C. J. M., *Relative analgesic potencies of ropivacaine and bupivacaine for epidural analgesia in labour*, ANESTHESIOLOGY, **90**, 944-50, 1999.
 18. VanKleef J. W., Veering B. T., Burm A. G. L., *Spinal anesthesia with ropivacaine : a double-blind study of efficacy and safety of 0,5% and 0,75% solutions in patients undergoing minor lower limb surgery*, ANESTH. ANALG., **78**, 1125-30, 1994.
 19. Vanna O., Chumsang L., Thongmee S., *Levobupivacaine and bupivacaine in spinal anesthesia for transurethral endoscopic surgery*, J. MED. ASSOC. THAI, **89** (8), 1133-9, 2006.