

# Ropivacaine versus Levobupivacaine for Minor Breast Surgery in Outpatients: Inversion of Postoperative Pain Relief Efficacy

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**Abstract.** *The number of ambulatory surgical procedures is growing and local anesthesia represents the technique of choice for outpatients undergoing minor surgery. The aim of this study was to verify whether differences exist in postoperative pain relief using equipotent doses of two long-acting local anesthetics, ropivacaine and levobupivacaine, in patients who underwent minor breast surgery. A series of 86 consecutive women (median age=55, range=39-75 years) with small (<2 cm in size) breast masses requiring surgical excision were prospectively enrolled in the study. Patients were randomly selected to receive 7.5 mg/ml ropivacaine (group A, 42 patients) or 5 mg/ml levobupivacaine (group B, 44 patient). For post-surgical measurement of pain intensity a visual analog scale (VAS) was used. The age of the patients (56.4±9.6 vs. 56.7±9.5 years; p=0.88) and operative time (38.4±4.3 vs. 39.8±5.0 min; p=0.16), did not differ significantly between the groups (A vs. B). Transient adverse effects were observed in 5 (11.9%) and 4 (9.1%) patients (p=0.49) of groups A and B, respectively. The pain VAS four (t4) and 24 (t24) hours from the end of surgery was significantly (p<0.05) different between the groups, but an inversion of pain relief efficacy and a crossing point of the two pain-time lines at the sixth hour was observed. In conclusion, ropivacaine results in more effective pain relief at time t4, while levobupivacaine should be the drug of choice when long-term postoperative analgesia is required.*

The number of ambulatory surgical procedures is growing and there are also studies suggesting methodologies to estimate the

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potential for moving inpatients to one-day surgery, with the aim of reducing healthcare costs (1, 2). Local anesthesia represents the technique of choice for patients undergoing minor surgery and drugs with short-acting duration are usually preferred for outpatients, allowing a quick for discharge of the patients. The use of local anesthesia-alone or combined with sedation currently represents a well-accepted and safe anesthetic method for several surgical procedures, including plastic surgery and breast surgery (3).

Ropivacaine and levobupivacaine are long-acting amino-amide local anesthetics, belonging to the n-alkyl-substituted piperidyl xylidine family (4). Both drugs have biphasic effects on skin microvessels and produce dose-dependent skin vasoconstriction, leading to a prolonged duration of effect, with limited systemic uptake (5). Ropivacaine has fewer potential cardiotoxic effects than does levobupivacaine, but its clinical efficacy does not substantially differ (4, 6). Few studies have considered the effectiveness of local anesthetics in the management of postoperative pain in breast surgery (7, 8).

The aim of this study was to verify whether differences exist in postoperative pain relief using equipotent doses of ropivacaine and levobupivacaine for patients who underwent minor breast surgery.

## Patients and Methods

A series of 86 women (median age=55, range=39-75 years) with small (<2 cm in size) breast masses requiring surgical excision were prospectively enrolled in the study. Once they had given informed consent for local anesthesia, patients were randomly selected to receive 7.5 mg/ml ropivacaine (group A, 42 patients) or 5 mg/ml levobupivacaine (group B, 44 patients). Patients who received more than 20 ml of solution, corresponding to doses exceeding 150 mg and 100 mg of ropivacaine and levobupivacaine, respectively, were excluded from the study, as well as those who required supplementation of drug administration at the end of surgery. Intra- and postoperative standard monitoring [*i.e.* continuous electrocardiogram (ECG), arterial blood pressure and pulse oximetry measurements], was used in all patients. Infiltration of the operative area was completed from 8 to 15 min (median of 10 min) before the incision.

Table I. Postoperative pain visual analog scale (VAS) scores at 2, 4, 6 and 24 hours from the end of surgery. Means±standard deviations.

VAS	Group A N=42	Group B N=44	Difference	t-Value	p-Value
2 h	2.14±0.93	2.50±1.55	0.36±1.24	-1.298	0.198
4 h	1.48±0.80	1.89±0.89	0.41±0.85	-2.243	0.028*
6 h	1.24±0.73	1.20±0.79	0.04±0.76	0.244	0.808
24 h	0.73±0.45	0.46±0.50	0.27±0.48	2.628	0.010*

\*Statistically significant difference (Student's t-test). Group A, Ropivacaine; Group B, levobupivacaine.

Table II. Number of patients with maximum postoperative pain visual analog scale (VAS) score at 2, 4, 6 and 24 hours from the end of surgery.

	2 h	4 h	6 h	24 h
VAS score	≥4	≥3	≥3	≥1
Group A	4 (9.5%)	4 (9.5%)	2 (4.8%)	28 (66.7%)
Group B	10 (22.7%)	12 (27.3%)	1 (2.3%)	19 (43.3%)
p-Value	0.080	0.032*	0.482	0.024*

\*Statistical significance (Fisher exact test). Group A, Ropivacaine; Group B, levobupivacaine.

For post-surgical measurement of pain intensity, a visual analog scale (VAS) was used. The pain VAS was a single-item continuous scale, self-completed by the respondent, 10 cm in length, anchored by 2 verbal descriptors, one for each symptom extreme (9, 10). A higher score (score of 10) indicated greater pain intensity, while a score of zero meant absolutely no pain. For each patient, data at time t2, t4, t6 and t24 were recorded, corresponding to 2, 4, 6 and 24 hours from the end of the surgical procedure, respectively.

All patients were informed about the purpose of the study, the mode of pain assessment and the need to communicate the t2, t4 and t6 value of pain before discharge and to undergo an interview by telephone the morning after surgery for t24 value recording. The study was double-blinded: the anesthetist was aware of the anesthetic product only at the time of local infiltration and interviewers of patients were unaware about the local anesthetic used. Patients did not know which group they belonged too.

The reported data are expressed as the mean±standard deviation (SD). Two-tailed Student's t-test for unpaired data and the Fisher's exact probability test, to compare means and categorical variables, respectively, were used. Differences were considered significant at a p-value <0.05.

## Results

The age of the patients (56.4±9.6 vs. 56.7±9.5 years; p=0.88) and operative time (38.4±4.3 vs. 39.8±5.0 min; p=0.16) did not differ significantly between the groups (A vs. B). Transient adverse effects (i.e. headache, nausea, numb

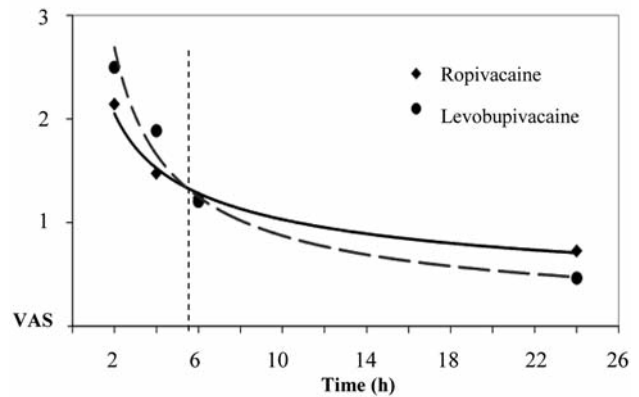


Figure 1. Pain visual analog scale (VAS) values (median) using ropivacaine (◆) and levobupivacaine (●). The crossing of the two pain-time lines is approximately at 6 hours from the end of surgery.

tongue, neck pain) were observed in 5 (11.9%) and 4 (9.1%) patients (p=0.49) of groups A and B, respectively.

Descriptive analysis of the postoperative pain VAS scores is presented in Table I. The average t4 and t24 VAS was significantly (p<0.05) different between the groups. An inversion of pain relief efficacy was found and a crossing point of the two pain-time lines, approximately at t6, was observed (Figure 1). The maximum VAS was reported by the patients two hours from the end of surgery, while the 24-hour VAS score was zero in 14 (33.3%) and 25 (56.8%) patients (p=0.024) of groups A and B, respectively (Table II).

## Discussion

Local anesthetics are used in a wide range of clinical situations, especially for outpatients and in minor surgery (11). Ropivacaine and levobupivacaine are pure left-isomers of bupivacaine which, due to their three-dimensional structure, have less central nervous system and cardiac toxicity than bupivacaine (12, 13). Several studies showed that equipotent doses of ropivacaine and levobupivacaine have similar efficacy in plexus block and walking spinal anesthesia in ambulatory patients, as well as when administered by topical application or local infiltration (6, 14, 15). Skeletal muscle toxicity is rarely observed and limited dose-dependent reversible myonecrosis represents an uncommon side-effect of intramuscular injection of all local anesthetics (16).

Pre-discharge anxiety is not infrequent in ambulatory patients and postoperative pain is usually better-tolerated by inpatients. Recently, Jones *et al.* (17) found that telephone calls from nurses during the immediate postoperative period may result in less symptom distress, significantly reducing anxiety and wound pain intensity. It has also been shown that

patients who underwent major breast surgery and post-incisional wound or muscle infiltration with bupivacaine had low postoperative pain following modified radical mastectomy and submuscular breast augmentation, respectively (18, 19).

Ropivacaine is a well-tolerated drug, effective for both surgical anesthesia and postoperative pain relief, leading to a lower incidence of motor block than bupivacaine (20). Moreover, it seems to have a better margin of safety in respect to all other long-acting anesthetics (4, 11). Levobupivacaine was found to be more effective than ropivacaine in terms of intensity and duration of analgesia, both in mastopexy and mini-abdominoplasty, especially between 4 and 10 hours from the end of surgery (3, 21). Our study confirms these results, suggesting that ropivacaine and levobupivacaine have similar analgesic effects at times t2 and t6, but ropivacaine was more effective 4 hours after surgery and levobupivacaine at t24.

In conclusion, the comparison of postoperative pain VAS score after local infiltration of equipotent doses of ropivacaine versus levobupivacaine shows an inversion of the efficacy of postoperative pain relief approximately six hours from the end of surgery, although levobupivacaine results in more effective long-acting pain relief.

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