The Pharmacodynamics of Ropivacaine and Bupivacaine in Combined Sciatic and Femoral Nerve Blocks for Total Knee Arthroplasty

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The potency of ropivacaine compared with bupivacaine in regional anesthesia remains controversial. Therefore, we compared the pharmacodynamics of equal concentrations of bupivacaine and ropivacaine in combined sciatic and femoral nerve blocks for patients undergoing knee arthroplasty. Fifty patients received 40 mL of either 0.5% bupivacaine (n = 25) or 0.5% ropivacaine (n = 25) divided between the sciatic (15 mL) and the femoral (25 mL) nerves before induction of anesthesia. Loss and recovery of sensory (% of cold sensation compared to opposite side) and motor (no contraction or normal muscle force) functions were recorded in the distribution of the femoral, saphenous, common peroneal, and tibial nerves. Pain scores and morphine consumption over 48 h were also evaluated. There were no difference between bupivacaine and ropivacaine in terms of onset of sensory and motor blockade. However, resolution of sensory and motor function was faster in the ropivacaine group but only significantly so for the sciatic nerve and between 24 to 28 h for sensory resolution and 12 to 20 h for motor function. Overall, pain scores and morphine consumption were similar. In conclusion, we showed that block resolution is different between bupivacaine and ropivacaine when administered for combined sciatic and femoral nerve blocks. A new systematic method to assess sciatic and femoral nerve blockade is proposed.

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Bupivacaine is the standard, long-acting local anesthetic used in regional anesthetic practice together with ropivacaine, a *N*-propyl homologue of bupivacaine and a pure S(-) enantiomer (1). Ropivacaine has shown a reduced potential for central nervous system toxicity and cardiotoxicity in laboratory experiments and in healthy volunteers (2). Some evidence suggests that ropivacaine produces a sensory and motor block that is clinically indistinguishable from that of racemic bupivacaine (3,4). However, this is a controversial issue and it is not yet clear whether the two compounds have the same potency (5–10). Indeed, it may depend on the particular block being performed.

For three-in-one blocks, in a study using the same concentration (0.5%) of ropivacaine and bupivacaine, Marhofer et al. (11) did not notice any difference between the two local anesthetics with respect to sensory onset time and quality of sensory block. Likewise, with a three-in-one block, ropivacaine 0.25%, ropivacaine 0.5%, and bupivacaine 0.25% provided comparable analgesia after total knee replacement (12). A comparison of ropivacaine 0.75% and bupivacaine 0.5% showed no difference in the mean time to onset of complete anesthesia of the foot or first request for postoperative analgesia after a sciatic nerve block (13). Furthermore, Fanelli et al. (14) compared 0.75% ropivacaine, 0.5% bupivacaine, and 2% mepivacaine during sciatic and femoral nerve blockade. Ropivacaine had an onset time similar to that of mepivacaine and a duration of postoperative analgesia between that of bupivacaine and mepivacaine. Ropivacaine and bupivacaine have also been compared in combined femoral and sciatic blocks for total knee replacement, and no difference in motor blockade recovery was found between the two except at 12 h, although sensory blockade was not assessed (15). Finally, Greengrass et al. (16) compared 0.5% ropivacaine and bupivacaine in lumbar plexus and sciatic nerve blocks for knee arthroplasty and found them to be similar, although motor function was evaluated using a Bromage score (17) and sensory blockade was measured in L1-S1 dermatomes and not along major nerve distributions.

Therefore, we designed a clinical trial for knee arthroplasty using combined sciatic and femoral nerve

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Table 1. Scoring System to Evaluate the Onset and Recovery of Motor and Sensory Blockade for the Sciatic and Femoral Nerves

	Motor block	Sensory block
	0 = no contraction 1 = normal muscle force	0% = no sensation 100% = normal sensation (Loss of cold sensation compared to opposite side)
Sciatic nerve		
Common peroneal nerve	Dorsiflexion of the foot	Lateral aspect of the calf
Tibial nerve	Plantar flexion of the foot	Plantar aspect of the foot
Femoral nerve	Ability to lift the heel with a semi-flexed thigh	Femoral: anterior aspect of the thigh Saphenous: medial part of the calf

Table 2. Demographic and Perioperative Period Data

	Bupivacaine (n = 21)	Ropivacaine (n = 25)
Age (yr)	65.1 (2.2)	67.1 (1.7)
Sex (M/F)	11/10	7/18
Weight (kg)	84.3 (4.4)	85.1 (3.2)
Height (cm)	165.5 (2.6)	159.5 (1.8)
Body mass index	30.8 (1.1)	33.4 (1.1)
ASA I/II/III	2/12/7	7/11/7
Sciatic nerve stimulation: common peroneal/tibial nerve	7/14	11/14
Sciatic nerve block threshold (mA)	0.34 (0.02)	0.37 (0.02)
Femoral nerve block threshold (mA)	0.36 (0.02)	0.36 (0.02)
Fentanyl (μg) use perioperatively	192.1 (10.7)	203.1 (17.4)
Ephedrine	5 (24%)	9 (36%)
Phenylephrine	2 (10%)	4 (16%)
Tourniquet time (min)	74.6 (9.4)	73.0 (7.8)
Surgical time (min)	108.2 (4.9)	102.6 (4.4)
Morphine use in recovery room (mg)	5.9* (1.1)	2.8 (0.7)

Data are mean (SEM) or percentage.

* $P < 0.05$.

blocks whose aim was to compare the pharmacodynamic profile of bupivacaine and ropivacaine administered at the same concentration using a standardized method of scoring nerve blockade.

METHODS

After approval by the local ethics committee of the CHUM-Hôtel-Dieu (Montréal) and after obtaining written informed consent, ASA physical status I–III patients undergoing unilateral total knee arthroplasty were enrolled into this prospective, randomized, double-blind study. Randomization was performed by the pharmacy of our institution using a computer-generated random list. Bupivacaine and ropivacaine were also prepared by the pharmacy in 20-mL syringes labeled only with the name of the patient (two syringes for each patient) and delivered just before the anesthesiologist performed the block. Only the pharmacist and the assistant delivering the local anesthetics knew the content of the two syringes; they were never involved in patient care thereafter. Exclusion criteria included coagulopathy, infection at the site of block, neurological injury on the operative side, chronic opioid consumption, and patient refusal.

Patients received 40 mL of either 0.5% bupivacaine (bupi group) (n = 25) or 0.5% ropivacaine (ropi group) (n = 25) for a combined sciatic-femoral nerve block. The sciatic nerve block was performed first according to the classic Labat posterior approach using 15 mL of the local anesthetic administered by increments of 5 mL after negative aspiration tests. The femoral nerve block, the injection being 1 cm lateral to the femoral artery at skin-crease level, consisted of the incremental injection of the remaining 25 mL of the allocated local anesthetic drug. Short-bevelled, Teflon-coated stimulating needles (Stimuplex, Braun, Germany) of 100 mm for the sciatic nerve and 50 mm for the femoral nerve were used with a nerve stimulator (Braun). The target was elicitation of adequate motor responses (i.e., dorsiflexion or plantar flexion of the foot and upper displacement of the patella for the sciatic and femoral nerves, respectively) with a current of 0.5 mA or less. Stimulation frequency was set at 2 Hz, with duration of 0.1 ms and paresthesia was never intentionally sought. Standard monitors were applied and light sedation using IV midazolam (1–3 mg) and/or fentanyl 50 μg was used during the procedure if deemed necessary by the anesthesiologist (P.B.) performing the blocks for this study.

After completion and evaluation of the blocks by the anesthesiologist who performed them (see below), all patients received a general anesthetic using propofol 2–3 mg/kg, fentanyl 1–2 μg/kg, and rocuronium 0.7 mg/kg. Anesthesia was maintained with sevoflurane 0.7%–2% in oxygen and air. Boluses of fentanyl, 1 μg/kg, were used as required to maintain arterial blood pressure levels within 20% of initial recordings. The use of vasopressors (boluses of 5 mg ephedrine or 0.1 mg phenylephrine) was allowed to achieve this goal and was recorded.

For each block, onset of nerve blockade was evaluated every 5 min and continued for 30 minutes after completion of the nerve blocks. If no block was present before induction of anesthesia, patients were excluded from the study. Sensory evaluation, using an ice cube, consisted of loss of cold sensation (patients were asked to rate the ice from 0%–100% on a continuum compared to the other side) in the sciatic (lateral aspect of the calf and plantar aspect

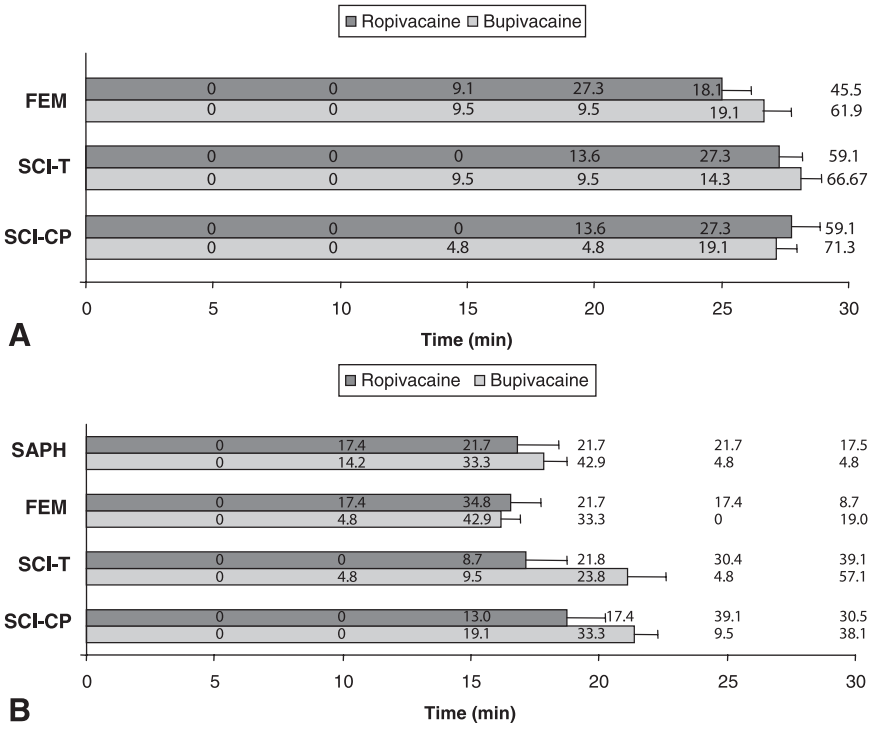

Figure 1. Onset of motor (A) and sensory (B) blockade for the lateral (common peroneal nerve = SCI-CP) and medial (tibial nerve = SCI-T) branches of the sciatic nerve, and for the femoral (FEM) and saphenous (SAPH) nerves. Onset times depict complete sensory and motor blocks. Ropivacaine (dark gray columns) and bupivacaine (gray columns). Numbers every 5-min period represent the percentage of patients with full motor (A) or sensory (B) blockade.

of the foot) and femoral (anterior aspect of the thigh at the level of the patella and anterior and medial part of the calf for saphenous distribution) nerve territories. Furthermore, motor blockade was evaluated simultaneously for the two main branches of the sciatic nerve, the common peroneal and tibial nerves (dorsiflexion and plantar flexion of the foot against manual resistance, respectively) and for the femoral nerve (ability to lift the heel from the bed with a semi-flexed thigh) (Table 1). The method used to evaluate motor function after femoral nerve block is similar to a method used by Casati et al. (18), whereas the evaluation of sensory block is derived from a method used by Marhofer et al. (11). Time from completion of the blocks to complete resolution of sensory and motor functions was performed by research nurses and recorded at regular intervals: hourly between 4 h and 8 h and 10 h after performance of the blocks, and every 4 h thereafter until 48 h post-sciatic and post-femoral blockade. Any complications associated with nerve blockade (venous puncture, paresthesia) and the use of local anesthetics (signs of toxicity) were also recorded.

All patients received 650 mg of acetaminophen per rectum as they arrived in the recovery room and then every 6 h for the length of the study. Pain scores were assessed using a numerical verbal scale (NVS; 0 = no pain, 10 = most severe pain). In the recovery room or later on the ward, IV boluses of 3 mg of morphine were given every 5 min as needed to achieve adequate analgesia (NVS <4). Then, all patients were given patient-controlled analgesia set to deliver IV morphine in 1-mg boluses, with a lockout interval of 6 min. All evaluations (nerve blocks and pain scores) were performed by two experienced pain research nurses blinded as to the treatment groups. The length of the study was 48 h post-nerve blockade.

Data are presented as mean ± SEM. Sample size calculation was performed by first estimating the mean duration of action of bupivacaine (20 h) for sensory block. For a 25% expected difference between bupivacaine and ropivacaine (15 h), with a common standard deviation of 7 h at a significance level of 5% and a power of 80%, this produced a sample size of 25 patients per group. Statistical analysis was performed using SigmaStat for Windows, version 2.03 (Systat Software Inc., Richmond, CA). Demographic data and onset of sensory and motor blocks were analyzed using Student's *t*-test or the Mann-Whitney rank sum test as appropriate. Resolution of sensory and motor block, pain scores and morphine consumption were compared using analysis of variance with Bonferroni correction for multiple comparisons or the Kruskal-Wallis test as appropriate. $P < 0.05$ was considered as statistically significant.

RESULTS

Four patients, all in the bupivacaine group, had failed blocks and were therefore excluded from the study. Details of the remaining patients are given in Table 2. There was no significant difference between the two groups regarding age, sex, body mass index, fentanyl administered perioperatively, surgical, or tourniquet time. However, morphine use (mg) in recovery was significantly higher in the bupivacaine group compared with the ropivacaine group. There was no difference perioperatively in the number of

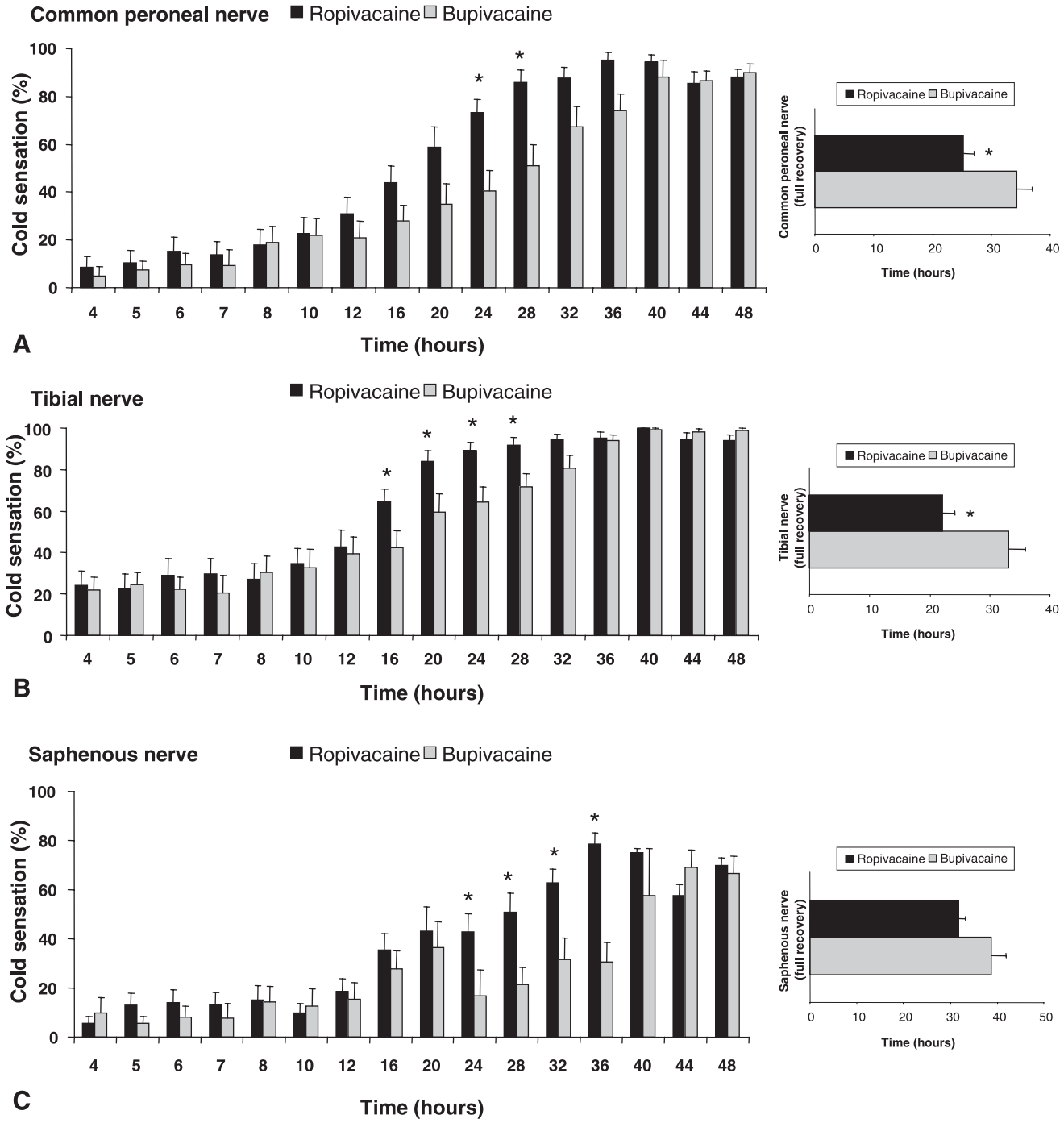

Figure 2. Recovery of sensory function (0% = no sensation; 100% = normal sensation) for the common peroneal nerve (A), tibial nerve (B), and saphenous nerve (C). *$P < 0.05$.

hypotensive episodes and the use of vasoactive drugs. Complications from nerve blockade included two venous and arterial punctures for each group of patients while performing sciatic and femoral nerve block, respectively. In three patients paresthesia was elicited while performing the block but disappeared immediately on withdrawal and on redirecting the stimulating needle.

No significant difference was found between bupivacaine and ropivacaine groups for the onset of sensory and motor blockade (Fig. 1). However, recovery of sensory and motor functions was different at some time points (particularly between 24 to 28 h for sensory resolution and 12 to 20 h for motor function) between the two groups as shown in Figure 2 and Figure 3, respectively, recovery being faster in the ropivacaine group. Overall, complete recovery of motor function was faster than sensory resolution with differences of approximately 8 h. The pattern of sensory block resolution was similar for the tibial and common peroneal nerves but faster in the ropivacaine group. Sensory block recovery was however never complete for the saphenous nerve even at 48 h, whereas femoral nerve motor function recovery was

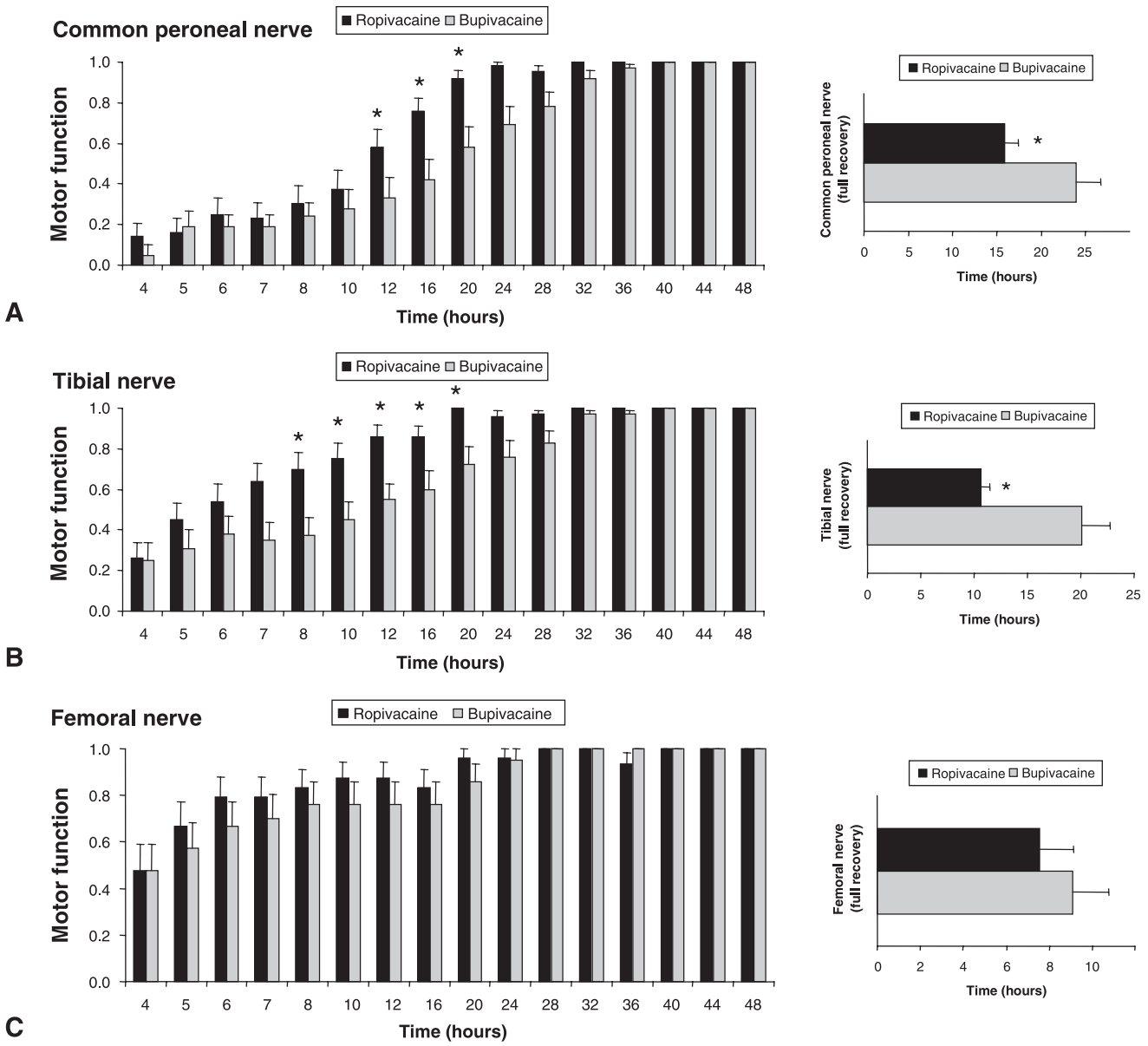

Figure 3. Recovery of motor function (0 = no recovery; 1 = full recovery) for the common peroneal nerve (A), tibial nerve (B), and femoral nerve (C). *$P < 0.05$.

complete at 28 h. Finally, tibial nerve motor function recovery was faster than that of common peroneal nerve and the ropivacaine group recovered earlier than the bupivacaine group. No major complications were recorded with the administration of local anesthetics, i.e., no signs of toxicity, convulsions, or cardiovascular collapse.

Pain scores at rest and on movement are presented in Figures 4A and 4B, respectively. Pain scores were slightly higher in the bupivacaine group for the first 10 h (and significantly higher at 7, 8, and 10 h), whereas they were higher in the ropivacaine group in the 20- to 32-h period (and significantly so at 28 h for pain scores on movement). The initial morphine loading dose was larger in the bupivacaine group. However, overall morphine consumption was not different between the two groups (Fig. 4C), except at 24 h, when it was significantly higher in the ropivacaine group.

There were no long-term complications associated with the nerve blocks.

DISCUSSION

This study shows that the use of bupivacaine and ropivacaine at the same volume and concentration in combined sciatic and femoral nerve blocks for knee arthroplasty was associated with a similar onset of motor and sensory blockade. Recovery of sensory and motor functions was faster with ropivacaine, except for the femoral nerve. Finally, the use of a new standardized method to quantify and evaluate onset and recovery of motor and sensory functions allowed a thorough comparison between the two local anesthetics.

The literature describes different ways of assessing motor and sensory blocks, but no one method has yet been validated or standardized. The use of a modified

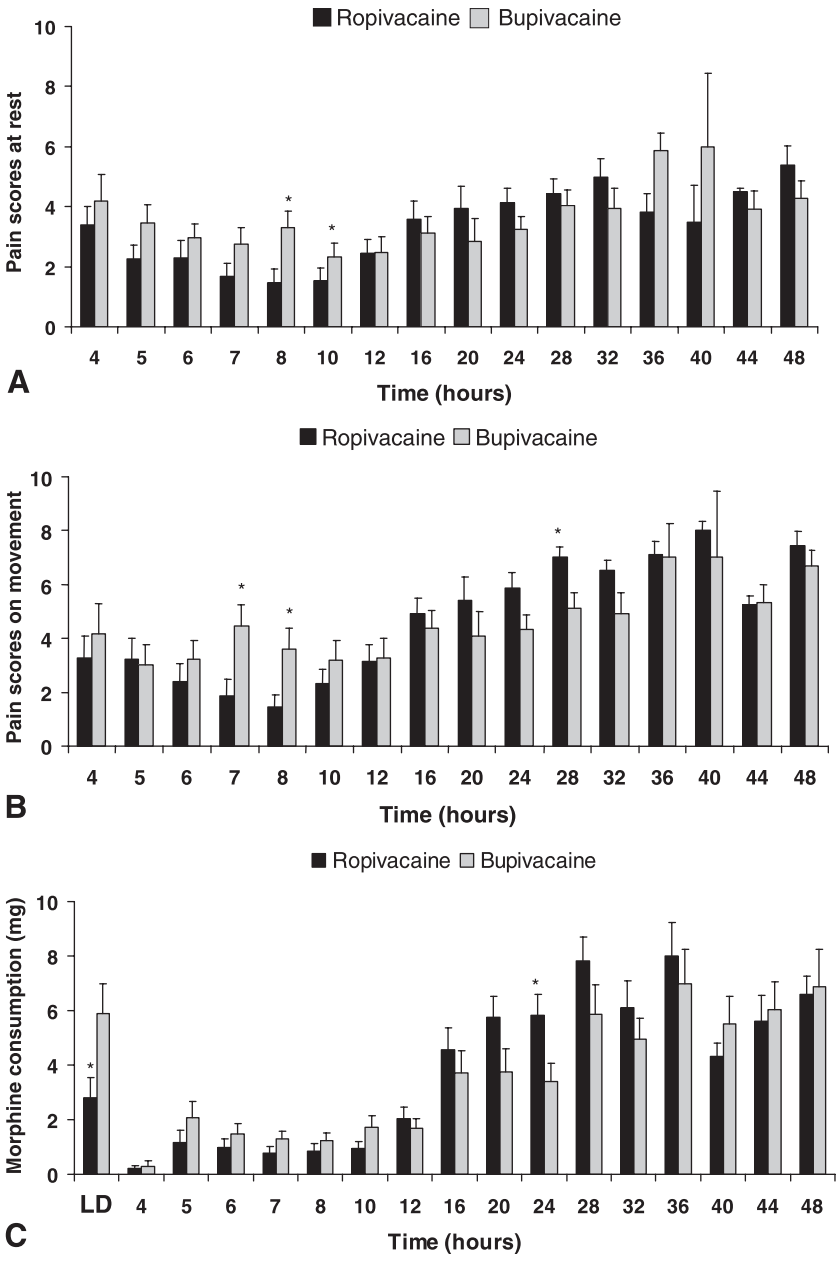

Figure 4. Verbal numerical pain scores (0–10) at rest (A), on movement (B) and morphine consumption (in mg) for each time period (C); LD = loading dose. *$P < 0.05$.

Bromage score to monitor motor function in regional anesthesia of the lower limb is frequently reported although this technique was originally described for the evaluation of epidural blockade, and therefore, its use in peripheral nerve blockade of the lower limb seems inadequate. For this reason we proposed the current method of scoring based on proper assessment of sensory and motor functions in the two main nerves of the lower limb and their branches. This method, although time-consuming, is precise and complete and may be recommended in everyday clinical practice. Its advantage is to offer a standard way to assess lower limb blockade when no accepted method is available. It could probably be refined and improved, and we are currently evaluating this option in our institution.

For situations such as total knee arthroplasty, when it is difficult to monitor femoral nerve sensory function, the saphenous nerve, the terminal branch of the femoral nerve, can be used instead. Furthermore, the fact that sensory function never recovered completely for up to 48 hours for the saphenous territory is surprising. Although surgical injury to the saphenous nerve is not usual after total knee arthroplasty (being medial to the skin incision and to major bone work) it may be an unrecognized transient "injury" for this kind of operation. Another explanation is that sensory testing on the anterior and medial part of the leg may not be very reliable. Finally, and as indicated by the rapid recovery of femoral nerve function, if the needle was inserted more medially when performing the femoral block, one could observe a nerve block that affected the saphenous nerve more than the femoral nerve, giving a predominantly sensory rather than motor block.

Sensory block, 0%–100%, was evaluated by comparing cold sensation of the operated limb with the

patient's sensation on the other side. This method of assessment in which the patient is asked to score sensory block is, of course, subjective but is quite similar to what is used when assessing pain scores using a NVS.

Pain scores at rest and on movement as well as morphine consumption were, in fact, only different between groups at 1–3 time points of the 16 evaluations made overall. Such a small difference may have been expected from a previous study performed in patients undergoing total knee replacement using combined sciatic-femoral blocks in which morphine consumption between 0.75% bupivacaine and 0.75% ropivacaine was not statistically significant (15). In this same study, pain scores were only different between the bupivacaine and ropivacaine groups at 24 and 28 hours. Finally, the increases in pain scores and morphine consumption were paralleled with the resolution of sensory function in a causal relationship; this was not so when compared to recovery of motor function.

An 8% block failure (4 patients of 50) in this population was not expected but in all cases, patients were morbidly obese, with body mass indexes between 30 and 35, and sciatic nerve blocks in particular proved to be impossible to perform using 100-mm stimulating needles.

In conclusion, the present study shows no difference in the onset time of bupivacaine and ropivacaine when used for combined sciatic and femoral nerve blocks, although there were significant differences in motor and sensory recovery, with recovery being faster with ropivacaine compared with bupivacaine. Furthermore, a new method of evaluating peripheral nerve blockade of the lower limb is described.

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