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Ropivacaine or 2% Mepivacaine for Lower Limb Peripheral Nerve Blocks

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Background: **Intra- and postoperative clinical properties of sciatic–femoral nerve block performed with either ropivacaine at different concentrations or mepivacaine have been evaluated in a multicenter, randomized, blinded study.**

Methods: **Adult patients scheduled for foot and ankle surgery were randomized to receive combined sciatic–femoral nerve block with 225 mg of either 0.5% (n = 83), 0.75% (n = 87), or 1% (n = 86) ropivacaine, or with 500 mg of 2% mepivacaine (n = 84). A thigh tourniquet was used in all patients. Onset time, adequacy of surgical anesthesia, time to offset of nerve block, and time until first postoperative requirement for pain medication were evaluated by a blinded observer.**

Results: **The adequacy of nerve block was similar in the four treatment groups (the ratios between adequate:inadequate: failed blocks were 74:9:0 with 0.5% ropivacaine, 74:13:0 with 0.75% ropivacaine, 78:8:0 with 1% ropivacaine, and 72:12:0 with 2% mepivacaine). The onset of the block was slower with 0.5% ropivacaine than with other anesthetic solutions ($P < 0.001$). Regardless of the concentration, ropivacaine produced a longer motor blockade (10.5 ± 3.8 h, 10.3 ± 4.3 h, and 10.2 ± 5.1 h with 0.5%, 0.75%, and 1% ropivacaine, respectively) than with mepivacaine (4.3 ± 2.6 h; $P < 0.001$). The duration of postoperative analgesia was shorter after mepivacaine (5.1 ± 2.7 h) than after ropivacaine (12.2 ± 4.1 h, 14.3 ± 5 h, and 14.5 ± 3.4 h, with 0.5%, 0.75%, or 1% ropivacaine, respectively; $P < 0.001$). Pain relief after 0.5% ropivacaine was 14% shorter than 0.75% or 1% ropivacaine ($P < 0.05$). During the first 24 h after surgery, 30–37% of patients receiving ropivacaine required no analgesics compared with 10% of those receiving mepivacaine ($P < 0.001$).**

Conclusions: **This study suggests that 0.75% ropivacaine is the most suitable choice of local anesthetic for combined sciatic–femoral nerve block, providing an onset similar to mepivacaine and prolonged postoperative analgesia. (Key words: Femoral nerve block; lower limb orthopedic surgery; regional anesthesia; sciatic nerve block.)**

ROPIVACAINE is a new long-acting local anesthetic with a greater therapeutic ratio than other long-acting local anesthetics.[1–3] Its physicochemical profile is similar to that of bupivacaine, and various controlled clinical trials have shown that ropivacaine provides anesthetic characteristics comparable to those of bupivacaine during epidural anesthesia[4–6] or brachial plexus blockade[7–10] when the same concentration is used. However, few clinical data are available on the use of ropivacaine for other techniques of peripheral nerve block, and it is unclear whether ropivacaine provides an onset of peripheral nerve block that is fast enough to be comparable to commonly used fast-onset–intermediate-duration local anesthetics, such as lidocaine or mepivacaine.

To gain more information about the use of ropivacaine during peripheral nerve blockade for orthopedic lower limb procedures, we conducted a multicenter, randomized, blinded study that evaluated the intra- and postoperative clinical properties of combined sciatic–femoral nerve block performed with 0.5%, 0.75%, or 1% ropivacaine or 2% mepivacaine.

Methods

After we received institutional review board approval from each of the 20 participating centers, we obtained informed consent from eligible adult patients classified as American Society of Anesthesiologists physical status I or II who were undergoing foot and ankle surgery expected to last at least 1 h. Patients receiving chronic analgesic therapy and patients with diabetes or peripheral neuropathy were excluded. At each of the 20 par-

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Names of participant clinicians are listed in the appendix.

ticipating hospitals, a senior anesthesiologist, who was a member of the Study Group on Orthopedic Anesthesia of the Italian Society of Anesthesia, Analgesia and Intensive Care and had substantial expertise in regional anesthesia (especially in peripheral nerve blocks performed with nerve stimulation), was selected as the study coordinator in his own hospital. Each coordinator received clear instruction about the standardization of data collection and setting of the nerve blockade and was responsible for the accuracy of data collected in his center. At each participating center, all the nerve blocks were performed by the coordinator, whereas a trained independent observer performed the blinded data collection.

After an 18-gauge intravenous cannula was inserted into the patients' forearms, the patients were premedicated with intravenous diazepam (0.05 mg/kg), and baseline arterial blood pressure and heart rate were recorded. Standard monitoring was used during the study, and all patients received a 5 ml · kg^{-1} · h^{-1} infusion of lactated Ringer's solution. A thigh tourniquet (100 mmHg > systolic arterial blood pressure) was always used during the surgical procedure.

Each participating center enrolled 20 patients and performed its own randomization using sealed envelopes. In each center, the 20 enrolled patients were randomized to receive 0.5%, 0.75%, or 1% ropivacaine or 2% mepivacaine. Sterile syringes containing the proper volume of local anesthetic solution were prepared by an anesthesia nurse who did not take part in the management of the patients being evaluated.

Nerve blocks were performed with the aid of a nerve stimulator using a short, beveled Teflon-coated stimulating needle. Stimulation frequency was set at 2 Hz, and the intensity of the stimulating current was set initially to deliver 1 mA and then gradually decreased to less than 0.5 mA. Paresthesia was never sought intentionally. A multiple injection technique was used, eliciting specific muscular twitches on nerve stimulation to confirm exact needle location.[11–13] First, we performed the femoral nerve block, which was followed by the sciatic nerve block. For the femoral nerve block, the stimulating needle was inserted lateral to the femoral artery at the intersection between the femoral artery and a line connecting the anterior superior iliac spine to the pubic tubercle, and then it was inserted again and redirected to elicit each of the three following muscular twitches: contraction of the vastus medialis, vastus intermedius, and vastus lateralis. The sciatic nerve block was performed according to the classic Labat approach: A line was drawn from the posterior superior iliac spine to the midpoint of the greater trochanter. A perpendicular line was drawn bisecting this line, which extended 5 cm caudally. A second line was drawn from the greater trochanter to the sacral hiatus. The intersection of this line with the perpendicular line indicated the point of needle entry. The stimulating needle was inserted and redirected in sequence to elicit each of the following muscular twitches: flexion of the foot, dorsiflexion of the foot, and contraction of the biceps femoris. If, after each of the considered muscular twitches had been observed, the injection of 1 ml of the study solution immediately stopped the twitch, the needle location was considered adequate. If it was not possible to elicit all the considered muscular twitches during the block placement, at least two of the considered twitches had to be elicited for each nerve block; otherwise the patient was removed from the study.

For both femoral and sciatic nerve blocks, the total volume of anesthetic solution was divided equally among each of the considered twitches. For ropivacaine, a total dose of 225 mg was used, divided into 90 mg for the femoral nerve block and 135 mg for the sciatic nerve block. Considering the three different ropivacaine concentrations, the volumes of local anesthetic available for block placement were as follows: for the femoral nerve block, 18 ml with the 0.5% concentration (6 ml per twitch), 12 ml with the 0.75% concentration (4 ml per twitch), and 9 ml with the 1% concentration (3 ml per twitch); for the sciatic nerve block, 27 ml with the 0.5% concentration (9 ml per twitch), 18 ml with the 0.75% concentration (6 ml per twitch), and 13.5 ml with the 1% concentration (4.5 ml per twitch). For mepivacaine, a total dose of 500 mg was used, divided into 200 mg (3 ml per twitch) for the femoral nerve block and 300 mg (5 ml per twitch) for the sciatic nerve block.

Arterial blood pressure, heart rate, and hemoglobin oxygen saturation and the evolution of both sensory and motor blockade on the operated limb were evaluated every 5 min after anesthetic injection by an independent blinded observer who had remained outside the operating thereafter during block placement. For the onset of the combined sciatic nerve block, we considered the onset of sensory and motor blocks: the onset of sensory block was defined as the time to complete loss of pinprick sensation (22-gauge hypodermic needle) on femoral and sciatic nerves distribution, and the onset of motor block was defined as the inability to move the ankle and the knee of the operated limb. The zero time for clinical assessments was the completion of the anesthetic injection at the sciatic nerve. The quality of the block was

Table 1. Demographic Data and Surgical Times of the Four Groups of Patients

	Ropivacaine 0.5% (n = 83)	Ropivacaine 0.75% (n = 87)	Ropivacaine 1% (n = 86)	Mepivacaine 2% (n = 84)
Age (yr)	45 ± 15	48 ± 15	48 ± 14	48 ± 15
Weight (kg)	65 ± 12	69 ± 11	66 ± 10	68 ± 10
Height (cm)	166 ± 9	164 ± 10	165 ± 9	165 ± 8
Sex (male/female)	26/57	25/62	25/61	24/60
Surgical times (min)	56 ± 26	62 ± 40	56 ± 30	60 ± 29

Data are mean ± SD except for sex (number of patients).

judged according to the need for supplementary intravenous analgesics and sedation: adequate nerve block = neither sedation nor analgesics required to complete surgery; inadequate nerve block = need for additional analgesia (0.01 mg intravenous bolus of fentanyl) and sedation (continuous intravenous propofol infusion 2 $mg \cdot kg^{-1} \cdot h^{-1}$) required to complete surgery; failed nerve block = general anesthesia required to complete surgery.

Resolution of motor blockade, the time to first request for pain medication, and details of any untoward event, side effect, or complication observed during the surgical procedure or in the postoperative period (including nausea, vomiting, hypotension, arrhythmia, dizziness, and any other unanticipated event) also were recorded. Postoperative analgesia consisted of 100 mg intravenous ketoprofen if required. At first request for pain medication, the degree of pain was measured using a 100-mm visual analog scale. Satisfaction with the anesthetic technique was evaluated 24 h after surgery using a two-point score: 1 = satisfactory ("If ever operated on again in the future I would accept the same anesthetic procedure") and 2 = unsatisfactory ("If ever operated on again in the future I would prefer a different anesthetic technique"). Patients were also questioned regarding neurologic complications (pain, dysesthesia, or both) at discharge from the orthopedic ward and 1 week after hospital discharge (at the first routine postoperative orthopedic examination).

Statistical Analysis

To calculate the required study size, we considered previous findings on combined sciatic-femoral nerve block with 0.75% ropivacaine.[14] We wished to detect a 2-h difference in the duration of postoperative pain relief between the 0.75% and the other two ropivacaine solutions, accepting a two-tailed α error of 5%, and a beta error of 10%.[15] Based on these figures, the required study size ranged from 58 to 84 patients per group.

Statistical analysis was performed using the program Stat-View 3.0 (Abacus Concepts, Berkeley, CA). A preliminary analysis was performed to exclude a "center effect" resulting from possible major discrepancies among the 20 participating hospitals; then the normal distribution of collected data was checked for each considered variable. Analysis of variance with Dunnett and Scheffé tests for multiple comparisons were used to evaluate demographic data, onset and resolution of the block, and duration of postoperative analgesia. Analysis of variance for repeated measures also was used to analyze changes in hemodynamic variables compared with baseline values. The adequacy of nerve blockade to surgical requirements and patient acceptance of the anesthetic procedure were analyzed by contingency table and chi-square analyses. $P < 0.05$ was considered significant. Continuous variables are presented as the mean (±SD), and ordinal data are presented as the median (range) or as the number.

Results

Three hundred forty-five patients were enrolled in the study. Hallux valgus repair was the most frequent operation (in 304 cases, or 88%), whereas ankle (in 13 cases, or 4%) and toe (in 28 cases, or 8%) procedures were performed in the remaining patients. No significant differences were observed among the 20 participating hospitals. Five anxious patients (two in the ropivacaine 0.5%, one in the ropivacaine 1%, and two in the mepivacaine 2% groups) required sedation during block placement and then were excluded from the final data analysis.

The four groups of patients were similar with respect to demographic data, American Society of Anesthesiologists physical status, and surgical times (table 1). No severe untoward event was reported in any patient. In all patients, at least two of the required twitches were elicited for sciatic and femoral nerve blocks. No failed

Table 2. Block Adequacy (Adequate/Inadequate/Failed), Tourniquet Pain, and Patient Acceptance Reported during Sciatic-femoral Nerve Block Performed with 0.5%, 0.75%, or 1% Ropivacaine or 2% Mepivacaine

	Ropivacaine 0.5% (n = 83)	Ropivacaine 0.75% (n = 87)	Ropivacaine 1% (n = 86)	Mepivacaine 2% (n = 84)
Block adequacy (adequate/inadequate/failed)	74/9/0	74/13/0	78/8/0	72/12/0
Tourniquet pain (yes/no)	75/8	81/6	80/6	75/9
Patient satisfaction (satisfactory/unsatisfactory)	81/2	84/3	83/3	80/4

Data are number of patients.

blocks were reported. No changes in arterial blood pressure, heart rate, or hemoglobin oxygen saturation were observed during the observation period, and no adverse hemodynamic events were reported.

Table 2 shows the adequacy of nerve block, incidence of tourniquet pain, and acceptance of the anesthetic procedure in the four groups. The onset of sensory and motor blocks, as defined before, are shown in the figure 1, whereas figure 2 shows the time from block placement to resolution of motor block on both the knee and the foot, and the first requirement for pain medication. No differences in the degree of pain measured at the first postoperative administration of pain medication were observed among the four groups (with visual analog score ranging from 51 to 62 mm). During the first 24 h after surgery, 25 patients in the ropivacaine 0.5% group (30%), 33 patients in the ropivacaine 0.75% group (37%), and 27 patients in the ropivacaine 1% group (32%) did not require any intravenous analgesic, compared with 7 patients (8%) in the mepivacaine 2% group ($P < 0.001$).

The day after surgery, four patients in the ropivacaine 0.5% group (5%), seven patients in the ropivacaine 0.75% group (8%), four patients in the ropivacaine 1% group (5%), and one patient in the mepivacaine 2% group (1%) reported dysesthesias on the operated limb (P = not significant). All patients reported complete resolution by 1 week after discharge.

Discussion

Clinically, the most valuable finding of this investigation is that 225 mg ropivacaine at concentrations greater than 0.5% is a practical agent for lower limb nerve blocks and provides nerve block onset times comparable to those of a widely used intermediate local anesthetic such as mepivacaine, with the advantage of prolonged postoperative pain relief. On the other hand, the advantage of long postoperative pain relief must be balanced against the delay in resolution of motor block. The use of ropivacaine concentrations greater than 0.5% for lower limb nerve blocks seems to be most appropriate when surgery is accompanied by relevant postoperative pain (such as hallux valgus repair) and when a delay in mobilizing the operated limb is not a problem for the surgeon or the patient.

Because the focus of this investigation was the evaluation of a long-acting local anesthetic, bupivacaine might

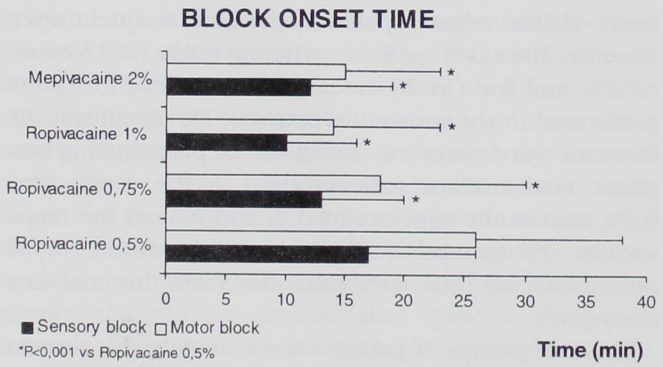

Fig. 1. Time required to achieve loss of pinprick sensation in both sciatic and femoral nerve distributions (sensory block) and inability to move both the ankle and knee of the operated limb (motor block) after combined sciatic–femoral nerve block performed with 0.5%, 0.75%, or 1% ropivacaine or 2% mepivacaine. Results are presented as the mean ± SD.

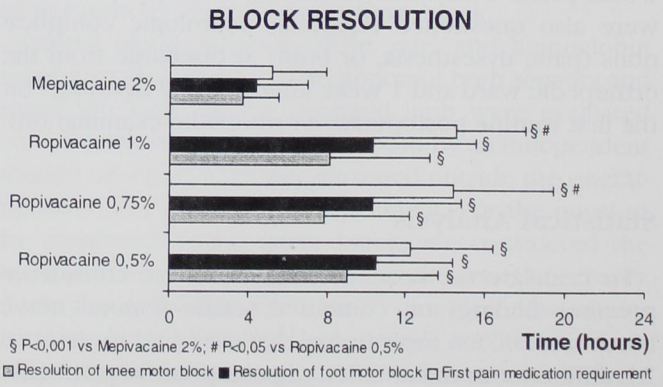

Fig. 2. Time from block placement to resolution of motor block at the knee, resolution of motor block at the foot, and first pain medication requirement after combined sciatic–femoral nerve block performed with 0.5%, 0.75%, or 1% ropivacaine or 2% mepivacaine. Results are presented as the mean ± SD.

appear more appropriate as a control agent than mepivacaine. However, the wide and unpredictable latency of sciatic–femoral nerve block performed with bupivacaine has made it less popular.[14] In contrast, mepivacaine is used widely for peripheral nerve blocks, because of its short onset and intermediate duration.[11,15,16] This is the reason we chose it.

The current investigation has confirmed in a larger population previous findings about the onset time of sciatic–femoral nerve block with ropivacaine, 0.75%,[14] and it has shown that increasing the ropivacaine concentration from 0.5% to 1% reduced block onset time and slightly delayed patients' first postoperative request for pain medication. This suggests that the dose of local anesthetic is not the only factor in the development of sensory and motor block. Previous investigations have shown that the total injected volume of local anesthetic solution is a crucial factor that improves the success rate of peripheral nerve blockade[17,18] because increasing the injected volume improves the impregnation of nerve roots involved in the nerve block. Furthermore, the penetration of local anesthetic molecules into nerve roots also is reported to be affected by the concentration of the local anesthetic solution.[19,20] Increasing the local anesthetic concentration around the nerves probably increased the gradient of concentration that allows for the diffusion of local anesthetic molecules into the peripheral nervous tissue. This could have increased the number of local anesthetic molecules that penetrate the blocked nerves, shortening the onset of nerve block and increasing the time required to wash out the anesthetic molecules from the blocked nerves. These results correspond with findings reported by Nolte *et al.*,[21] who blocked the ulnar nerve with different concentrations of ropivacaine and found that reducing the ropivacaine concentration significantly decreased the duration of the nerve block. On the other hand, the concentration-related effect on the duration of nerve block was evident for sensory block only, although the time required to recover the motor function of the blocked limb was not influenced by changes in local anesthetic concentration. This significantly increased the time from the resolution of motor blockade to the first pain medication requirement when using either the 0.75% or 1% concentrations.

Recently, the use of highly concentrated solutions of local anesthetic for regional anesthesia has prompted some concerns because of the theoretical risk for direct local neurotoxicity.[22] Previous *in vitro* and *in vivo* studies on ropivacaine failed to produce evidence of direct neurotoxicity,[2,3,19,23] and our results show that the use of 1% ropivacaine does not affect the complete recovery of neurologic function after combined sciatic–femoral nerve block.

Because we compared the clinical properties of combined sciatic–femoral nerve block performed with 225 mg 0.5%, 0.75%, or 1% ropivacaine with those of 2% mepivacaine, the results of this investigation are relevant in comparison to mepivacaine only. However, because the quick onset of the block and prolonged postoperative analgesia are important goals in regional anesthesia, 0.75% ropivacaine is the most suitable choice of local anesthetic for combined sciatic–femoral nerve block, providing an onset similar to mepivacaine and prolonged postoperative analgesia, with a more adequate volume of local anesthetic solution available to the anesthesiologist for block placement.

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Appendix 1. Study Group on Orthopedic Anesthesia of the Italian Society of Anesthesia, Analgesia, and Intensive Care

The following clinician-participants are coauthors:

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