Duration of analgesia is similar when 15, 20, 25 and 30 mL of ropivacaine 0.5% are administered via a femoral catheter

[La durée de l'analgésie est similaire quand 15, 20, 25 et 30 mL de ropivacaïne à 0,5 % sont administrés par un cathéter fémoral]

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Purpose: This dose-response study was designed to determine the most appropriate dose of ropivacaine 0.5% injected via an indwelling femoral catheter for perioperative peripheral analgesia for total knee replacement (TKR).

Methods: 84 patients were allocated randomly to four groups and received, via a femoral catheter, either 15, 20, 25 or 30 mL of ropivacaine 0.5% in a double-blind fashion. An anterior sciatic block with 20 mL bupivacaine 0.5% was also performed. The evolution of sensory block of femoral, obturator and lateral femoral cutaneous nerves and motor block of femoral nerve were tested every five minutes during the first 30 min. The percentage of patients with complete sensory block of both femoral and obturator nerves determined success rate. General anesthesia was then induced. After surgery, patient-controlled analgesia (PCA) with ropivacaine 0.2% was available via the femoral catheter. The interval between the initial injection and the first PCA administration determined duration of action.

Results: The duration of action was not different between the four solutions tested i.e., 534 ± 379 min for 15 mL, 799 ± 364 min for 20 mL, 624 ± 342 min for 25 mL and 644 ± 266 min for 30 mL. The percentage of patients with complete sensory femoral and obturator blocks was, respectively, 60%, 95%, 85% and 70% for 15, 20, 25 and 30 mL ($P = 0.008$/15 mL *vs* 20 mL).

Conclusion: Although there is no difference in duration of analgesia, because of better sensory spread, 20 mL of ropivacaine 0.5% appears to be the most appropriate dose for peripheral analgesia after TKR.

Objectif : *L'étude dose-réponse visait à déterminer la meilleure dose de ropivacaïne à 0,5 % injectée par cathéter fémoral à demeure pour l'analgésie périopératoire périphérique lors d'une arthroplastie totale du genou (ATG).*

Méthode : *Nous avons réparti au hasard, en quatre groupes, 84 patients qui ont reçu par cathéter fémoral 15, 20, 25 ou 30 mL de ropivacaïne à 0,5 % en double insu. Un bloc sciatique antérieur a aussi été réalisé avec 20 mL de bupivacaïne à 0,5 %. L'évolution du bloc sensitif des nerfs fémoral, obturateur et cutané latéral de la cuisse et du bloc moteur du nerf fémoral a été vérifiée toutes les cinq minutes pendant les 30 premières minutes. Le pourcentage de patients qui présentait un bloc sensitif complet des nerfs fémoral et obturateur a déterminé le taux de succès. L'anesthésie générale a ensuite été induite. Après l'opération, l'analgésie auto-contrôlée (AAC) avec de la ropivacaïne à 0,2 % était disponible par cathéter fémoral. L'intervalle entre l'injection initiale et la première administration d'AAC a donné la durée d'action.*

Résultats : *La durée d'action a été comparable dans tous les groupes : 534 ± 379 min avec 15 mL, 799 ± 364 min avec 20 mL, 624 ± 342 min avec 25 mL et 644 ± 266 min avec 30 mL. Le pourcentage de patients présentant un bloc sensitif complet des nerfs fémoral et obturateur a été respectivement de 60 %, 95 %, 85 % et 70 % pour les doses de 15, 20, 25 et 30 mL ($P = 0,008$/15 mL vs20 mL).*

Conclusion : *Même si la durée de l'analgésie est équivalente, grâce à une meilleure diffusion sensitive, 20 mL de ropivacaïne à 0,5 % semble être la dose la plus appropriée pour l'analgésie périphérique après une ATG.*

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IN the last decade, analgesia through neuraxial and peripheral nerve blocks has been shown to be superior to *iv* opioids and has gained increased acceptance for pain relief during total knee replacement (TKR).[1,2] Although continuous epidural and continuous femoral nerve blocks provide excellent analgesia of comparable quality, because of fewer side effects, continuous femoral nerve blocks appear to be the most appropriate analgesic technique for this surgical procedure.[1,2]

Sensory innervation of the knee is provided by the lumbar plexus and sciatic nerve.[3] The lumbar plexus supply is predominant and includes the femoral nerve (anterior aspect of the knee) and the obturator nerve (medial aspect of the knee). Blockade of these two nerves is mandatory to obtain satisfactory analgesia during TKR surgery. The third main branch of the lumbar plexus, the lateral femoral cutaneous nerve, provides sensory supply to the lateral side of the thigh, and its blockade allows better tolerance to thigh tourniquet during TKR. A local anesthetic can be administered in the lumbar plexus using the anterior 3-in-1 block[4] or a posterior approach.[5] The anterior approach does not consistently produce anesthesia of the obturator and lateral femoral cutaneous nerves,[6,7] whereas the posterior approach appears to be more reliable in blocking the three major branches.[6,8]

By introducing an indwelling femoral catheter in a cephalad direction, one can expect that the tip of the catheter will be located much closer to the site of injection achieved by a posterior approach to the lumbar plexus. Thus a more reliable blockade of the three main branches can be expected. In addition, the higher cephalad administration of a local anesthetic could, in theory, allow a decrease in the volume and dose of a local anesthetic usually given for a 3-in-1 block, which varies between 30 and 40 mL.[6,7,9–11] A reduction in dose and volume could decrease the risk of systemic toxicity in the context of peripheral block for TKR when the combination of both femoral and sciatic blocks is followed by the administration of local anesthetics over several days via a femoral catheter.

This study was designed to evaluate, in patients undergoing TKR, the analgesic effects of various doses of ropivacaine 0.5% injected via a femoral catheter threaded 12 cm in a cephalad direction. The main endpoint was duration of analgesia and the ancillary endpoints were success rate of blockade and quality of postoperative analgesia.

Methods

After approval from the Ethics Committee of our institution, 84 orthopedic patients, ASA physical status class I–III, scheduled to undergo a TKR under combined peripheral block/general anesthesia, gave informed consent to participate in this study. Hemorrhagic diathesis, peripheral neuropathy, local infection, allergy to amide local anesthetics, preoperative use of opioids and psychiatric disease or dementia were exclusion criteria.

Patients received midazolam 7.5 mg orally 30 to 45 min before their scheduled arrival in the operating room and were monitored with continuous electrocardiogram, peripheral oxygen saturation, and noninvasive blood pressure measurement. A peripheral venous catheter was inserted in all patients, whereas more invasive monitoring such as urinary, central venous and arterial catheters were placed only when required by the patient's clinical condition.

Prior to insertion of a femoral catheter (Contiplex® D Set, Braun, Melsungen, Germany), all patients received fentanyl 1.5 $\mu g \cdot kg^{-1}$ *iv*. Using Winnie's landmarks,[4] the femoral nerve was located using a nerve stimulator (Stimuplex® HNS 11, Braun, Melsungen, Germany). After observing contraction of the quadriceps femoris (patella ascension) at a stimulus rate of 2 Hz, a stimulus duration of 0.1 msec and an amplitude lower than 0.4 mA, 2 mL of normal saline were injected in the sheath before the catheter was introduced to a depth of 12 cm from the needle tip.

Using sealed envelopes, patients were randomly assigned to one of four study groups and received, in a double-blind fashion, one of the following solutions via the femoral catheter:

- Group Ropivacaine-15 mL (R15): 15 mL of ropivacaine 0.5% = 75 mg (Naropin®, Astra, Dietikon, Switzerland)
- Group Ropivacaine 20 mL (R20): 20 mL of ropivacaine 0.5% = 100 mg
- Group Ropivacaine 25 mL (R25): 25 mL of ropivacaine 0.5% = 125 mg
- Group Ropivacaine 30 mL (R30): 30 mL of ropivacaine 0.5% = 150 mg

The study solutions were prepared and injected by the attending anesthesiologist who was not involved in patient care or data collection. Sensory block of the three main branches was assessed by the anesthesiologist in charge, every five minutes during the first 30 min after injection, by loss of temperature discrimination with ether drops. Testing was performed on the anterior aspect of the knee (femoral nerve), medial aspect of the knee (obturator nerve) and the lateral aspect of the thigh (lateral femoral cutaneous nerve). The block was considered complete when no cold discrimination was observed, partial when cold discrimi-

TABLE I Patient characteristics (mean ± SD)

Group	*Ropivacaine 0.5% 15 mL (n = 20)*	*Ropivacaine 0.5% 20 mL (n = 20)*	*Ropivacaine 0.5% 25 mL (n = 20)*	*Ropivacaine 0.5% 30 mL (n = 20)*	*P value*
Age (yr)	72 ± 8	72 ± 9	68 ± 9	69 ± 7	NS
Height (cm)	166 ± 9	158 ± 25	161 ± 27	163 ± 8	NS
Weight (kg)	81 ± 12	74 ± 12	82 ± 17	76 ± 13	NS
Female/male	12/8	14/6	10/10	15/5	NS
ASA I-II/III	13/7	17/3	14/6	16/4	NS

ASA = American Society of Anesthesiologists physical status.

nation was decreased, and absent when normal cold discrimination was observed. Femoral motor block was also assessed during the same period by testing knee extension, and was considered complete when no extension was observed, partial when quadriceps motor force was decreased and absent when normal quadriceps function was observed. The percentage of patients with complete sensory block of the femoral and obturator nerves after 30 min determined the success rate of the tested dose of ropivacaine 0.5%.

Thereafter a sciatic nerve block with 20 mL bupivacaine 0.5% (Carbostesin®, Astra, Dietikon, Switzerland) with epinephrine 1:200,000 was performed in all patients using an anterior approach.[12] A 100-mm long needle was attached to a nerve stimulator and the anesthetic solution was injected after obtaining dorsal or plantar flexion of the foot with similar stimulation variables as those described above. The block was assessed by the same investigator, after surgery, in the recovery room by loss of temperature discrimination with ether drops on the dorsal side of the foot.

General anesthesia was induced with sodium thiopental 4 to 6 $mg \cdot kg^{-1}$ and rocuronium 0.6 $mg \cdot kg^{-1}$ and maintained with isoflurane (end-tidal 0.3–1%) and nitrous oxide 60 to 70% in oxygen. Intraoperatively, fentanyl 1 $\mu g \cdot kg^{-1}$ was given when heart rate and/or mean arterial blood pressure increased more than 30% above pre-induction levels with 1% end-tidal isoflurane concentrations.

After surgery, a patient-controlled analgesia (PCA) device was set to deliver 20 mL boluses of ropivacaine 0.2% with a lockout of 120 min via the femoral catheter. All patients were instructed to quantify postoperative pain intensity on a visual analogue scale (VAS) ranging from 0 to 10 cm and to locate pain, when possible, in either the anterior or posterior knee area. They were further instructed to use the PCA device when the pain score in the anterior knee area was above 3 cm, or to ask for rescue morphine in the event of persistent pain in the posterior knee area. The interval between the initial ropivacaine injection and the first PCA injection determined the duration of analgesic action of the tested dose of ropivacaine 0.5%.

Pain scores at rest every four hours after the initial ropivacaine injection and over 24 hr were recorded by nurses in charge. Intervals between the initial ropivacaine injection (time zero) and first PCA injection, as well as consumption of ropivacaine 0.2% over 24 hr were recorded by a single investigator blinded to group assignment.

Rescue morphine (0.1 $mg \cdot kg^{-1}$ *sc*, maximum six doses/24 hr) was prescribed for a residual pain score in the anterior knee area higher than 3 cm during the lockout interval or for pain in the posterior knee area. Paracetamol 1 g (Dafalgan®, UPSA, Baar, Switzerland) and/or ibuprofen 400 mg (Brufen®, Knoll, Liestal, Switzerland) were given orally for other pains (headache, back pain, arthritic pain) as required. Analgesic requirements over 24 hr were obtained from the nurses' records.

According to our previous report where duration of analgesia with 20 mL ropivacaine 0.5% was 657 ± 345 min,[13] the sample size was computed to detect an increase of duration of 50%, i.e., 5 ½ hr with a power of 80% or greater and a 5% or less chance of a type 1 error ($\beta = 0.2$; two-tailed $\alpha = 0.05$). For four study groups a minimal sample of 18 patients per group met these criteria. Taking into account possible catheter failure or inappropriate use of the PCA pump, we decided to test 21 patients per group.

Data are expressed as mean ± SD or number (*n*) and percentage (%). The statistical analyses were performed using analysis of variance (ANOVA) with Bonferroni post-hoc or Chi-square as required, using the Statistical Package for the Social Sciences (SPSS for Windows, version 9.0, Chicago, IL, USA). A P value < 0.05 was considered statistically significant.

TABLE II Success rate of blocks after 30 min

Group		*Ropivacaine 0.5% 15 mL (n = 20)*	*Ropivacaine 0.5% 20 mL (n = 20)*	*Ropivacaine 0.5% 25 mL (n = 20)*	*Ropivacaine 0.5% 30 mL (n = 20)*	*P value*
Sensory femoral	complete	13 (65%)	19 (95%)	17 (85%)	15 (75%)	NS
	partial	6 (30%)	1 (5%)	3 (15%)	4 (20%)	NS
	absent	1 (5%)	0	0	1 (5%)	NS
Sensory obturator	complete	14 (70%)	19 (95%)	17 (85%)	16 (80%)	NS
	partial	3 (15%)	1 (5%)	2 (10%)	4 (20%)	NS
	absent	3 (15%)	0	1 (5%)	0	NS
Sensory lateral	complete	6 (30%)	12 (60%)	8 (40%)	10 (50%)	NS
femoral cutaneous	partial	8 (40%)	6 (30%)	7 (35%)	7 (35%)	NS
	absent	6 (30%)	2 (10%)	5 (25%)	3 (15%)	NS
Motor femoral	present	14 (70%)	19 (95%)	14 (70%)	16 (80%)	NS
	partial	6 (30%)	1 (5%)	6 (30%)	4 (20%)	NS
	absent	0	0	0	0	NS

Number of patients with blocked nerves with % in parentheses.

Results

Four of the 84 patients enrolled (one in each group) were withdrawn from the study for the following reasons: obvious failure of femoral catheter in three patients and impossibility to reliably test the block in one patient. Among the remaining 80 patients, 20 were allocated to each group. No differences between the four groups were noted with respect to patient characteristics (Table I).

The success rate of blockade of each nerve 30 min after the injection of the local anesthetic is presented in Table II. The differences between the groups are not significant. Complete block of both the femoral and obturator sensory nerves was observed in 12 patients in R15, 19 in R20, 17 in R25 and 14 in R30 group. The difference between R15 and R20 group is significant ($P = 0.008$).

The duration of anesthesia, defined as time between ropivacaine 0.5% injection and extubation (about three hours), and tourniquet time (about 30 min) were comparable between the four groups. During surgery, no patient in groups R20 and R30, one patient in the R15 group and two in the R25 group received 75 µg of fentanyl for hypertension during tourniquet inflation.

In the recovery room, complete sensory sciatic block was present in 19 out of 20 patients in groups R15, R20 and R30 and in 18 out of 20 patients in group R25. The block was partial in one patient of each group and absent in one patient of the R25 group.

Five patients (one in groups R15, R25 and R30 and two in group R20) were not considered for analysis of duration of analgesia because the first ropivacaine 0.2% administration was incompatible with the study design (the PCA pump was activated by the patient or patient's family to test the device and not for pain treatment).

The duration of analgesia was not statistically different between the four study groups i.e., 534 ± 379 min in R15, 799 ± 364 min in R20, 624 ± 342 min in R25 and 644 ± 266 min in the R30 group.

The 24 hr consumption of ropivacaine 0.2% was significantly lower in group R20 (44 ± 29 mL) when compared to group R15 (83 ± 46 mL), ($P = 0.009$) and group R25 (79 ± 37 mL), ($P = 0.027$), but not different from group R30 (67 ± 28 mL). During this period six patients in R15, three in R20, four in R25 and three in R30 received one dose of rescue morphine (always for posterior knee pain and always after the first PCA injection of ropivacaine 0.2%).

The evolution of pain scores of both anterior and posterior aspects of the knee, over 24 hr after blockade, is illustrated in the Figure. The mean values remained under 3 cm in the four groups. Four hours after the initial injection, pain scores in group R15 were higher when compared to R20 ($P = 0.02$), R25 ($P = 0.031$) and R30 ($P = 0.013$).

A comparable number of patients in each group received paracetamol and/or ibuprofen during the first 24 hr, 42% in R15, 44% in R20, 32% in R25 and 37% in R30 group.

Discussion

Our results show that the duration of analgesia was similar in all groups. However, considering the initial sensory spread, postoperative ropivacaine 0.2% requirements and VAS values (Figure), 20 mL of ropi-

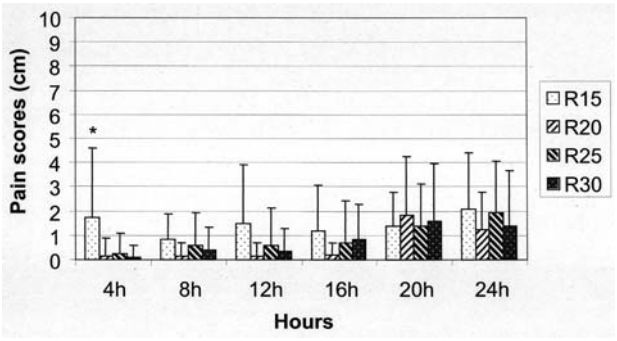

FIGURE Evolution of pains scores of both anterior and posterior aspects of the knee over 24 hr after nerve blockade in the four groups (mean ± SD). R15 = 15 mL of ropivacaine 0.5%, R20 = 20 mL of ropivacaine 0.5%, R25 = 25 mL of ropivacaine 0.5% and R30 = 30 mL of ropivacaine 0.5%. *$p < 0.05$ between R15 and the other groups four hours after the initial injection.

vacaine 0.5% appear to be superior to 15 mL of ropivacaine 0.5%, whereas 25 and 30 mL of the same ropivacaine solution do not provide any further advantage.

Dose response studies using femoral plexus blocks are incomplete and inconclusive. With a single injection of local anesthetic at the femoral crease, Seeberger[7] found no difference in the extension of a 3-in-1 block between 20 mL and 40 mL of mepivacaine 1%. By using an up-and-down method, Casati reported that the minimum local anesthetic volume required to provide a successful femoral nerve block in 50% of subjects was 14 mL of ropivacaine 0.5% and 15 mL of bupivacaine 0.5%[14] and that the average dose was 23 mL of ropivacaine 0.5%.[15] Using indwelling femoral catheters, different authors injected between 20 and 40 mL of different anesthetic solutions with or without epinephrine and/or opiates.[1,2,13,16–19] Among these, only one reported the duration of analgesia of the initial dose of local anesthetic,[13] only one reported extent of the block,[16] and a dose response study has never been described previously. Our study in patients undergoing TKR demonstrates that there was no significant difference in duration of analgesia between the four anesthetic solutions studied. In our opinion, performing a sciatic nerve block improved our ability to measure this variable.

Although a sciatic block is mandatory to perform TKR surgery when using a peripheral block, there is controversy regarding it's usefulness for postoperative pain relief after surgery. Allen observed no advantage on postoperative analgesia when a sciatic block is combined with a femoral block.[20] Capdevila using a continuous femoral block with a mixture of local anesthetic, clonidine and morphine reported that the pain located in the posterior knee area was disturbing in patients undergoing TKR.[2] Recently we have shown that a sciatic block was required in two thirds of patients to improve postoperative pain relief after TKR.[21] We feel that, in the present study, a long lasting sciatic nerve block contributed to the excellent analgesia observed during the first 24 postoperative hours (Figure), and that the small doses of fentanyl given in all patients before the catheter insertion and in only three during surgery did not affect the time of first ropivacaine 0.2% request. Since rescue morphine was always given after the first PCA administration of ropivacaine 0.2%, there is a high probability that these morphine injections were required for pain originating from the anterior or medial knee areas innervated by branches of the femoral plexus, thus allowing a very precise determination of duration of analgesia with different doses of ropivacaine 0.5%. However, we have no valid explanation as to why there is no difference in duration of analgesia with different volumes of local anesthetic. Variability of the catheter tip location may be involved.

In our study, the position of catheters was not verified by *x-ray*. Thus, catheter coiling or migration must be taken into account. Ganapathy[22] evaluated, by computed tomography, the position of 20 femoral catheters advanced 20 cm cranially. Only eight (40%) were placed in an "ideal" position, defined as location of the catheter tip within 2 cm of the cephalad portion of the sacroiliac joint and the lateral borders of L4 to L5 vertebrae. The position of the remaining catheters was not reported. Capdevila[16] verified radiologically the position of 100 femoral catheters inserted 16 to 20 cm in the fascia sheath and reported that, in 23% of the patients, the tip of the catheter reached the lumbar plexus, in 33% lay deep in the medial part of the fascia iliaca and in 37% was placed in the lateral part of the fascia iliaca. After injection of 30 mL of a mixture of lidocaine 2% and bupivacaine 0.5%, a 3-in-1 block was obtained in 91% of patients when the catheter was placed in the lumbar plexus. With the catheter positioned more medially, femoral and obturator nerves were blocked in 84% and the lateral femoral cutaneous nerve in 52% of patients. However, when the catheters were placed more laterally, femoral and lateral femoral cutaneous nerves were blocked in 91% and the obturator nerve in only 27% of patients. We inserted the catheter 12 cm i.e., 4 to 8 cm less than Ganapathy or Capdevila, respectively, and obtained, with 20 mL ropivacaine 0.5%, femoral and obturator

sensory blocks in 95% of patients, whereas the lateral femoral cutaneous nerve was blocked in only 75% of subjects. Thus, threading the catheter over a shorter distance appears to provide a consistent sensory block of both femoral and obturator nerves which is mandatory for effective perioperative analgesia during TKR. Additionally, this shorter distance could decrease the risk of epidural distribution of local anesthetic which has been described with a catheter inserted 24 cm.[23] Further studies are needed to determine the most appropriate length of the indwelling segment of the catheter. The use of the stimulating catheter would be helpful to elucidate this question.

In summary, in the present study, duration of analgesia, our main endpoint, was similar when 15, 20, 25 or 30 mL ropivacaine 0.5% are used for a continuous femoral block. However, ancillary endpoints such as sensory extent of the block after 30 min, postoperative local anesthetic requirements and evolution of VAS values suggest that 20 mL (100 mg) ropivacaine 0.5% injected via the indwelling femoral catheter threaded blindly 12 cm in the lumbar plexus may be the most appropriate dose for perioperative peripheral analgesia during TKR. Larger volumes add no benefit and a smaller volume appears to be less effective.

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