Original Article

Minimum effective concentration 90 (EC90) of ropivacaine for Femoral nerve block: A biased-coin up-and-down sequential method study

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ABSTRACT

Background and Aims: The femoral nerve (FN) is commonly blocked using ropivacaine to provide postoperative analgesia after knee surgery. However, the minimal required concentration has not yet been defined. The aim of this study was to estimate the minimal ropivacaine concentration required to achieve adequate analgesic FN block in 90% of cases (EC_{90}). **Methods:** This study included 50 patients who were scheduled for knee ligament reconstruction under combined nerve block and general anaesthesia. The FN block was performed using 15 mL of ropivacaine with varying concentrations and considered adequate when associated with pain-free recovery. The sciatic, obturator, and lateral femoral cutaneous nerves were blocked to negate other knee pain generators, and their block success was confirmed. We used the biased-coin design up–down sequential method where the adequacy of an FN block altered the ropivacaine concentration used for the next block. The adequacy of the analgesic block or lack of it was analysed to calculate the analgesic EC_{90}. The quadriceps motor power and morphine requirement were also recorded. **Results:** The recommended analgesic ropivacaine EC_{90} was 0.05% w/v. The associated quadriceps weakness and morphine requirement were minimal. **Conclusion:** FN block using ropivacaine 0.05% w/v may provide adequate analgesia in 90% of patients.

Keywords: Anaesthesia, anaesthetics local, analgesia, femoral, lower limb, regional, ropivacaine, ultrasound

INTRODUCTION

The hip and knee joints have multiple nerve supplies. However, the femoral nerve (FN) is the main innervation.[1] Therefore, its block is indicated for pain control after almost any lower-limb surgery.[2-8] Ropivacaine is a long-acting local anaesthetic (LA) with a relatively high cardiac safety profile. It is commonly used for postoperative analgesia.[2-8] The LA concentration affects the block success rate and its side effects. Decreasing LA concentration lowers the risk of toxicity while also sparing the motor fibres, but too low a concentration may result in an unsuccessful block.[2-4] Various low ropivacaine concentrations have been used to achieve analgesic FN block,[3-8] yet the minimal effective concentration (EC) of ropivacaine is still unknown.

The primary objective of this study was to estimate the minimum ropivacaine EC required to achieve analgesic FN block in 90% of patients (EC_{90}). The secondary objectives included assessing the associated quadriceps weakness and the morphine requirement.

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METHODS

This study followed the principles of the Declaration of Helsinki (2013) and Good Clinical Practice guidelines. The study was approved by the Healthpoint Research Ethics Committee (vide approval number MF2467-2021-14, dated March 2021), clinical trials registration (NCT04834440, accessible at https://www.clinicaltrials.gov/study/NCT04834440), and was conducted between May 2021 and September 2021. Written informed consent was obtained for participation in the study and use of the patient data for research and educational purposes.

Patients with knee ligament reconstruction under combined nerve blocks and general anaesthesia formed the study group. Patients aged <18 years, with American Society of Anesthesiologists physical status class > III, body mass index >40 kg/m^2, or any contraindication for medications used in this study were excluded.

In the block room, all patients had neurological assessments of both lower limbs. Oxygen supplementation (5–7 L/min) was applied, as well as routine monitoring (electrocardiogram, pulse oximeter, and non-invasive blood pressure) using Infinity® M540 device (Draeger Medical Systems Inc., Telford, PA, USA). All patients were premedicated with intravenous (IV) midazolam 2 mg, dexamethasone 8 mg, and cefazolin 2 g. Ropivacaine 0.2% (Naropin®, Aspen, Dublin, Ireland) was diluted according to the desired concentration (as explained in the statistical section). When a certain volume (x mL) of ropivacaine 0.2% is diluted with normal saline to 20 mL, the resultant ropivacaine concentration would be 0.0x%. Thus, to prepare a solution of 0.04%, 4 mL of ropivacaine 0.2% was added to 16 mL of normal saline.

All blocks were performed by one operator (AMT) under aseptic conditions and ultrasound guidance (S-Nerve, SonoSite Inc, Bothell, WA, USA). With the patient in the supine position, the linear probe (13–6 MHz) was placed on the inguinal crease to identify the femoral vessels and FN. The probe was adjusted to achieve the best resolution of the FN image. The block needle was inserted lateral to the probe and advanced using an in-plane technique towards the FN. After careful aspiration, 15 mL of the prepared ropivacaine solution was slowly injected. The needle tip was adjusted to confirm that the ropivacaine solution bathed the nerve all around. Thirty minutes later, the FN block was assessed. The cutaneous block was assessed using pinprick sensation along the skin at the medial aspect of the leg and differentiated into three grades: 0 (normal sensation), I (decreased pinprick sensation), and II (absent or touch sensation). The motor block (quadriceps weakness) was assessed by asking the patient to extend a flexed knee against resistance and differentiated into four grades: 0 (normal power), I (extension against resistance), II (extension against gravity), and III (no extension).

The sciatic, obturator, and lateral femoral cutaneous nerves were blocked using ropivacaine 0.5% (20 mL), 0.3% (10 mL), and 0.3% (5 mL), respectively, and their successful blocks were confirmed.[9] Therefore, any residual postoperative pain was considered inadequate FN block (as explained later). In the operating room, under routine monitoring (as described before), general anaesthesia was induced with IV propofol 2–2.5 mg/kg and a laryngeal mask (Supreme™; Teleflex Medical, Athlone, Co. Westmeath, Ireland) was inserted. Anaesthesia was maintained with sevoflurane (1.5%–2% end-tidal concentration in a 50% air/oxygen mixture) and remifentanil IV infusion (0.05–0.1 μg/kg/min). Pressure support/controlled ventilation was initiated to maintain end-tidal carbon dioxide as 35–45 mmHg. After draping, the surgeon (SO) infiltrated the skin overlying the grafted tendon and portal sites with 5 mL of ropivacaine 0.2%. At the end of the procedure, the sevoflurane and remifentanil were stopped. The laryngeal mask was removed when the patient regained consciousness (with adequate respiratory depth and rate).

In the recovery unit, the patients were observed for at least 1 hour. Pain was defined as a numerical rating scale ≥3 (0 = no pain and 10 = worst pain imaginable) and was treated with IV morphine 2 mg increments. Patients who had postoperative pain in the recovery unit were considered to have an inadequate FN block. Meanwhile, patients discharged pain-free from the recovery unit were considered to have an adequate FN block. In the inpatient ward, patients received IV paracetamol 1 g and ketorolac 30 mg four times daily. Any further pain was treated with IV morphine 2 mg increments. They were discharged home after 24 h. An assessment was performed neurologically before discharge and during physiotherapy visits for 3 weeks. Block adequacy, sensory and motor blocks, and morphine supplementation, as well as any complications, were recorded.

The ropivacaine concentration used for the FN block was adjusted according to the biased-coin design up-and-down sequential method.[10] When a patient had an inadequate FN block, ropivacaine concentration was increased by 0.01% w/v in the next patient. However, when a patient had an adequate FN block (as defined above), the next patient was randomised to receive the same ropivacaine concentration (with a probability of 0.89) or 0.01% w/v less (with a probability of 0.11). We used ropivacaine 0.03% w/v in the first FN block, based on a previous report where an FN block using ropivacaine 0.025% w/v provided some analgesia after knee arthroplasty.[6] To calculate the EC_{90}, a fixed minimal number of 45 adequate blocks were needed. Isotonic regression with bias-corrected 95% confidence interval (CI) derived by bootstrapping was used to estimate EC_{90}. The mean value of dose estimator Mu3 was obtained from 2000 bootstrap samples. Statistical analysis was performed using Statistical Package for the Social Sciences v16 (SPSS Inc., Chicago, IL, USA), Excel 2007 (Microsoft, Seattle, WA, USA), and Minitab 16.1 Statistical Software 2010 (Minitab, Inc., State College, PA, USA). Data are presented as frequency, percentage, mean (standard deviation [SD]), or mean (95% CI) as appropriate.

RESULTS

Fifty patients completed the study [Figure 1, Table 1]; 45 had adequate blocks, whereas five did not [Figure 2]. The estimated ropivacaine EC_{90} was 0.045% w/v [95% CI: 0.29, 0.43]. However, at that concentration, the dose-response curve seemed very steep, resulting in a wide variability in its success rate (0.83 [95% CI: 0.47, 0.90]) [Figure 3]. Ropivacaine 0.05% w/v was associated with a higher success rate and less variability. Grade 0, I, and II sensory blocks were achieved in 10%, 84%, and 6% of patients, respectively, while grade 0, I, and II motor blocks were achieved in 22%, 62%, and 8% of patients, respectively (grade 3 motor block was not recorded). Of the 45 patients with adequate block, 41 (91.1%) remained pain-free, with no morphine supplementation used until home discharge. No complications were recorded.

Table 1: Patients' characteristics and block assessment

Parameters	Values (*n*=50)
Age (yr) [mean (SD)]	28.6 (7.5)
Gender: male/female [*n*]	48/2
BMI (kg/m^2) [mean (SD)]	26.6 (4)
ASA class I/II/III [*n*]	37/11/2
Reconstructed ligament [*n*]	-
Anterior cruciate primary	45
Anterior cruciate revision	3
Posterior cruciate	2
Graft/Tendon used [*n*]	-
Hamstring (semitendinosus/gracilis)	41
Patellar (bone to bone)	6
Quadriceps	3
Other performed procedures [*n*]	
Extra-articular fixation	16
Meniscus repair	14
Meniscectomy	11
Other*	10
Nerve block supplemented [*n*]	
Sciatic nerve block	1

Data expressed as mean (standard deviation) and numbers. ASA=American Society of Anesthesiologists; BMI=body mass index, *n*=number of patients. *Include plica excision, micro-fracture, notchplasty, fat pad resection, synovectomy, and foreign body removal

DISCUSSION

This study showed statistically that though ropivacaine 0.045% w/v was estimated to induce adequate analgesic FN block in 90% of patients, ropivacaine 0.05% w/v was the recommended concentration due to the lower variability of success rate, without impairment of its analgesic or motor block effect, along with the ease of preparation. Most patients had minimal motor block and remained pain-free for 24 h.

The ease with which any operator conducted block and the efficient postoperative enhanced recovery after surgery (ERAS) protocol success were the strengths of this study. The FN is superficial at the inguinal crease, and its block is relatively easy. The FN is the main nerve supply to both hip and knee joints.[1] It's rectus branch supplies the hip, while its three vasti branches supply the knee.[1] Unlike the adductor canal block, the FN block anaesthetises all vasti nerves, thereby all femoral innervations to the knee. Nevertheless, the associated quadriceps muscle weakness hinders patients' ambulation. In modern anaesthesia, pain-free recovery and early ambulation/physiotherapy are important targets of ERAS, especially after arthroplasty, sport-related, and outpatient procedures.[11] Decreasing LA concentration could spare or minimise the associated motor fibre blocks and risk of toxicity; however, a concentration that is too low would neither block sensory nor motor fibres.[3]

For postoperative analgesia, the onset of a preoperatively performed block is unimportant, and no time limit was used in the current study. Therefore, very low ropivacaine concentrations could be tested. In the current study, the recommended ropivacaine

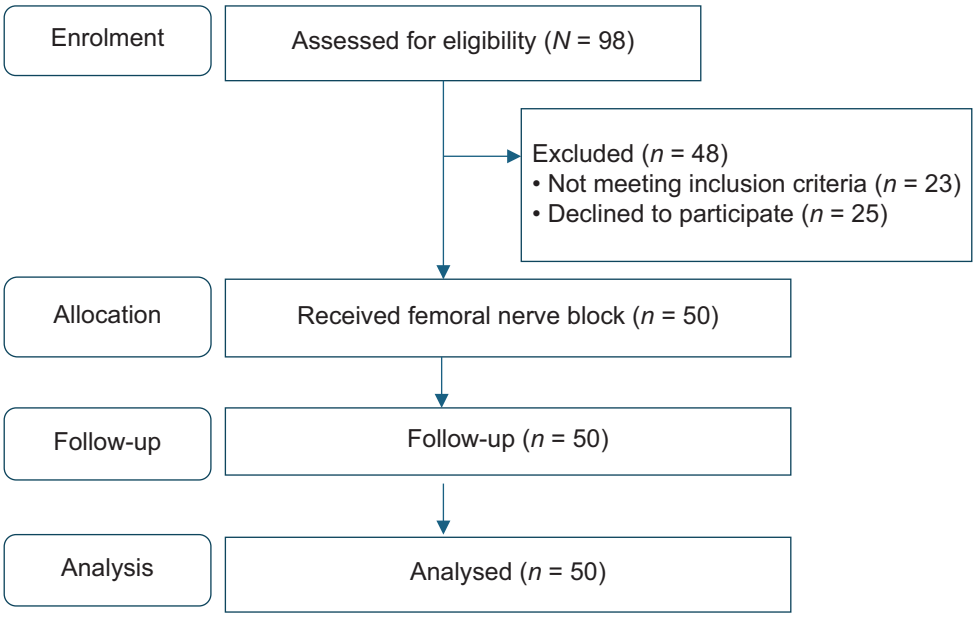

Figure 1: Patients' flow chart

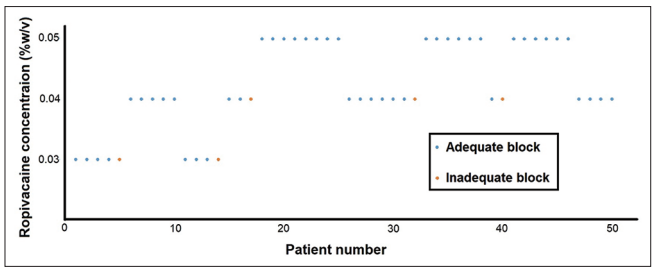

Figure 2: Femoral nerve block analgesic adequacy with different ropivacaine concentrations

EC_{90} for analgesic FN block was 0.05%. Similarly, FN block using ropivacaine 0.1% and 0.05% could provide adequate analgesia after a knee scope and arthroplasty, respectively.[6,12] In addition, ropivacaine 0.88% was reported to provide sensory block in 50% of geriatric patients.[3] However, for continuous infusion, ropivacaine 0.15% (10 mg/h) is required to achieve analgesic FN block.[13] Veneziano *et al*. (in a retrospective study in paediatric patients) and Yao *et al*. evaluated various ropivacaine concentrations to determine the ropivacaine EC for analgesic FN block; they recommended ropivacaine 0.5% and 0.2%, respectively.[7,8] The sciatic/obturator-mediated pains were not excluded in Veneziano's study, while Yao and colleagues used ropivacaine 0.2% to block the sciatic nerve and FN. Unlike the above two studies, we assessed FN selectively using the biased-coin design up-and-down sequential method, which can accurately calculate the EC at any quantile. Using the same statistical method, ropivacaine 0.17% was reported to induce anaesthetic FN block.[2] In that study, a time limit (35 min) was set to achieve a complete motor block. Otherwise, the block was considered unsuccessful.[2]

The quadriceps weakness was minimal and, theatrically, should not delay ambulation. Similar results were reported using low ropivacaine and bupivacaine concentrations.[2-5,12] Fortunately, the duration of analgesia was not affected in the current and some previous studies,[12] yet impairment was still reported.[4] The use of IV dexamethasone might improve the duration of analgesia in the current study.[14]

There are certain limitations to this study. We considered postoperative pain as an inadequate FN block. In a surgery like a knee ligament reconstruction, the pain generators are multiple, with the hamstring graft having a sciatic and obturator nerve origin and the lateral knee incision having a lateral femoral cutaneous nerve origin. Therefore, a successful block of the sciatic, obturator, and lateral femoral cutaneous nerves was confirmed preoperatively. This minimised the false negative results but made assessing patients' ambulation difficult. The current analgesic ropivacaine concentration was estimated in patients who had received LA infiltration at the site of the skin incision. However, to achieve a complete cutaneous block, a higher ropivacaine concentration may be required.[3]

One operator conducted all blocks. This may increase the consistency of our results but may also decrease

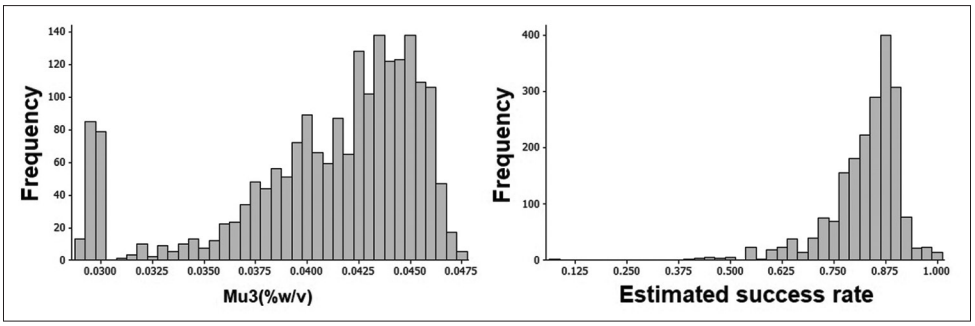

Figure 3: Histogram of isotonic regression estimator (Mu3) and estimated success rate

its general application. However, FN block using an LA volume of 15 mL can be performed by operators of different experience levels. The calculated EC_{90} in this study may or may not be altered by factors such as a) the tested nerve, localising technique, and injection technique (needle vs perineural catheter); b) LA type, volume, and adjuvant; c) definition of adequate block, especially regarding time limit; d) the use of systemic analgesics and intra-articular LA injection or lack of subcutaneous LA infiltration; and e) type of patient. All included patients were relatively healthy middle-aged males and had knee ligament reconstruction; thus, our results (EC_{90}) may not be valid in patients with comorbidities (especially neuropathy).[3]

CONCLUSION

FN block using ropivacaine 0.05% w/v may provide adequate analgesia in 90% of patients.

Study data availability

De-identified data may be requested with reasonable justification from the authors (email to the corresponding author) and shall be shared after approval as per the authors' Institution policy.

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Conflicts of interest

There are no conflicts of interest.

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