ORIGINAL RESEARCH PAPER

Anesthesiology

MINIMUM EFFECTIVE ANESTHETIC CONCENTRATION (MEAC90) OF ROPIVACAINE IN ULTRASOUND GUIDED POPLITEAL SCIATIC NERVE BLOCK: A DOSE FINDING STUDY.

KEY WORDS: Local anesthetics, Ropivacaine, Regional anesthesia, Sciatic nerve, Ultrasonography, Paraneurium.

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ABSTRACT

Background: Peripheral nerve blocks provide excellent regional anaesthesia for limb surgeries. Ultrasound guidance improves the precision and success of the peripheral nerve blocks; and appears to reduce both the concentration and volume of the local anaesthetics required for successful blocks.

Objectives: This study was aimed at estimating the minimum effective anesthetic concentration of ropivacaine for ultrasound guided popliteal sciatic nerve block, successful in 90% of patients ($MEAC_{90}$).

Materials and Methods:

Design: Prospective, Interventional, Single Group, Double blind (subject and outcome assessor) study.

Setting: The study was carried out in the Pre anesthesia procedure room of a tertiary care hospital in India.

Patients: 47 ASA functional status 1 – 2 adult patients aged 18years and above, scheduled to undergo unilateral leg procedures of less than 90 minutes duration were included.

Intervention: 47 patients scheduled to undergo lower leg surgeries received popliteal sciatic nerve block using 15 ml of ropivacaine in sub-paraneural plane starting with 0.2% w/v. The concentration of ropivacaine administered to the subsequent patient was determined by the effectiveness of nerve block in the previous patient, using the biased-coin design sequential up-down method. If the nerve block was effective in a patient, then the next patient was randomized to receive either the same concentration as the previous patient(probability of 0.89) or a concentration 0.02% w/v less than the previous patient(probability of 0.11). If the nerve block was not effective in a patient, then ropivacaine concentration was increased by 0.02% w/v in the next patient. The block efficacy was assessed by an independent observer every 5 minutes for 30 minutes following the block.

Measurements: Time to onset of block, Duration of procedure, Time to first rescue analgesic and complications of procedure were recorded.

Results and Conclusion: Out of the 47 patients, 45 had successful blockade. Minimum Effective Anesthetic Concentration in 90% of subjects ($MEAC_{90}$) was estimated to be 0.139%w/v (95% confidence interval, 0.129% - 0.158%).

Ultrasound guided sub-paraneural popliteal sciatic nerve block with 15 ml of 0.139% w/v ropivacaine can produce successful blockade in 90% of patients.

INTRODUCTION

Peripheral nerve blocks provide excellent regional anaesthesia for the extremities. It helps to avoid general anaesthesia which may be risky in patients with co-morbidities. General anaesthetics and opioids lead to cardio respiratory and neurological depression. There is possible deterioration of the hepatic and renal systems also, which may be detrimental in high risk patients. No or minimal sedation only is required for the safe and comfortable administration of these blocks, as well as for the intra-operative management.

Surgery under regional anaesthesia does not trigger stress response unlike under general anaesthesia. General anaesthesia only attenuate the stress response to various levels and do not obtund the stress response completely. Stress may decompensate poorly functional organ systems leading to failure.

Regional anaesthesia provides prolonged post operative analgesia for a duration of 12- 18 hours when long acting local anaesthetics like bupivacaine or ropivacaine is used[1]. No narcotic or non-narcotic analgesics are warranted during this period, which benefits the severely co-morbid patients.

Success rate of landmark based peripheral nerve blocks of the lower limb in general, and especially of the sciatic nerve in the popliteal fossa, is poor. Nerve stimulation improves the success rate, but a larger concentration and volume of local anaesthetics are generally used. Technical problems, delayed onset, variable reliability, nerve damage and local anesthetic systemic toxicity have deterred the anesthesiologists in performing peripheral nerve blocks[2].

Ultrasound guidance is recently used for regional anaesthesia. It helps in the localization of the target nerves, real-time needling and injection. The needle tip can be maneuvered precisely to the close proximity of the nerve without entering into it, thus avoiding nerve damage. Intravascular injections and local anaesthetic systemic toxicity can be easily avoided by ultrasound guidance. Spread of the local anaesthetic can be appreciated live. Post procedural scan will reveal the extent of spread. Spread of local anaesthetic for about 2 cm along the nerve is needed for the successful blockade. An additional volume may be injected if the spread is found inadequate. This helps to reduce the dose of local anaesthetic both in terms of volume and concentration.

Systemic toxicity of local anesthetics is to an extend dose dependent. Prevention of such adverse events is important in promoting patient safety during regional anesthesia. Using lower doses of local anesthetics provides a wider safety margin[18]. Ropivacaine is a long acting amide local anesthetic, structurally related to bupivacaine but with relatively better safety margin as compared to bupivacaine. Moreover ropivacaine being less lipophilic than bupivacaine is less likely to penetrate large myelinated motor nerve fibers producing relative sensory blockade[19]. The dosage of local anesthetic has been directly linked to neuro toxicity and hence using lower concentrations can be beneficial[20].

More and more of invasive and painful surgical procedures are being performed on ambulatory basis, under the precise ultrasound guided peripheral nerve blocks[2,3]. Paraneurium is the soft tissue condensation around a nerve. Epineurium, which is the outermost layer of the nerve, and lies beneath the paraneurium.

Injection within the epineurium is considered intraneural and considered injurious to the nerve. The closest extraneural injection is sub paraneural and extra epineural. The local anaesthetic injected in this plane will spread around and along the nerve evenly, producing an early and dense block. So a lower concentration and volume of local anaesthetic may be sufficient for the neural blockade in this plane.

Ultrasound guided sub-paraneural popliteal sciatic nerve block at the bifurcation of sciatic nerve into the tibial and a common peroneal component is now an accepted technique of nerve blockade. This method is simple, safe, effective and has faster onset of action[4–6]. Lower leg surgeries require blockade of the tibial and common peroneal component of sciatic nerve as well as the saphenous component of femoral nerve.

Multiple nerve blockades using larger volumes and concentration may lead to use of maximum allowed safe doses of local anesthetics[7,8]. This can lead to untoward side effects and local anesthetic toxicity. There have been studies aimed at minimizing the local anesthetic doses while still producing reliable nerve blockade[7–12] .

This study was aimed at estimating the minimum effective anesthetic concentration of ropivacaine in ultrasound guided sub-paraneural popliteal sciatic nerve block, successful in 90% of patients($MEAC_{90}$).

MATERIALS AND METHODS

The study was started after obtaining approval from the research and institutional ethics committee of Jubilee Mission Medical College and Research Institute, India(26/16/IEC/JMMC&RI). The study was then registered in the Clinical Trials Registry of India (CTRI/2016/12/007563). The study was conducted from August 2016 to December 2016. After obtaining written informed consent, consecutive ASA physical status 1-2 patients aged 18 years and above, who were scheduled to undergo unilateral leg surgeries of less than 90 minutes expected duration were enrolled in to this study. Patients who had preexisting neuropathy, coagulopathy, severe hepatic and renal dysfunction, who are unable to report pain/paresthesia and allergic to ropivacaine were excluded from this study.

All patients were taken to the block room from the pre anesthesia holding area and standard monitoring consisting of ECG, pulse oximetry and non invasive arterial blood pressure was applied. Intravenous access was secured and sedation in titrated doses was given up to a maximum of 2mg Midazolam and 10mcg of dexmedetomidine. All blocks were performed by one experienced anesthesiologist to exclude difference in technique and expertise. Patients were made to lie down in lateral position and popliteal sciatic nerve block was performed with 15ml of ropivacaine after skin asepsis and sterile draping. Saphenous nerve block in the adductor canal was also performed after making them supine with 15ml of 0.2% ropivacaine. The volume and concentration for saphenous nerve block remained the same for all patients while the concentration of ropivacaine varied according to biased coin up down method for sciatic nerve block.

Table-1

Patient Demographics and Characteristics -	
Age in years –Median Range	53 25-75
Gender-Male/Female in numbers in %	35/ 12 74.5%/2 5.5%
ASA I/ ASA II in numbers in %	13/34 27.7%/72.3%

Ultrasound guidance with a M-Turbo machine (Sonosite Inc., Bothell, WA, USA)and a linear transducer(HFL38x,13-6MHz) was used to perform the nerve block. A 25G standard quincke spinal needle(Spinocan, B.Braun Medical Inc., PA, USA) and a 100cm plastic extension tubing were used to deliver the drug from a 20ml syringe. The transducer after sterile sheathing was placed in the popliteal fossa and the point of bifurcation of sciatic nerve to common peroneal and posterior tibial branches were identified. The needle was advanced precisely between the two nerves at the bifurcation. Saphenous nerve block was performed after identifying the nerve in adductor canal at mid-thigh level.

The time immediately after performing nerve blockade was taken as zero and sensory blockade was assessed every 5minutes for the next 30 minutes using a 26G sterile hypodermic needle for pin prick sensation. The sensory blockade was arbitrarily graded as Grade 0 – Normal sharp sensation, Grade 1 – reduced sharp sensation and Grade 2 – absent sensation. Patients with a Grade 2 sensation by 30 minutes of blockade were considered to have a successful blockade and were allowed to proceed for surgery. Intra-operatively they were monitored for pain and discomfort. Any pain during surgery was supplemented with inhalational or intravenous anesthesia and those patients were considered as failed block. Those with lesser grades of sensory blockade received some form of supplemental anesthesia and they were also grouped as failed nerve block.

The sensory blockade was assessed by an independent observer, who was unaware of the concentration of ropivacaine used. Intra-operative pain, time to rescue analgesic request and any complications arising out of blockade were recorded. Rescue analgesic prescribed was aliquots of 25 mg of intravenous tramadol. All patients underwent a neurological assessment of the lower limb before discharging from the hospital.

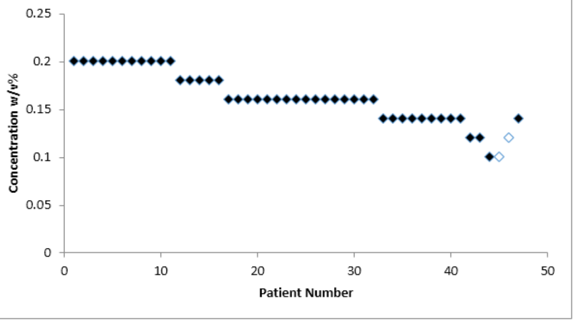
As per the biased coin sequential up down design, the ropivacaine concentration given to a patient depends on the response of the previous patient[7,8,10] . Had the block been a failure in a patient, then the next patient received 0.02% higher concentration of ropivacaine. Had the block been a success, then the next patient received either the same concentration of ropivacaine (probability of 0.89) or a concentration 0.02% lower(probability of 0.11). The ropivacaine concentration used in the first patient was fixed at 0.2% as per a previous study done by a different methodology quoting the 95% Effective Concentration(EC_{95}) as 0.198%[13].

At least 45 successful blocks (smallest multiple of 9 that is more than 40) were required to calculate the $MEAC_{90}$. This minimum sample size required was estimated using simulations for different scenarios of dose distribution, number of positive responses and sample size[10,14–16] . Isotonic regression with bias corrected 95% confidence interval (CI) derived by bootstrapping was used to estimate the $MEAC_{90}$. Dose estimator m2, defined as the dose with an estimated probability of success closest to 90% was used in this study stated as the mean value of the dose with its confidence interval(CI)[10,17]. Statistical analysis was performed using SPSS statistics for windows, version 17.0(SPSS Inc., Chicago, Illinois, USA). Continuous variables are presented as mean (standard deviation) or median (range) and categorical variables as frequency (percentage).

RESULTS

Forty seven patients were recruited to the study to obtain forty five successful blocks. No patients were excluded from the study after inclusion. Patient demographics and characteristics are summarized in Table 1. The Minimum Effective Anesthetic Concentration ($MEAC_{90}$) of 15 ml of ropivacaine in ultrasound guided popliteal sciatic nerve block in the sub-paraneural plane was estimated to be 0.139% w/v (95% CI 0.129%-0.158%) (Figure 1). Out of the two patients, who had failed blockade, first was a 61 year old male for open fixation of lateral malleolus in whom the block became adequate 40 minutes after injection and the surgery proceeded without any further supplementation. Second patient was a 52 year old lady posted for drainage of an abscess on her foot in which the block did not work and needed supplemental general anesthesia. No complications were observed in any of these 47 patients.

Figure 1:Patient response to successful (black) and failed (white) block with different ropivacaine concentrations



DISCUSSION

Summary of findings: The factors influencing the success of peripheral nerve blockade are volume and concentration of local anesthetic and the precision at which the drug is deposited closely around the nerve[11]. The use of ultrasound helps to deliver the local anaesthetic close to the nerve and helps in reducing the total amount of local anaesthetic needed to block a particular nerve[3]. In this study, we injected the drug close to the sciatic nerve in the popliteal fossa in the sub paraineural plane, under ultrasound guidance. A fixed volume, 15 ml, of ropivacaine, at decreasing concentrations was injected. Our study employing the up and down methodology to determine the minimum effective anesthetic concentration of ropivacaine in ultrasound guided popliteal sciatic nerve block has proved that it is possible to achieve a successful block with lower concentrations of ropivacaine. The onset of the block is delayed with the reducing concentrations. We found that 0.139% of 15ml ropivacaine provided adequate anesthesia in 90% of patients. This low concentration of 0.139% of ropivacaine has not been previously established for ultrasound guided popliteal sciatic nerve block.

Comparison of results: The minimum effective volume of 0.5% ropivacaine for ultrasound guided popliteal sciatic nerve block has been found to be 16ml in a previous study[21]. In another study to find out the minimum effective concentration of ropivacaine for sciatic nerve blockade, it was found to be 0.198% even though they used a different methodology (probit regression model)[13]. In this study we used a fixed volume of ropivacaine, 15 mls, at decreasing concentrations to find out the minimum effective concentration. The biased coin sequential up down design can estimate the minimum effective anesthetic concentration at any quantile[10]. The minimum effective anesthetic concentration (MEAC) can be affected by multiple factors like the type of local anesthetic, the volume, the use of adjuvant, the nerve to be blocked, the block level, and the localizing technique[10,11,22,23]. The minimum effective anesthetic concentration of ropivacaine in 90% of population ($MEAC_{90}$) for popliteal sciatic nerve block in the sub-paraneural plane has not been established accurately by previous studies.

Strength and limitations: In this study, the precise deposition of drug under ultrasound visualisation around the nerve in the sub-paraneural plane is likely to be the reason for the successful blockade with low concentrations of ropivacaine. No complications attributable to nerve blockade were detected in patients at discharge. The following issues should be taken in to consideration while applying the results of this study in general population. The definition of successful blockade and the success rate depended on the fixed 15ml volume of ropivacaine and the 30 minute time after blockade. Any change in the volume of drug and time interval after blockade will definitely change the results with smaller volumes and shorter time interval after blockade decreasing the success of the block. Volume of drug injected outside the suggested plane will be less effective. All blocks were performed by an anesthetist with extensive experience in regional anesthesia which can also influence the success rate. The outcome of the blocks depends on the quality of the ultrasound device and the skill of the anaesthetist performing the block. Most of our patients were middle aged males, which might have affected the results. Patient factors like age, sex, obesity and co-morbidities like diabetic neuropathy and metabolic dysfunction, intractable chronic pain in the blocked area, might have an impact on minimum effective anesthetic concentration (MEAC)[24–27].

Conclusion:

We found that sub para-neural injection of 0.139% of 15ml of ropivacine around sciatic nerve block in popliteal fossa produces successful blockade in 90% of the patients.

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