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SCIENTIFIC ARTICLE

Minimum effective volume of bupivacaine 0.5% for ultrasound-guided retroclavicular approach to infraclavicular brachial plexus block

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KEYWORDS
Retroclavicular block;
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Minimum effective volume

Abstract
Background and objectives: The current study aimed to determine the minimum effective volume (MEV) of bupivacaine 0.5% in 50% of patients for an ultrasound-guided retroclavicular approach to infraclavicular brachial plexus block.
Methods: A total of 25 adult patients who were scheduled for upper limb surgery received an ultrasound-guided retroclavicular approach to infraclavicular brachial plexus block with bupivacaine 0.5%. The needle insertion point was posterior to the clavicle and the needle was advanced from cephalad to caudal. Block success was defined as a composite score of 14 at 30 min after local anesthetic (LA) injection. The minimum effective volume in 50% of patients was determined using the Dixon-Massey up-and-down staircase method. Minimum effective volume for a successful block in 95% of the patients was also calculated using logistic regression and probit transformation.
Results: The minimum effective volume of bupivacaine 0.5% resulting in successful block in 50% of patients (MEV50) according to the up-and-down staircase method was found to be 9.6 mL (95% confidence interval (CI), 5.7–13.4). The calculated minimum effective volume required for a successful block in 95% of patients (MEV95) using the probit transformation and logistic regression analysis was 23.2 mL (95% CI, 18.8–36.7).
Conclusions: The MEV50 of bupivacaine 0.5% for US-guided retroclavicular approach to infraclavicular brachial plexus block was 9.6 mL and the calculated MEV95 was 23.2 mL. Future studies are required for infraclavicular brachial plexus block with different approaches, other LA agents and different concentrations of bupivacaine.

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PALAVRAS-CHAVE
Bloqueio retroclavicular;
Guiado por ultrassom;
Bloqueio do plexo braquial por via infraclavicular;
Volume mínimo efetivo

Volume mínimo efetivo de bupivacaína a 0,5% para abordagem retroclavicular guiada por ultrassom no bloqueio do plexo braquial por via infraclavicular

Resumo
Justificativa e objetivos: Determinar o volume mínimo efetivo (VE) de bupivacaína a 0,5% em 50% dos pacientes para uma abordagem retroclavicular guiada por ultrassom no bloqueio do plexo braquial por via infraclavicular.
Métodos: Um total de 25 pacientes adultos agendados para cirurgia do membro superior receberam abordagem retroclavicular guiada por ultrassom para o bloqueio do plexo braquial por via infraclavicular com bupivacaína a 0,5%. O ponto de inserção da agulha foi posterior à clavícula e a agulha foi avançada de cefálica para caudal. O sucesso do bloqueio foi definido como um escore composto de 14 aos 30 min após a injeção do anestésico local. O VE em 50% dos pacientes foi determinado com o método de escalonamento progressivo-regressivo de Dixon-Massey. O VE para um bloqueio bem-sucedido em 95% dos pacientes também foi calculado com regressão logística e transformação *probit*.
Resultados: O volume mínimo efetivo (VE50) de bupivacaína a 0,5% que resultou em bloqueio bem-sucedido em 50% dos pacientes, de acordo com o método de escalonamento progressivo-regressivo, foi de 9,6 ml (intervalo de confiança de 95%, IC 5,7-13,4). O cálculo do volume mínimo efetivo necessário para um bloqueio bem-sucedido em 95% dos pacientes (VE95) com a análise de transformação *probit* e regressão logística foi de 23,2 ml (IC 95%, 18,8-36,7).
Conclusões: O VE50 de bupivacaína a 0,5% para abordagem retroclavicular guiada por US para o bloqueio do plexo braquial por via infraclavicular foi de 9,6 ml e o VE95 calculado foi de 23,2 ml. Estudos futuros são necessários para o bloqueio do plexo braquial por via infraclavicular com diferentes abordagens, outros anestésicos locais e diferentes concentrações de bupivacaína.

Introduction

The Ultrasound (US) guided posterior approach to Infraclavicular Brachial Plexus Block (IBPB) was first described by Hebbard and Royse.[1] Charbonneau et al. reported that retroclavicular block was a quick, safe, and reliable alternative for distal arm block.[2] Unlike the coracoid approach, the needle insertion point is posterior to the clavicle in the retroclavicular approach. Therefore, the needle shaft is aligned perpendicular to the Ultrasound (US) beam, thereby allowing better needle tip and shaft visibility. In a recent study by the current authors, retroclavicular and coracoid approach to US-guided infraclavicular brachial plexus block (IBPB) were compared.[3] The retroclavicular approach was found to be superior to the coracoid approach in terms of performance and anesthesia related time, needle passes and paraesthesia during block performance. It was concluded that these results were due to better needle tip and shaft visibility. On the assumption that good needle visibility affects the Local Anesthetic (LA) requirement, it was aimed in the current study to estimate the Minimum Effective Volume (MEV) of bupivacaine 0.5% in 50% of patients for a retroclavicular approach to IBPB.

Methods

This study was carried out in accordance with the Declaration of Helsinki, approved by the Ethics Committee of the Training and Research Hospital, Antalya, Turkey (approval no. 3/13), and registered in the Clinicaltrials.gov clinical trials registry (no. NCT03472911). Written informed consent was obtained from all patients before they were included in the study. A total of 25 patients who received IBPB for elective elbow, forearm, wrist, or hand surgery were enrolled in the study. Exclusion criteria were patients <18 years old, with a Body Mass Index (BMI) <20 or >35 $kg.m^{-2}$, inability to provide written informed consent, refusal of regional anesthesia, pregnancy or contraindication for regional anesthesia.

All blocks were performed by single anesthesiologist (N.K.O.) experienced in this technique. This experience included, during the most recent 5 years, the performance of more than 500 infraclavicular brachial plexus blocks with ultrasound guidance and more than 100 retroclavicular approaches to IBPB.

On arrival in the operating room, a peripheral venous line was established. Standard monitoring including non-invasive blood pressure, five lead electrocardiography and pulse oximetry. Patients were premedicated with a 0.05 $mg.kg^{-1}$ intravenous bolus of midazolam 5 min before the block. Before all the blocks, the skin was cleaned with chlorhexidine and the skin and subcutaneous tissue were anesthetized with 2–4 mL of 1% lidocaine. A 21 gauge 85 mm needle (Echoplex+®, Vygon, Ecouen, France) was used for the blocks. Patients were positioned supine, the arm was adducted, and the head was rotated to the contralateral side of the blockade. A Mindray (Shenzhen, China) DC-T6 ultrasound machine with a 10 MHz linear probe with a sterile cover was used to perform the blocks. The retroclavicular

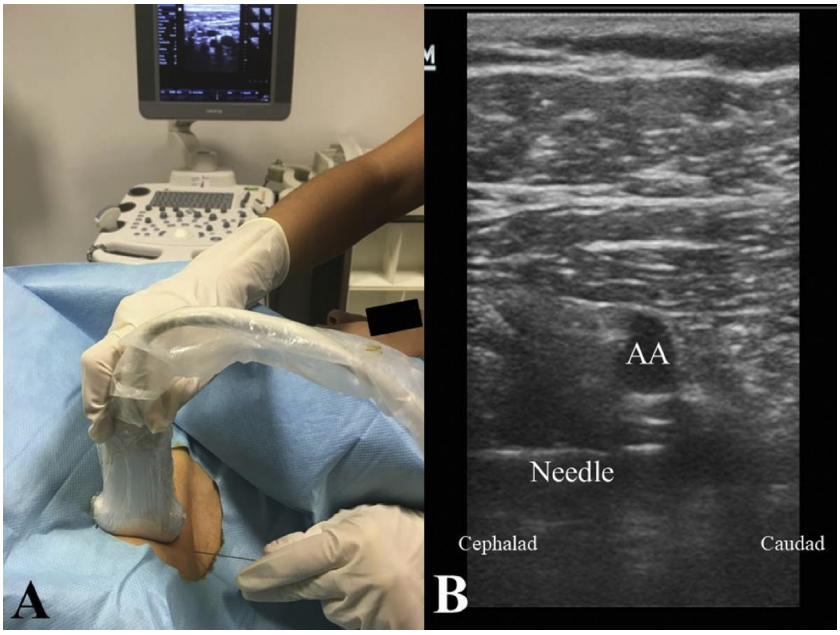

Figure 1 Retroclavicular approach for ultrasound-guided infraclavicular brachial plexus block. (A) Position of the transducer and block needle insertion point. (B) Ultrasound image demonstrating the needle tip and shaft. AA, axillary artery.

approach to the IBPB was performed as described by Charbonneau et al.[2] The US probe was placed parasagittally just medial to the coracoid process and caudal from the clavicle. The needle insertion point was located in the supraclavicular fossa, just medial to the shoulder at a point sufficiently posterior to the clavicle and medial to the trapezius muscle insertion point on the clavicle. The needle was inserted immediately above the clavicle in the space between the coracoid process and the clavicle and advanced from cephalad to caudal. After US visualization of the nerve roots, saline boluses (less than 0.5 mL) were used to verify the correct position before injecting the bupivacaine (Fig. 1). The aim of the injections was to administer local anesthetic with the aim of providing a U-shaped spread around the axillary artery. Therefore, 25% of the local anesthetic was injected at the 5 o'clock position of the axillary artery for medial cord coverage. Then, the needle was withdrawn to the 6 o'clock position of the artery and 50% of the local anesthetic was injected to posterior cord anesthesia. Finally, the needle was withdrawn to the 7 o'clock position and 25% of the local anesthetic was injected to guarantee the covered of the lateral cord.[4]

The first patient who agreed to participate in the study received a volume of 25 mL. Based on a recent study, a volume of 25 mL 0.5% bupivacaine to retroclavicular approach to IBPB had provided sensory block success of 96%.[3] The up-and-down method design was applied to succeeding patients. The volume for consecutive patients was defined by the block effect in the preceding patient. If the previous block was successful, the block was performed by a reduction of the volume by 2.5 mL in the next patient. In case of failure, the volume was increased by 2.5 mL.

A blinded observer, who was not present during performance of the block and who was unaware of the volume of anesthetic used, was asked to assess the sensory and motor blockade. Sensory assessments were performed every 5 min after needle removal for 30 min in the regions of the radial, median, ulnar, and musculocutaneous nerves of the forearm based on a three-point scale with a cold test [0: normal sensation, 1: analgesia (patient can feel touch but not cold), 2: anesthesia (patient cannot feel touch)]. Motor block was evaluated for flexion of the elbow, opposition of the thumb, abduction of the thumb, and adduction of the thumb based on a three-point scale (0: no block, 1: paresis, 2: paralysis). The maximum composite score was 16 points. Block success was defined as a composite score of 14 at 30 min. The number of needle passes and the block performance time were recorded by an independent observer. Any retraction of a least 10 mm and re-advancement of the needle was counted as an additional needle pass. Block performance time was defined as the time from the first insertion of the blocking needle to its removal. Onset time was defined as the time required for a composite score of 14 points. If the composite score was >4 after 30 min, the patient was transferred to the operating room to begin the surgery, and the onset time was not recorded in this case. If the composite score was less than 14/16, additional intravenous analgesia, rescue blocks or general anesthesia was administered.[5] The total anesthesia-related time was the sum of the performance and onset times. Complications such as needle-induced paraesthesia, vascular puncture, and symptoms of local anesthetic toxicity were recorded by a blinded observer.

Statistical analysis

In this study, the primary objective was to estimate the MEV_{50} for a retroclavicular approach to US-guided IBPB. Two rules were used to stop the study. The first was a fixed sample size. An up-and-down method was used to estimate the threshold for an all-or-none response in the present study design. Therefore, for sample size calculation, the

Table 1 Patient characteristics. Values expressed as mean ± SD or number with percentage.

Age (years)	40.5 ± 10
BMI (kg.m^{-2})	23.6 ± 2.6
Gender	
Male	13 (52)
Female	12 (48)
ASA physical status	
ASA I	9 (36)
ASA II	16 (64)
Types of surgery	
Hand	7 (28)
Wrist	10 (40)
Forearm	4 (16)
Elbow	4 (16)

BMI, Body Mass Index; ASA, American Society of Anesthesiologists.

Dixon and Massey formula was applied; $n = 2$ (SD/SEM)^2 (SD, Standard Deviation and SEM, Standard Error of Mean).[6,7] SD was assumed to be 5 mL and SEM 1.5 mL. The formula suggested 22 patients for the study, so 25 patients were included to replace any dropouts. The second rule for stopping included the demonstration of a minimum of five consecutive up-and-down sequences. On the basis of previous studies with similar binary outcomes,[8] it was estimated that a priori a minimum of five negative-positive up-and down deflections was required to calculate MEV_{50}. As the volume interval should lie between 0.5 and 2 times the anticipated SD, 2.5 mL 0.5% bupivacaine volume interval was used in the present study.[6] The determination of MEV_{50} and its Confidence Interval 95% (95% CI) was based on the staircase up-and-down method by Dixon and Massey (MEV50, $X = (\sum fiX_i/n) + d/2$); Xi, the LA volume used leading to a failed or successful block, f_i, frequency of failed or successful blocks associated with X_i; n, the total number of patients with failed or successful blocks; d, volume interval.[6] The secondary objective was to estimate the MEV in 95% of patients (MEV95). To calculate the MEV95, data were analyzed using probit transformation and logistic regression. Continuous variables are presented as mean ± SD, 95% CI, or both. Categorical variables are presented as number and percentage. Ordinal variables are presented as the median and range. Statistical analysis was performed using the SPSS version 24 statistical software (SPSS Inc., Chicago, IL, USA).

Results

A total of 25 patients were enrolled, and all were successfully followed up according to the study protocol. The characteristics of the patients are presented in Table 1. Block performance data are summarized in Table 2. The sequence of successful and failed blocks is depicted in Fig. 2. The volumes of LA administered ranged from 5 mL to 25 mL. The minimum effective volume of bupivacaine 0.5% resulting in successful block in 50% of patients (MEV50) according to the up-and-down staircase method was found to be 9.6 mL (Confidence Interval 95% – 95% CI 5.7–13.4). The calculated minimum effective volume required for successful block in 95% of patients (MEV95) using the probit transformation and logistic regression analysis was 23.2 mL (95% CI 18.8–36.7).

Table 2 Block data and complications. Values expressed as mean ± SD, median (range) or number with percentage.

Block performance time (min)[a]	1.3 ± 0.5
Onset time (min)[a]	24.2 ± 5
Anesthesia related time (min)[a]	25.6 ± 4.8
Number of needle passes	2 (1–3)
Number of needle passes for successful blocks	
1	6 (24)
2	6 (24)
3	4 (16)
Number of needle passes for failed blocks	
1	6 (24)
2	1 (4)
3	2 (8)
Complications	
Paraesthesia during block performance	3 (12)
Vascular puncture	0
Local anesthetic toxicity	0
Pneumothorax	0

[a] Mean and SD based on only the patients with a minimal composite score of 14 points at 30 min.

Paraesthesia during block performance occurred in 3 cases. There was no vascular puncture or LA toxicity in any patient. Sensory and motor functions were completely recovered in all patients at the 24 h follow-up. No neurological deficit was diagnosed in any patient at 24 h and 1 week follow-up (Table 2).

Discussion

In the current study, the minimum volume required to provide an effective block in 50% of patients of bupivacaine 0.5% for an US-guided retroclavicular approach to IBPB was 9.6 mL (95% CI 5.7–13.4) and the calculated effective volume for US-guided retroclavicular approach to IBPB in 95% of patients was 23.2 mL (95% CI 18.8–36.7).

In previous studies of the retroclavicular approach to ICBP, the volume of LA required for surgical anesthesia has been reported at doses ranging from 25 to 40 mL.[2,3,9] However, no studies have calculated the MEV50 or MEV95. Charbonneau et al. reported a 96% rate of surgical success and 90% of block success with 40 mL of mepivacaine 1.5% with epinephrine 2.5 μg.mL^{-1}.[2] In the previous study by the current authors, a 96% surgical success rate was achieved with 25 mL of bupivacaine 0.5%.[3] Unlike that study, in which a 14 point minimal composite score was accepted as block success, Charbonneau et al. defined block success as a sensory score of 10 at 30 min. Luftig et al. also reported a series of 3 cases with successful block performed using 30 mL of 1%–1.5% lidocaine with epinephrine.[9] Although there have been no studies for MEV of LA in the retroclavicular approach to IBPB, the MEV of LA for different approaches to IBPB has been reported in a few studies. Flohr-Madsen et al.

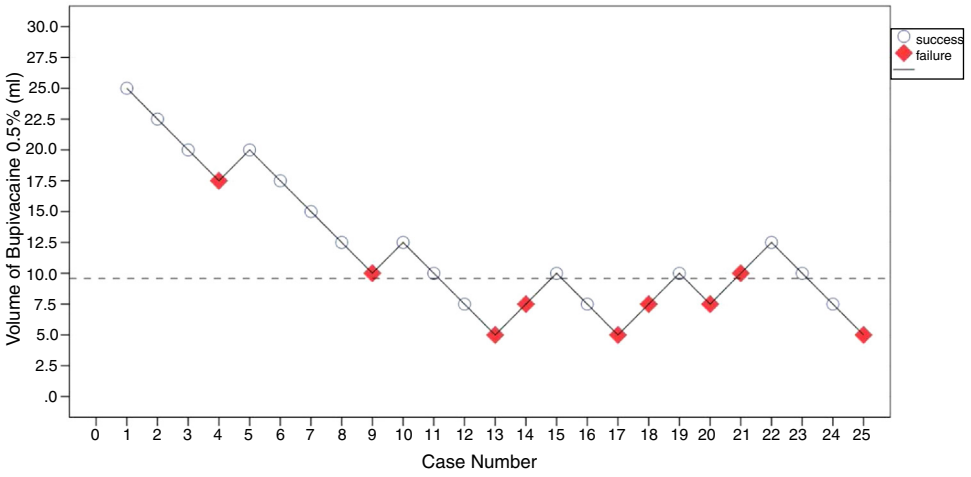

Figure 2 Up-and-down sequences of ultrasound-guided retroclavicular approach to infraclavicular brachial plexus block using 0.05% bupivacaine. The horizontal dotted line represents the minimum effective volume of local anesthetic required for effective ultrasound-guided retroclavicular approach to infraclavicular brachial plexus block in 50% of the patients: 9.6 mL.

reported a MEV50 of 19 mL and MEV95 of 31 mL in a study of ultrasound-guided lateral sagittal infraclavicular block with ropivacaine 7.5 mg.mL^{-1}.[8] Tran et al. reported that the MEV90 of lidocaine 1.5% with epinephrine 5 μg.mL^{-1} for single injection US-guided ICB was 35 mL.[10] Sotthisopha et al. stated that the MEV90 of lidocaine 1.5% with epinephrine 5 μg.mL^{-1} was 34.0 mL for costoclavicular IBPB.[11]

It can be seen that the previous studies of different approaches to IBPB have indicated a higher volume requirement compared to the current study findings for the retroclavicular approach. In addition to factors such as choice of LA and the statistical methodology, the approach used to perform the block may also affect this difference. In the retroclavicular approach to IBPB, the needle insertion point posterior to the clavicle provides perpendicular alignment of the ultrasound beam and needle shaft. Positioning the needle path in a parallel plane to the probe and aligning the needle shaft perpendicular to the ultrasound beam increases the needle tip and shaft visibility.[2] The ability to accurately keep track of the needle tip contributes to the avoidance of unintentional contact with the neurovascular bundle and reduces procedural complications.[12] In addition, better needle visibility may provide guaranteed needle orientation and may allow distribution around the target nerve as desired by increasing the deposition of LA. This may result in reducing the amount of LA required to successfully block the nerve.[13]

Sutton et al. reported that if the lateral cord was separated from the artery by a small distance, the LA failed to reach the cord.[14] It was reported that when the needle was withdrawn slightly and redirected anteriorly to deposit a small aliquot of LA at the lateral cord, onset was more rapid. However, the presence of the clavicle may sometimes prevent the redirection of the needle. Uppal et al.[4] suggested that injecting the LA at three different points along the needle trajectory provided a more rapid onset of the block.[4] Therefore, in the current study, 25% of the LA was injected at the 5 o'clock position to the artery for medial cord coverage, 50% at the 6 o'clock position to the artery for posterior cord coverage and 25% at the 7 o'clock position to the artery for lateral cord coverage, as described by Uppal et al.[4] In addition, it was considered that better LA distribution could be provided at lower volumes.

This study has several limitations. Although the up-and-down method constitutes the most popular and simple study design to estimate the MEV50 for peripheral nerve blocks, it may not be able to accurately determine the MEV95.[15] Probit and logistic regression analyses may be used to calculate MEV95. Probit and logistic regression analyses posit that the tolerance distribution is symmetrical and normally distributed with a mean equal to the estimated 50th quantile. Therefore, these analyses may carry significant bias.[16] Furthermore, probit and regression analyses are imprecise for the calculation of the MEV95, as evidenced by the wide range of the 95% CI 18.8–36.7 mL. However, due to its clinical importance especially for the anesthesiologists, reporting of the MEV95 may be important for comparisons with the results of future studies.

In conclusion, the results of this study showed that the MEV50 of bupivacaine 0.5% for the US-guided retroclavicular approach to IBPB is 9.6 mL and the calculated MEV95 is 23.2 mL. Further studies are required of IBPB with different approaches, other LA agents and different concentrations of bupivacaine.

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Conflicts of interest

The authors declare no conflicts of interest.

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