Minimum effective volume of 0.5% bupivacaine with epinephrine in ultrasound-guided interscalene brachial plexus block


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Editor’s key points

- Ultrasound-guided regional anaesthesia can reduce local anaesthetic volumes needed for effective analgesia.
- The minimum effective volume of 0.5% bupivacaine required for interscalene brachial plexus block was studied.
- A comprehensive assessment of sensory and motor changes was used along with pain scores.
- The MEV of 0.5% bupivacaine with epinephrine was found to be 0.95 ml.
- Further work is needed on block duration and dose variation.

Background. The use of ultrasound (US) in regional anaesthesia enables a reduction in the local anaesthetic volume. The present study aimed to determine the minimum effective volume (MEV90) of 0.5% bupivacaine with epinephrine for interscalene brachial plexus block (ISBPB).

Methods. The volume of the anaesthetic was determined using a step-up/step-down method and was based on the outcome of the preceding block. A positive or negative block resulted in a 1 ml reduction or increase in volume, respectively. The success of the block was defined as the presence of motor block in three muscle groups and the absence of thermal and pain sensations in three dermatomes within 30 min of the injection. Diaphragmatic paralysis and analgesia were assessed at 30 min, 4, and 6 h.

Results. The MEV90 for US-guided brachial plexus block under the conditions of the present study was 0.95 ml ($R^2$: 0.97, 95% confidence interval (CI): 0.6–1.22 ml). The estimated maximum volume that did not cause diaphragmatic block was 4.29 ml ($R^2$: 0.84, 95% CI: 3.56–4.98 ml). Effective postoperative analgesia was achieved with 2.34 ml ($R^2$: 0.87, 95% CI: 0.48–11.47 ml).

Conclusions. The MEV90 of 0.5% bupivacaine with epinephrine (1:200 000) for US-guided ISBPB was 0.95 ml. Adequate postoperative analgesia and a reduced incidence of diaphragmatic block can be obtained using from 2.34 to 4.29 ml.

ClinicalTrials.gov. Registry NCT01244932.

Keywords: anaesthetic, local; brachial plexus; bupivacaine; ultrasonography

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Interscalene brachial plexus block (ISBPB) is one of the most commonly used techniques for regional anaesthesia of the upper limbs. Before the introduction of ultrasound (US)-guided ISBPB, large volumes of local anaesthetics (LAs) were used to increase the success rate of this procedure. US-guided interscalene,1–3 axillary,4 femoral,5 6 and ilioinguinal7 blocks require lower LA doses. The maximum reduction in anaesthetic volume for ISBPB resulting in anaesthesia of the upper limb, adequate postoperative analgesia, and minimal influence on diaphragmatic block is unknown.

Despite these benefits, the interscalene approach may present risks and complications, and phrenic nerve paralysis has been described in as many as 100% of patients when using high volumes of LA,8 a technique that is still widely used. Ventilation may consequently be compromised, thus restricting the use of this technique in patients with limited pulmonary reserve.

The present study was therefore conducted to identify the minimum effective LA volume (MEV90) required for both adequate anaesthesia of the brachial plexus and minimization of the complications inherent in the interscalene procedure.

Methods

A step-up/step-down study, single blinded, was used to determine the MEV90 of 0.5% bupivacaine with epinephrine in US-guided ISBPB.

This protocol was approved by our institution’s Research Ethics Committee (Ref: 1310/09) and registered at ClinicalTrials.gov under the protocol number NCT01244932. Patients
aged 21–65 yr who were candidates for an elective surgical intervention on the shoulder, with an indication for brachial plexus block for anaesthesia and analgesia, a physical condition of I or II according to the ASA, and a BMI $\leq 35$ kg m$^{-2}$, were included in the study between 2010 and 2011 after written informed consent. Patients with chronic obstructive pulmonary disease, cognitive impairment or an active psychiatric condition, an infection at the site of the puncture for the block, coagulopathy, or a history of a bupivacaine allergy were excluded from the study.

After inclusion, patient characteristic data were recorded for all patients. The patients were then referred to the regional anaesthesia station, where the entire procedure and the differences between tactile and painful sensations were explained to achieve a greater accuracy of the collected information. Routine monitoring of the surgical procedure was performed.

The US-guided brachial plexus block was performed by a single experienced anaesthesiologist (MicroMaxx$^{TM}$, SonoSite, Bothell, WA, USA). The procedure was performed using a peripheral nerve stimulator (PNS), with a 50 mm, 22 G needle (Stimuplex$^{TM}$ A, B. Braun, Melsungen, Germany). The patient was placed in the dorsal decubitus position with the neck extended towards the contralateral side. Aspesis of the skin was achieved and a local infiltration was performed with 1 ml of 1% lidocaine. After US visualization of the nerve roots and the trunks of the brachial plexus between the anterior and middle scalene muscles, the identification of the injection site was confirmed using the PNS (1 Hz frequency, 0.1 ms pulse, 1 mA current) with a progressive reduction to 0.4 mA. When a maintained motor response was observed, 15 ml of 0.5% bupivacaine with epinephrine (1:200 000) was injected, with a direct view of the injection site. The injection was given in two equal aliquots of 7.5 ml: one between the upper and middle trunk and one between the middle and lower trunk of the brachial plexus. A single puncture was used for both injections.

The end of the second injection was considered time 0 for evaluating the effectiveness of the block. A blinded assistant, who was not present during the injection and who was unaware of the volume of anaesthetic used, was asked to assess the nerve blocks. The block was tested using motor, thermal, and pain assessments every 10 min for up to 30 min after the procedure. Upon an effective block, the subsequent patient received a reduction of 1 ml in the total volume of the anaesthetic. Upon failure of the block, the volume of LA was increased by 1 ml for the next patient, and the MEV90 for postoperative analgesia was estimated for 4 and 6 h after the block or when requested by the patient. The MEV90 for postoperative analgesia was estimated for complete absence of pain and no use of analgesics for 6 h.

After 30 min of evaluation, general anaesthesia was induced with 2–2.5 mg kg$^{-1}$ propofol, 2.5 $\mu$g kg$^{-1}$ fentanyl, and 0.5 mg kg$^{-1}$ atracurium. The airway was maintained by tracheal intubation, and ventilation was provided with 40% oxygen and 60% nitrous oxide. General anaesthesia was maintained with 0.5–1% isoflurane. The patients who exhibited an increase in intraoperative heart rate or arterial pressure above 25% of the pre-induction baseline values received 25 $\mu$g of i.v. fentanyl. At the end of surgery, all

The modified Bromage scale$^{4}$ was used to evaluate motor function (Table 1). The evaluated muscles included the deltoid, biceps, triceps, finger flexors (median nerve), finger extensors (radial nerve), and finger abductors (ulnar nerve).

<table>
<thead>
<tr>
<th>Degree</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>Full strength in relevant muscle groups</td>
</tr>
<tr>
<td>3</td>
<td>Strength reduction, but able to move against resistance</td>
</tr>
<tr>
<td>2</td>
<td>Ability to move against gravity, but not against resistance</td>
</tr>
<tr>
<td>1</td>
<td>Discrete movements (trembling) of muscle groups</td>
</tr>
<tr>
<td>0</td>
<td>Absence of movements</td>
</tr>
</tbody>
</table>

The assessment of thermal sensation in the upper limb was performed using gauze and alcohol. Pain sensation was assessed by a pinprick test using a 23 G needle. The thermal and pain sensitivities of dermatomes C4 to T1 were examined. The block was considered positive when there was absence of thermal distinction and absence of pain.

Phrenic nerve block was assessed via US using real-time movement of the diaphragm ipsilateral to the ISBPB at four distinct time points: immediately before the block and at 30 min, 4, and 6 h after the block. The block was positioned at the midpoint of the hemiclavicular and midaxillary lines, at the level of the hemidiaphragm on the ipsilateral side of the block. The US was performed using a curvilinear 2–5 MHz probe (MicroMaxx$^{TM}$) with the patient in the dorsal decubitus position while inhaling deeply. The excursion of the caudal diaphragm was designated positive, and paradoxical cephalic motion (negative) was considered paralysed.

Postoperative analgesia was assessed in the recovery room using a numeric pain rating scale (0 indicating no pain, 10 indicating the worst pain ever experienced) and the amount of analgesic used at two distinct times (4 and 6 h after the block) or when requested by the patient. The MEV90 for postoperative analgesia was estimated for complete absence of pain and no use of analgesics for 6 h.
of the patients had the neuromuscular block reversed by 0.01 mg kg\(^{-1}\) of atropine and 0.03 mg kg\(^{-1}\) of neostigmine.

After the surgical procedure, the patients were admitted to the recovery room, where they were monitored until they met the conditions for discharge into an outpatient regimen.

For the sample size calculation, the risk levels of \(\alpha\)≤0.05 and \(\beta\)≤0.20 were considered for a power/efficiency of 90%. Success was considered for regression coefficient \(R^2\) >0.9, while failure was considered for \(R^2\)<0.8. \(R^2\) values close to 1 indicate that the LA volume used in the block adheres to the up/down method, demonstrating its appropriateness. The necessary sample size was thus calculated as 25 patients.

The means and standard deviations were used to analyse parametric data, whereas medians and quartiles were used to analyse non-parametric data. The continuous variables were analysed using the unpaired Student’s t-test. The \(\chi^2\) test was used for the statistical comparison of pre- and post-block diaphragmatic movement.

The effective volume of 0.5% bupivacaine was estimated using the step-up/step-down sequence according to the formulae proposed by Dixon, focusing on the analysis of the minimum anaesthetic volume with a 50% probability of effective nerve block. The sequences were also examined using probit regression to calculate the effective volume for 90% of the cases. The volume–response curves resulting from these calculations were compared at the points corresponding to EV\(_{50}\) (50% of effective volume). The critical values for \(\alpha\) were set at 0.05.

The calculations were conducted in electronic spreadsheets using Microsoft Excel for Windows (Microsoft Corp., Redmond, WA, USA), IBM SPSS Statistics 20.0 for Mac (SPSS Inc., Chicago, IL, USA), and GraphPad Prism 4.0 for Windows (GraphPad Software Inc., San Diego, CA, USA).

Figure 1 illustrates the flowchart for the study design.

**Results**

The 29 patients who met the inclusion criteria were assessed. Among these patients, four were excluded: two due to protocol violations (errors in the LA volume sequence), one due to an ipsilateral motor deficit, and one due to contralateral sensory alterations. These differences could have potentially distorted the motor, thermal, and sensory evaluations, given that these assessments were made in a comparative manner. Among the 25 patients, we experienced difficulty with only one in performing the block (9 ml LA). This failure was associated with a technical difficulty and not with the LA volume; proper visualization of the plexus was not possible for this patient. None of the patients received sedation before the block, allowing for adequate assessment responses. A total of 25 patients completed the study and were analysed. The study ended when five successes and four consecutive failures of the block were achieved and when a sufficient \(R^2\) was reached to calculate the minimum effective volume \(R^2\geq0.90\). The patients’ characteristics are presented in Table 2.

The sequence of the positive and negative blocks in the evaluated patients is presented in Figure 2. The MEV\(_{90}\) of 0.5% bupivacaine with epinephrine for US-guided brachial plexus block was 0.95 ml \(R^2\): 0.97, 95% confidence interval \(\text{CI}\): 0.6–1.22 ml). No difference in intraoperative fentanyl consumption was noted between the patients receiving the MEV\(_{90}\) and those receiving the highest volume \(P=0.84\).

When evaluating the block of the individual trunks of the brachial plexus (Table 3), the MEV\(_{90}\) for (i) the upper trunk was 1.34 ml \(R^2\): 0.97, 95% CI: 0.66–1.35 ml), (ii) the middle trunk was 1.64 ml \(R^2\): 0.92, 95% CI: 0.76–2.3 ml), and (iii) the lower trunk was 2 ml \(R^2\): 0.95, 95% CI: 0.98–2 ml). The difference in volume was noted between the MEV\(_{90}\) of the three trunks (analysis of variance, \(P<0.0001\)) or for the upper vs middle, upper vs lower, or middle vs lower trunks (Student–Newman–Keuls post hoc test, \(P<0.0001\)).

When considering a 1 ml volume for performing the block, the time to the initiation of the block and the percentage of patients who exhibited block of each muscle group and dermatome (thermal and sensory) were estimated using a receiver operating characteristic curve. An earlier block was noted in the proximal regions than for distal regions. A low percentage of successes (20–35%) was noted for the block of the distal muscles (flexors, extensors, and abductors of the fingers) when compared with proximal muscles (deltoid, biceps, triceps) (90–95%).

The estimated maximum volume for the non-occurrence of diaphragmatic paralysis in 95% of patients was 4.29 ml \(R^2\): 0.84, 95% CI: 3.56–4.98 ml).

Effective postoperative analgesia, with complete absence of pain and no use of analgesics for 6 h, was possible when a minimum volume of 2.34 ml of 0.5% bupivacaine with epinephrine was used \(R^2\): 0.87, 95% CI: 0.48–11.47 ml). No difference in intraoperative fentanyl consumption was noted when using this volume in comparison with patients blocked with smaller or larger volumes \(P=0.3\).

No intraneuronal injections were given. There were no adverse events associated with the blocks.

**Discussion**

We have demonstrated an MEV\(_{90}\) of 0.95 ml \(R^2\): 0.97, 95% CI: 0.6–1.22 ml) of 0.5% bupivacaine with epinephrine for US-guided brachial plexus block.

US allows for easy visualization of the nerve, the needle, and the dispersion of the anaesthetic, facilitating adequate injection in the perineural region. US-guided blocks have been associated with high success rates, reduced latencies, and reduced LA doses. Under the conditions of the present study, the US-guided technique significantly reduced the volume of 0.5% bupivacaine with epinephrine necessary for upper-limb block.

A recent study by McNaught and colleagues determined the MEV\(_{50}\) for 0.5% ropivacaine using either a US-guided interscalene block or a nerve stimulator technique, reporting volumes of 0.9 (95% CI: 0.3–2.8) and 5.4 (95% CI: 3.4–8.6) ml, respectively. However, their results could have underestimated the
required volume, given that the patients received a subcutaneous infiltration with 10 ml of a mixture of 1% lidocaine and epinephrine and 0.25% bupivacaine at the site of incision before the surgery. Another potential confounder in this previous study was the lack of an objective evaluation. A score of 0 in the numerical pain scale (positive block) 30 min after admission to the recovery room was considered a determining factor for the change in the dose in the step-up/step-down model, and the residual analgesic effect could have been strongly influenced by the opioid used for general anaesthesia. In the present study, we confirmed the low LA volume required for a brachial plexus block (0.95 ml) using objective criteria: motor, thermal, and sensory block. However, when analysing the trunks individually, with stricter criteria for positivity (complete motor, thermal, and sensory block in all of the regions innervated by each trunk), it was possible to note the requirement for larger volumes, with a volume of 1.35 ml required for the upper trunk, 1.64 ml required for the middle trunk, and 2 ml required for the lower trunk. There were statistically significant differences between these values.

Shoulder surgery is one of the most painful surgical procedures, especially when performed in a day hospital regimen.14 The ISBPB procedure provides these patients...
with adequate analgesia.\textsuperscript{15} In the present study, an MEV\textsubscript{90} of 2.34 ml was associated with a complete absence of pain for 6 h after the block. A complete absence of pain was defined as 0 on the numerical pain scale and no use of analgesics in the postoperative period. None of the patients received i.v. analgesics at the end of the surgery. This fact may indicate that the volume of LA was overestimated, given that analgesics are routinely given to patients before extubation in daily clinical practice.

Recent studies\textsuperscript{11, 6} using US-guided nerve block techniques have demonstrated that a reduction in LA volume preserves respiratory function. Altintas and colleagues\textsuperscript{17} detected significant reductions in forced vital capacity, end-expiratory volume (EEV\textsubscript{1}), and peak expiratory flow in patients subjected to interscalene block with bupivacaine when compared with those anesthetized using ropivacaine. Riazi and colleagues\textsuperscript{1} compared two LA volumes, 20 and 5 ml, in US-guided ISBPB and identified significant reductions in the incidence of diaphragmatic paralysis. Under the conditions of the present study, the highest volume not associated with diaphragmatic block in 95% of cases was calculated as 4.29 ml ($R^2$: 0.84, 95% CI: 3.56–4.98 ml), suggesting the need for smaller volumes than those that are currently indicated for ISBPB.

We acknowledge that the present study has certain limitations. A single anaesthetist performed all of the blocks. Although this eliminates the possibility of operator variability in performing the technique, it may be an important limiting factor with respect to generalizing the results. The use of a single anaesthetist may also reflect that a high technical proficiency is necessary to achieve successful blocks with extremely reduced volumes. Another important point to consider is that all of the blocks were accompanied by general anaesthesia, limiting the use of low volumes for shoulder surgery with regional anaesthesia only. However, under the conditions of the present study, it was possible to obtain the MEV\textsubscript{90}, that is, the minimum effective volume for ISBPB effective in 90% of patients, confirming a high similarity with the MEV\textsubscript{50} reported by McNaught and colleagues.\textsuperscript{3}

Future studies are required to determine the duration of the block using extremely low volumes in US-guided techniques and the effects of different concentrations on the duration and quality of the block.

In summary, the MEV\textsubscript{90} of 0.5% bupivacaine with epinephrine for US-guided ISBPB was 0.95 ml. The ideal volume for an efficient block with adequate postoperative analgesia and reduced incidence of diaphragmatic paralysis is between 2.34 and 4.29 ml.

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**Table 2** Patient characteristic data (n=25)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Median (P25–P75)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>54 (50.5–58.5)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>75 (69.5–82)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>160 (156–171)</td>
</tr>
<tr>
<td>BMI (kg cm\textsuperscript{-2})</td>
<td>28.1 (24.9–29.9)</td>
</tr>
<tr>
<td>Duration of surgery (min)</td>
<td>102 (73.7–131.2)</td>
</tr>
<tr>
<td>Gender (male/female)</td>
<td>10/15</td>
</tr>
<tr>
<td>Physical condition (ASA)</td>
<td>I 8, II 17</td>
</tr>
<tr>
<td>Surgical procedure</td>
<td>Rotator cuff injury/arthroscopy 14, Rotator cuff injury/open repair 9, Bankart/arthroscopy 1, Humerus fracture 1</td>
</tr>
</tbody>
</table>

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**Table 3** The minimum effective volume of 0.5% bupivacaine with epinephrine for brachial plexus block (overall assessment and according to the upper, middle, and lower trunks)

<table>
<thead>
<tr>
<th>Location</th>
<th>MEV\textsubscript{90} (ml)</th>
<th>$R^2$</th>
<th>95% CI (ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brachial plexus block (overall)</td>
<td>0.95</td>
<td>0.97</td>
<td>0.6–1.22</td>
</tr>
<tr>
<td>Upper trunk</td>
<td>1.35</td>
<td>0.97</td>
<td>0.66–1.35</td>
</tr>
<tr>
<td>Middle trunk</td>
<td>1.64</td>
<td>0.92</td>
<td>0.76–2.3</td>
</tr>
<tr>
<td>Lower trunk</td>
<td>2</td>
<td>0.95</td>
<td>0.98–2</td>
</tr>
</tbody>
</table>

**Fig 2** The step-up/step-down sequence of patients subjected to US-guided ISPB with 0.5% bupivacaine with epinephrine.
Declaration of interest
None declared.

References
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