Minimum Effective Volume of Lidocaine for Ultrasound-Guided Infraclavicular Block

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Background: The aim of this study was to determine the minimum effective volume of lidocaine 1.5% with epinephrine 5 μg/mL in 90% of patients (MEV_{90}) for single-injection ultrasound-guided infraclavicular block (ICB).

Methods: Using an in-plane technique, a single-injection ultrasound-guided ICB was performed: a 17-gauge, 8-cm Tuohy needle was advanced until the tip was located dorsal to the axillary artery. Volume assignment was carried out using a biased coin design up-and-down sequential method, where the volume of local anesthetic administered to each patient depended on the response of the previous one. In case of failure, the next subject received a higher volume (defined as the previous volume with an increment of 2.5 mL). If the previous patient had a successful block, the next subject was randomized to a lower volume (defined as the previous volume with a decrement of 2.5 mL), with a probability of \( b = 0.11 \), or the same volume, with a probability of 1 − \( b = 0.89 \). Lidocaine 1.5% with epinephrine 5 μg/mL was used in all subjects. Success was defined, at 30 mins, as a minimal score of 14 of 16 points using a composite scale encompassing sensory and motor block. Patients undergoing surgery of the elbow, forearm, wrist, or hand were prospectively enrolled until 45 successful blocks were obtained.

Results: Fifty-five patients were included in the study. Using isotonic regression and bootstrap confidence interval (CI), the MEV_{90} for single-injection ultrasound-guided ICB was estimated to be 35 mL (95% CI, 30–37.5 mL). The probability of a successful response at 35 mL was estimated to be 0.91 (95% CI, 0.8–1.0). All patients with a minimal composite score of 14 points at 30 mins achieved surgical anesthesia intraoperatively.

Conclusions: For single-injection ultrasound-guided ICB, the MEV_{90} of lidocaine 1.5% with epinephrine 5 μg/mL is 35 mL. Further dose-finding studies are required for other concentrations of lidocaine, other local anesthetic agents as well as techniques involving multiple injections, a more medial approach to ICB, or precise location of all 3 cords of the brachial plexus.

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Ultrasoundography (US) is being increasingly used for brachial plexus block because of allows operators to visualize the needle, nerve, and spread of local anesthetic agents (LA). For upper-limb surgery at or below the elbow joint, US-guided infraclavicular block (ICB) represents an attractive option: despite a similar success rate, it results in shorter performance time and fewer adverse effects than its axillary and supraclavicular counterparts, respectively. Ultrasound-guided ICB is commonly achieved with a single injection of LA dorsal to the axillary artery. The single-injection method has been shown to provide a similar efficacy to the double- and triple-injection techniques. Although success has been reported with volumes as low as 20 mL, the minimum effective volume (MEV) for US-guided ICB remains unknown. Determination of MEV is important to prevent the unnecessary administration of potentially toxic doses. Furthermore, when multiple blocks are performed in the same patient, knowledge of MEV ensures success without sacrificing safety.

Thus, using lidocaine 1.5% with epinephrine 5 μg/mL, the aim of this study was to determine the MEV in 90% of patients (MEV_{90}) for single-injection US-guided ICB.

MATERIALS AND METHODS

After obtaining ethics committee approval (McGill University Health Center, Montreal, Quebec, Canada) and written informed consent, patients undergoing surgery of the elbow, forearm, wrist, or hand were prospectively enrolled. Inclusion criteria were age between 18 and 70 years, American Society of Anesthesiologists status I to III, and body mass index between 20 and 35 kg/m². Exclusion criteria were inability to consent to the study, preexisting neuropathy, coagulopathy, chronic obstructive pulmonary disease, hepatic or renal failure, allergy to LA, pregnancy, and prior surgery in the infraclavicular region.

After arrival in the induction room, an 18- or 20-gauge intravenous catheter was placed in the upper limb contralateral to the surgical site, and standard intravenous premedication (0.03 mg/kg of midazolam and 0.6 μg/kg of fentanyl) was administered to all patients. Supplemental oxygen (nasal cannulas at 4 L/min) and pulse oximetry were applied throughout the procedure. All patients received a single-injection US-guided ICB. Confirmatory neurostimulation was not used. All blocks, performed by residents, fellows, and staff anesthesiologists, were supervised by the first author (D.Q.H.T.). Independently of their status, operators were considered experts if, prior to the start of the study, they possessed an experience level equal or superior to 60 US-guided ICB. Otherwise, they were considered trainees. The nerve block kits (Arrow StimuCath Continuous Nerve Block Set; Arrow International, Reading, Pa), portable ultrasound machine (SonoSite M-Turbo; SonoSite Inc, Bothell, Wash), and 6- to 13-MHz linear probes were the same for all patients.

The US probe was applied in a sterile fashion in the infraclavicular fossa, immediately medial to the coracoid process, to obtain a short-axis view of the axillary artery. A skin wheal was raised with 3 mL of lidocaine 1%. Using an in-plane technique, a 17-gauge, 8-cm Tuohy needle was advanced until the tip was located dorsal to the artery. Were the latter to be a clock, this would correspond to the 6-o-clock position. Although hydrodissection was not used to locate the 3 cords of the brachial plexus, a small volume of saline (<1 mL) was initially injected...
to ensure that the needle tip was correctly positioned, and a “double-bubble” sign achieved. Subsequently, the predetermined volume of lidocaine 1.5% with epinephrine 5 µg/mL was incrementally injected. Blinding of patient and primary operator to volume was ensured by having an assistant perform the injection. After the bolus of LA, a 19-gauge styletted catheter was advanced under direct vision 3 to 4 cm past the needle tip. The purpose of the catheter was to allow LA reinfusion or infusion for postoperative pain control. A video clip of US-guided ICB can be found on the authors’ free-access, educational Web site, www.regionalworks.ca.

During the performance of the block, the imaging time (defined as the time interval between contact of the US probe with the patient and the acquisition of a satisfactory picture) and the needling time (defined as the time interval between the start of the skin wheal and the end of LA injection through the Tuohy needle) were recorded. Thus, performance time was defined as the sum of imaging and needling times. The number of needle passes was also recorded. The initial needle insertion counted as the first pass. Any subsequent needle advancement that was preceded by a retraction of at least 10 mm counted as an additional pass. Furthermore, the incidence of vascular puncture and paresthesia (sensation of electrical shock) was also noted.

Subsequently, measurements of brachial plexus blockade were carried out every 5 mins until 30 mins by a single, blinded observer. Sensory blockade of the musculocutaneous, median, radial, and ulnar nerves was graded according to a 3-point scale using a cold test: 0 = no block, 1 = analgesia (patient can feel touch, not cold), and 2 = anesthesia (patient cannot feel touch). Sensory blockade of the musculocutaneous, median, radial, and ulnar nerves was assessed on the lateral aspect of the forearm, the volar aspect of the thumb, the lateral aspect of the dorsum of the hand, and the volar aspect of the fifth finger, respectively. Motor blockade was also graded with a 3-point scale: 0 = no block, 1 = paresis, and 2 = paralysis. Motor blockade of the musculocutaneous, radial, median, and ulnar nerves was evaluated by elbow flexion (musculocutaneous), thumb abduction (radial), thumb opposition (median), and thumb adduction (ulnar). Overall, the maximal composite score was 16 points.

We considered the block a success if a minimal composite score of 14 points was achieved, provided the sensory block score was equal or superior to 7 of 8 points. This scale has been shown to provide a reliable estimate of the rate of surgical anesthesia. Thus, onset time was defined as the time required to obtain 14 points. Therefore, the anesthesia-related time was equal to the sum of the performance and onset times. For all subjects in whom a minimal composite score of 14 points was achieved at 30 mins, we also verified that surgical anesthesia was indeed present. The latter, recorded by the same blinded observer, was defined as the ability to proceed with surgery without the need for intravenous narcotics, general anesthesia, rescue blocks, or local infiltration by the surgeon. However, for anxiolysis, subjects could receive a propofol infusion (25–75 µg/kg per min), provided that response to verbal stimulus was maintained. However, if, after 30 mins, the composite score was inferior to 14 points, the ICB was considered a failure, and the patient received supplemental nerve blocks.

The blinded observer also recorded the patient’s anthropometric data as well as the level of procedural pain immediately after the block placement using a 10-cm visual analog scale (0 cm = no pain; 10 cm = worst, imaginable pain). The incidence of dyspnea and symptoms suggestive of LA toxicity was also noted.

Postoperatively, pain control was managed by reinjecting or infusing the perineural catheter. This was left to the discretion of the treating anesthesiologist and was not recorded for the purpose of the study. Furthermore, 1 week after the surgery, all patients were contacted by the blinded investigator to inquire about complications such as persistent paresthesias (numbness) or motor deficits (weakness) in the surgical limb.

### Statistical Analysis

In this study, the primary objective was to estimate MEV$_{90}$ for single-injection US-guided ICB. Volume assignment was carried out using a biased coin design (BCD) up-and-down sequential method (UDM), where the volume administered to each subject depended on the response of the previous one. The first subject recruited received 25 mL. Because data were absent for ICB, this initial volume was derived from a study showing that the MEV in 50% of patients (MEV$_{50}$) for US-guided supraclavicular block is 23 mL. Subsequently, volume assignment was based on the response of the previous patient. In case of failure, the next subject received a higher volume (defined as the previous volume with an increment of 2.5 mL). If the previous patient had a successful block, the next subject was randomized to a lower volume (defined as the previous volume with a decrement of 2.5 mL), with a probability of $b = 0.11$, or the same volume, with a probability of $1 - b = 0.89$. We also decided a priori not to exceed a maximal volume of 40 mL to avoid LA toxicity. In other words, if the previous patient did not respond but had been administered the maximal volume (40 mL), the next subject would also receive 40 mL.

To estimate the minimum sample size required for stabilization of the MEV$_{90}$ calculation, we used simulations (assuming a fixed-sample BCD and a fixed minimal number of positive

### Table 1. Patient Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD), y</td>
<td>39.1 (16.8)</td>
</tr>
<tr>
<td>Sex (male/female), n</td>
<td>38/17</td>
</tr>
<tr>
<td>BMI, mean (SD), kg/m²</td>
<td>25.9 (3.3)</td>
</tr>
<tr>
<td>ASA physical status (I/II/III), n</td>
<td>43/7/5</td>
</tr>
<tr>
<td>Types of surgery (hand/wrist/forearm/elbow), n</td>
<td>32/11/6/6</td>
</tr>
</tbody>
</table>

Continuous variables are presented as mean (SD); categorical variables are presented as counts.

ASA indicates American Society of Anesthesiologists.

### Table 2. Block Performance Data

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Imaging time, sec</td>
<td>35.8 (25.3)</td>
</tr>
<tr>
<td>Needling time, min</td>
<td>3.9 (2.0)</td>
</tr>
<tr>
<td>Performance time, min, SD, min</td>
<td>4.5 (2.2)</td>
</tr>
<tr>
<td>Onset time, mean, SD, min</td>
<td>21.3 (5.5)</td>
</tr>
<tr>
<td>Total anesthesia-related time, min</td>
<td>25.4 (5.7)</td>
</tr>
<tr>
<td>Operator’s experience level (trainee/expert), n</td>
<td>46/9</td>
</tr>
<tr>
<td>No. passes, mean, SD</td>
<td>1.7 (1.2)</td>
</tr>
<tr>
<td>Block-related pain (scale 0–10), mean, SD</td>
<td>2.0 (2.1)</td>
</tr>
<tr>
<td>Paresthesia, n (%)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Vascular puncture, n (%)</td>
<td>1 (1.8)</td>
</tr>
</tbody>
</table>

Continuous variables are presented as means (SD); categorical variables are presented as count or percentage. Imaging, needling, performance, and total anesthesia-related times are calculated only for patients with a minimal composite score of 14 points at 30 mins.
responses, i.e., successful blocks) for different scenarios of dose distribution, sample size, and number of positive responses. The different scenarios and starting rules were performed according to Durham et al.\(^1\) The first simulation design showed stabilization of the estimated parameters after a minimum of 40 subjects. This result was supported by Pace and Stylianou\(^4\) as well as George et al.\(^5\) A second simulation design was performed using the additional assumption that the probability of receiving a lower volume after a successful (previous) response is exactly equal to the theoretical one (\(b = 0.11\)). For this, it was necessary to keep the minimal number of successful responses fixed to a multiple of 9. Again, stabilization of estimated parameters occurred after 40 subjects; however, the standard errors of the estimated parameters were smaller for this second simulation design. A fixed minimal number of 45 positive responses (the smallest multiple of 9 that is \(>40\)) was then chosen for our dose-finding study. Thus, we continuously recruited subjects until 45 successful blocks were obtained and 45 envelopes (containing the random volume assignments for successful blocks) were opened. The final sample size was not known a priori but was estimated from the simulations to be 52 (SD, 2). The MEV\(_{90}\) was calculated using isotonic regression with a 95% confidence interval (CI) derived by bootstrapping. We used the dose estimator \(\hat{\mu}_2\), which is defined as the dose with an estimated probability of success closest to 90%, because it is less variable than the classic isotonic estimator \(\mu_1\) and because, in contrast to the estimator \(\mu_3\), its value, as well as those of the CI, is always equal to a dose used in the study.\(^1\)

Statistical analysis was performed using the R statistical software package (R Foundation for Statistical Computing, Vienna, Austria; ISBN 3-900051-07-0, URL http://www.R-project.org.).

RESULTS

Fifty-five patients were recruited to obtain 45 successful blocks (Table 1). Block performance data are presented in Table 2. The BCD up-and-down sequence is presented in Figure 1.

Using lidocaine 1.5% with epinephrine 5 \(\mu\)g/mL, the MEV\(_{90}\) for single-injection US-guided ICB was estimated with isotonic regression to be 35 mL (95% CI, 30–37.5 mL). The probability of a successful response at 35 mL was 0.91 (95% CI, 0.8–1.0). All patients with a minimal composite score of 14 points at 30 mins achieved surgical anesthesia intraoperatively.

There were minimal adverse events associated with the performance of the block (Table 2). One case of vascular puncture occurred. No patient reported dyspnea or symptoms suggestive of LA toxicity. Patient follow-up 1 week after the surgery revealed no instances of postoperative neurological deficits.

DISCUSSION

Single-injection US-guided ICB provides a reliable method to anesthetize the brachial plexus. In our study, despite the high prevalence of trainee operators (83.6%), the quick performance time (4.5 mins), small number of needle passes (1.7), mild procedural pain (2.0), and low rate of adverse events echo previously published results.\(^1\) Furthermore, the onset (21.3 mins) and total anesthesia-related (25.4 mins) times are also in keeping with the latter.\(^2\) Using the BCD method, we found that the MEV\(_{90}\) of lidocaine 1.5% with epinephrine 5 \(\mu\)g/mL for single-injection US-guided ICB is 35 mL.

Biased coin design is a relatively new method to approximate MEV for US-guided peripheral nerve blocks. To date, published dose-finding studies have focused exclusively on MEV\(_{50}\) and relied on the Dixon and Massey UDM.\(^3\) With the latter, if the previous subject achieved success, the next one received a lower volume. In case of failure, the next subject received a higher volume.\(^4\) Thus, UDM represents a simplified variant of BCD, which uses \(b = 0.5\) and \(1 - b = 0.5\) probabilities.\(^4\)

Historically, UDM has been used to investigate the concentration of inhalational anesthetic agent required to prevent movement on surgical incision in 50% of patients (ED\(_{50}\)), also known as minimal alveolar concentration.\(^5\) Because the concentration-response relation for inhaled anesthetics is steep, ED\(_{50}\) can be approximated with ED\(_{50}\). Furthermore, the sample sizes required by UDM are usually small.\(^5\) These 2 factors have contributed to its great popularity. Unfortunately, the concentration (or volume)-response curve may not be as steep for other anesthetic drugs (such as LA); thus, ED\(_{50}\) (or MEV\(_{50}\)) may not be as clinically relevant. As a remedy, maximum likelihood logistic or probit regression is commonly used to compute ED\(_{50}\) or MEV\(_{50}\) and to extrapolate to higher quantiles, such as ED\(_{95}\) or MEV\(_{95}\).\(^6\) However, the use of maximum likelihood logistic or probit regression in up-and-down designs, as well as extrapolation to higher quantiles, has been criticized by many.\(^4,5,\) In contrast, BCD allows the direct investigation of ED or MEV at any quantile.\(^1\) In a recent study, George et al.\(^1\) successfully used BCD to determine the ED\(_{50}\) of phenylephrine for the treatment of hypotension in patients undergoing cesarean section with spinal anesthesia. Thus, in this study, we also opted for BCD to determine the MEV\(_{90}\) of lidocaine for US-guided ICB. Furthermore, our estimation of the MEV\(_{90}\) was carried out using isotonic regression with 95% CI derived by bootstrapping, as recommended by Pace and Stylianou.\(^4\)

The relatively large MEV\(_{90}\) (35 mL) deserves mention. By enabling anesthesiologists to visualize LA spread and to reposition the needle tip in real time, US is purported to decrease the amount of LA required. Compared with neurostimulation, Casati et al.\(^7\) and Danelli et al.\(^8\) have reported 42% and 37% reductions in MEV\(_{50}\) for the femoral and (subgluteal) sciatic nerve, respectively, with US. Furthermore, dose-finding studies for the midfemoral sciatic nerve and axillary brachial plexus have concluded that volumes as low as 5.7 and 1.0 mL can reliably anesthetize the sciatic nerve\(^1\) and terminal branches of the brachial plexus.\(^1\) In stark contrast, Fredrickson et al.\(^9\) and Duggan et al.\(^10\) have calculated the MEV\(_{95}\) of the interscalene and supraclavicular brachial plexus block to be 20.5 and 42 mL, respectively. Their results seem more in keeping with our own findings. However, because of differences in study subjects (patient vs volunteer), body mass indices, nerve blocks,
techniques (in-plane vs out-of-plane; bolus through needle vs catheter), LA, concentrations, definitions of success, and statistical methods, caution must be exercised when comparing these studies. Nonetheless, a paradox seems to exist as US reduces LA requirement for some blocks but not for others. We speculate that this dichotomy can be explained by the choice of technique. For instance, in all reports where the neural structure was visually identified and LA incrementally injected to surround the latter, a sparing effect or low volumes of LA were noted.\(^{17-21}\) However, in studies that used a single-injection technique (such as ours), a larger volume was invariably required.\(^{13,22}\) Thus, we emphasize that the MEV\(_{90}\) reported in this trial applies only to single-injection US-guided ICB.

In light of the small sample size (n = 55), one limitation of our protocol pertains to the variability in operator. Our study was open to trainees as well as staff anesthesiologists. However, all blocks were supervised by the first author (D.Q.H.T.), and the end point (6-o’clock position of the axillary artery) was always the same. Thus, the final position of the needle tip was identical in all patients. Therefore, only the performance time, number of passes needed, and procedural pain (all secondary variables) changed according to the level of experience of the operator. These should have a minimal impact on the primary outcome (MEV\(_{90}\)).

Another limitation relates to the definition of success. We used a 14-point composite score as a surrogate marker for surgical anesthesia. This decision was based on our 3 previous randomized trials on US-guided supraclavicular, infraclavicular, and axillary blocks.\(^{2,5,11}\) In a combined total of 300 patients, the proportion of subjects achieving a minimal score of 14 points at 30 mins (87.0%–95.4%) provided a reliable estimate of the incidence of surgical anesthesia (93.1%–97.5%).\(^{2,5,11}\) In fact, review of patient files showed that, of 272 subjects who reached 14 points at 30 mins, only 2 (0.7%) failed to achieve surgical anesthesia. However, because the 14-point success rates were always slightly inferior to the rates of surgical anesthesia, we cannot exclude the possibility that subjects in this trial who did not attain a score of 14 points could have achieved surgical anesthesia nonetheless. To circumvent this problem, we would have needed to measure the true incidence of surgical anesthesia regardless of the composite score. We decided a priori against this course of action because it could have exposed patients with low scores (with little chance of surgical anesthesia) to pain at the beginning of surgery. This was deemed unethical in the context of a dose-finding study. Instead, we purposefully allowed treating anesthesiologists to provide supplemental blocks for patients whose scores were inferior to 14 points. Thus, although not perfect, we consider that the estimation of surgical anesthesia was reliable and reproducible. In fact, because the latter tends to slightly underestimate the true incidence of surgical anesthesia, the MEV\(_{90}\) reported in this study may in fact overestimate the MEV\(_{90}\) needed for surgical anesthesia.

In summary, the MEV\(_{90}\) of lidocaine 1.5% with epinephrine 5 \(\mu\)g/mL is 35 mL for single-injection US-guided ICB. Further dose-finding studies are required for other concentrations of lidocaine, other LA as well as techniques involving multiple injections, a more medial approach to ICB, or precise location of all 3 cords of the brachial plexus.

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