

## ORIGINAL INVESTIGATION

## Determination of the minimum effective volume of bupivacaine for ultrasound-guided infraclavicular brachial plexus block: a prospective, observer-blind, controlled study



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Received 30 January 2020; accepted 19 December 2021

Available online 29 December 2021

### KEYWORDS

Brachial plexus block;  
Bupivacaine;  
Drug dose-response  
relationship;  
Regional anesthesia

### Abstract

**Background:** We aimed to determine the minimum effective volume (MEV) of 0.5% bupivacaine for infraclavicular brachial plexus block.

**Methods:** We assigned patients to volume groups consisting of five consecutive patients. Local anesthetic was sequentially reduced from a starting dose of 30 mL by 2 mL to form the volume groups. Five patients were included in each volume group, and at least 3 of 5 injections had to be successful to consider the volume of the anesthetic as sufficient. The study ended when the anesthetic volume of a group was determined to be unsuccessful (two or fewer successful blocks). Block was successful if the patient reported a sensorial block score of 7 or more on an 8-point scale and sensorial and motor block's total score of 14 on a 16-point scale.

**Results:** The MEV of 0.5% bupivacaine for infraclavicular brachial plexus block was 14 mL. A successful block was achieved in all patients (n = 45) in 9 volume groups, which received 30 mL down to 14 mL. Three blocks were unsuccessful in the 12-mL group. Time to onset of block and time to first postoperative anesthetic administration was 15 (10–15) min and more than 24 h in the 30-mL bupivacaine group, but 40 (30–45) min and 14 (10–24) h were determined for the 14-mL group, respectively.

**Conclusions:** The MEV of 0.5% bupivacaine for ultrasound-guided infraclavicular brachial plexus block was 14 mL. However, this low-dose block has a long onset time of 40 (30–45) min on average.

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<https://doi.org/10.1016/j.bjane.2021.12.008>

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## Introduction

Several blocks can be performed without ultrasound guidance, but the use of ultrasonography has become standard. Ultrasonography has various advantages, including reduced local anesthetic (LA) requirement, better visualization of patient anatomy, and the possible identification of anatomical variations that would otherwise be overlooked.<sup>1</sup>

A small LA volume is preferred owing to the possibility of systemic anesthetic toxicity with high doses.<sup>2</sup> The incidence of systemic toxicity due to peripheral block is low (0.18–0.2%), but such toxicity is a serious complication that may be fatal.<sup>3–5</sup> Reducing the volume of LA in routine practice can play a crucial role in preventing complications in rare situations, such as the administration of bilateral blocks when the LA volume should be reduced.<sup>4</sup> Thus, the minimum effective volume (MEV) of any anesthetic administered with any approach is important. When the MEV of a procedure is determined, the procedure can be safely performed without excessive anesthetic. To our knowledge, few studies have investigated the MEVs of various LAs administered for infraclavicular blocks with different approaches.<sup>6,7</sup> We aimed to determine the MEV of bupivacaine for ultrasound-guided (USG) infraclavicular brachial plexus block.

## Methods

This study was performed in accordance with the ethical standards of our institution, the national research committee (Ankara Numune Training and Research Hospital Clinical Research Ethical Committee; Reference No. 646, approved November 11, 2015), the 1964 Declaration of Helsinki and its later amendments, and other comparable ethical standards.

The study was registered at ClinicalTrials.gov (No. NCT03838120). Informed consent was obtained from all patients before inclusion in this controlled, patient- and observer-blind, single-center study. We included patients between 18 and 70 years of age with American Society of Anesthesiologists (ASA) physical status I–III who underwent upper limb surgery from November 2015 through November 2016.

We excluded patients who refused to participate; those with ASA physical status IV or V; those with serious cardiac,

respiratory, hepatic, or renal comorbid conditions; those with neuromuscular and/or neurological disease, mental disorders, and coagulopathy; those who were pregnant; and those with an allergy to LA and infection at the injection site. We excluded eight patients (two because of coagulopathy, three because of respiratory disease, and three who refused to participate) during the preoperative evaluation period.

All procedures were performed by the same physician (S. B.). Routine anesthesia monitoring was performed, and each patient was administered 0.03 mg.kg<sup>-1</sup> of midazolam and 1 µg.kg<sup>-1</sup> of fentanyl for sedation. The injection site was prepared according to aseptic and antiseptic guidelines.

We performed the lateral sagittal infraclavicular block technique, as reported by Klaastad.<sup>8</sup> The technique was modified to include ultrasound guidance, which was performed with a 6–12 MHz linear ultrasound probe. The patient was placed in the supine position, with the head turned away from the application side and the shoulder relaxed. The arm on the operative side was slightly abducted; the elbow was flexed 90° and placed on the patient's torso. The anesthesiologist was positioned beside the head of the patient. The ultrasound probe was placed 1 cm inferior to the intersection of the clavicle and the coracoid process on the sagittal axis. The in-plane technique was used, and a 21G, 5-cm needle (Locoplex, Vygon, Ecouen, France) was visualized at all times. To obtain appropriate anesthetic spread, the LA (0.5% [5 mg.mL<sup>-1</sup>] bupivacaine) was applied in a U-shaped pattern from 3 to 11 o'clock around the axillary artery; if this spread could not be achieved, the needle was repositioned as necessary (0.5% bupivacaine, which is the only long-acting LA available in our hospital).

The patients were assigned to the groups in order of admission, and the volume of LA was reduced from a starting dose of 30 mL in the first group. Five patients were included in each volume group, and at least 3 of 5 injections had to be successful to consider the volume of LA as sufficient. If the previous group's anesthesia was successful, the anesthesiologist reduced the dose by 2 mL every five patients. We ended the study when the anesthetic dose of a group of patients was insufficient (two or fewer successful blocks) (Table 1).

**Table 1** Volume groups and outcomes.

Volume group	Volume, mL	Patients, n	Outcome
1	30	5	≥ 3 Patients with successful block
2	28	5	≥ 3 Patients with successful block
3	26	5	≥ 3 Patients with successful block
4	24	5	≥ 3 Patients with successful block
5	22	5	≥ 3 Patients with successful block
6	20	5	≥ 3 Patients with successful block
7	18	5	≥ 3 Patients with successful block
8	16	5	≥ 3 Patients with successful block
9	14	5	≥ 3 Patients with successful block
10	12	5	≤ 2 Patients with successful block (end of study)
1–9	14–30	45 (93.8% of total)	Successful block
10	12	3 (6.3% of total)	Unsuccessful block

X, the first group in which anesthetic dose is insufficient; Y, the first volume of anesthetic dose which is insufficient.

The researcher who determined whether the block was successful (N.A.E.) was blind to the study protocol. We evaluated sensorial and motor blocks to determine block success. To measure sensorial block, we used touch and cold sensation tests to evaluate these sensations in each region innervated by the musculocutaneous, median, radial, and ulnar nerves. Touch sensation was evaluated with the cotton wool test, and cold sensation was evaluated with ice packs. Each region was compared with the corresponding contralateral region. A score of 0 indicated no block; 1, some analgesia achieved (touch sensation present, but temperature sensation absent); and 2, complete sensorial block in that specific region.

Motor block was graded on a 3-point scale: 0, no block; 1, partial motor block; and 2, complete motor block. To evaluate motor block, we evaluated motor responses in the muscles innervated by the musculocutaneous, median, radial, and ulnar nerves. Lack of movement indicated complete block, slight movements indicated partial motor block (i.e., initiation of motor block), and normal movements indicated an absence of motor block.

Evaluations were performed every 5 minutes during the first 60 minutes after injection. The maximum total score of sensorial and motor block was 16. Anesthesia and block were considered unsuccessful if the score was less than 14. Furthermore, a sensorial block score of at least 7 on an 8-point scale was required for a successful block.

If the block was unsuccessful during the first 60 minutes after the procedure, we administered laryngeal mask airway anesthesia.

We defined initiation of motor and sensorial block as the time at which the score on the Bromage scale changed from 0 to 1, and we defined time of regression as the time at which this score decreased to less than 1. Postoperative pain was evaluated with a visual analogue scale (VAS) at 2, 4, 8, 12, 16, and 24 hours. VAS was assessed with a 10-cm ruler, with numbers ranging from 0 to 10. Additional analgesic was administered when the VAS score increased to greater than 4.

Statistical analysis was performed with IBM SPSS 21.0 (IBM Corp., Armonk, NY) and MedCalc 15.11.4 (MedCalc Software bv, Ostend, Belgium; <https://www.medcalc.org>). Descriptive statistical methods (frequency, percentage, mean, standard deviation, median, min–max) were used to evaluate study data. Normality was evaluated with the Shapiro-Wilk test, skewness-kurtosis, and graphical methods (histogram, Q-Q Plot, Stem and Leaf, Boxplot). In the study, categorical variables were presented as n/%, normally distributed quantitative data as mean  $\pm$  SD, and non-normally distributed data as median (min–max). The Kruskal-Wallis test was used to compare volume groups. In cases where there was a difference, the (post-hoc) Tukey HSD test was used to find out which volume(s) caused the difference. The relationship between local anesthetic volume and the different times evaluated as outcomes (onset of successful block, regression of sensory and motor block, and first operative analgesic rescue) were evaluated by the Spearman correlation test. This test yields values ( $\rho$ ) between -1.00 (perfect negative correlation or inverse relationship) and +1.00 (perfect positive correlation or direct relationship) with a value of 0.00 representing the absence of correlation. In this study,  $p \leq 0.05$  was considered significant.

## Results

The mean age of our patient group was  $37.3 \pm 13.7$  years, 66.7% were men, the mean weight was  $73.4 \pm 11.8$  kg, the mean height was  $171.3 \pm 10.8$  cm, the mean body mass index was  $25.0 \pm 3.3$ , and 83.3% had ASA II physical status. Block was successful in 93.8% of patients (Tables 1 and 2).

The overall median time to onset of successful block was 20 (10–45) min, the median sensorial block regression time was 18 (10–24+) h, the median motor block regression time was 18 (8–24+) h, and the median time of first postoperative analgesic administration was 24 (10–24+) h. Consistently reducing the LA volume from 30 to 14 mL increased the time to onset of successful block from 15 to 40 minutes and shortened the time required for sensory and motor block regression from more than 24 hours to 12 hours. Patients in groups that received decreased LA required additional analgesia at an earlier time (Table 3).

Volume was negatively associated with time to onset of successful block ( $r = -0.89$ ) but positively associated with sensorial and motor block regression times ( $r = 0.80$  and  $r = 0.77$ , respectively), and positively associated with time to first postoperative analgesic administration ( $r = 0.77$ ). These relationships were statistically significant ( $p < 0.05$ ). The MEV of 0.5% bupivacaine for brachial plexus block was 14 mL (Table 4).

## Discussion

The administration of a brachial plexus block with USG techniques has important positive effects, such as a reduced number of needle passes, less pain during the procedure, and higher success and lower complication rates.<sup>7,9</sup>

The incidence rates of complications such as systemic toxicity,<sup>3</sup> phrenic paralysis,<sup>10</sup> and Horner syndrome<sup>11</sup> are low in patients who receive infraclavicular block, but these serious complications may be fatal. Reducing the volume of LA in routine practice can play a crucial role in preventing complications, especially in rare situations such as bilateral block administration<sup>4</sup> and the treatment of patients with comorbid conditions that require a reduced dose (e.g., those with renal failure).

**Table 2** Patient characteristics.

Variable	n (%) or mean $\pm$ SD
Sex <sup>a</sup>	
Female	16 (33.3%)
Male	32 (66.7%)
Age <sup>b</sup>	$37.3 \pm 13.7$
Weight, kg <sup>b</sup>	$73.4 \pm 11.8$
Height, cm <sup>b</sup>	$171.3 \pm 10.8$
BMI <sup>b</sup>	$25.0 \pm 3.3$
ASA <sup>a</sup>	
I	8 (16.7%)
II	40 (83.3%)

ASA, American Society of Anesthesiologists physical status; BMI, body mass index; SD, standard deviation.

<sup>a</sup> n/%.

<sup>b</sup> Mean  $\pm$  SD.

**Table 3** Anesthetic duration according to volume, median (minimum to maximum).

Volume	Time to onset of successful block, min	Time to regression of sensorial block, h	Time to regression of motor block, h	Time to first additional postoperative analgesic, h
12 mL	—	—	—	—
14 mL	40 (30–45) <sup>a</sup>	12 (10–18) <sup>a</sup>	12 (8–18) <sup>a</sup>	14 (10–24) <sup>a</sup>
16 mL	35 (25–40) <sup>a,b</sup>	16 (10–18) <sup>a,b</sup>	14 (10–18) <sup>a,b</sup>	16 (12–24) <sup>a,b</sup>
18 mL	30 (20–35) <sup>b,c</sup>	12 (10–24) <sup>a,b</sup>	12 (10–20) <sup>a,b</sup>	20 (14–24) <sup>a,b,c</sup>
20 mL	25 (20–30) <sup>c,d</sup>	18 (12–24) <sup>a,b</sup>	18 (12–22) <sup>a,b,c</sup>	22 (16–24) <sup>a,b,c,d</sup>
22 mL	25 (20–25) <sup>c,d</sup>	18 (10–24) <sup>a,b</sup>	18 (10–24) <sup>a,b,c</sup>	22 (15–24) <sup>b,c,d</sup>
24 mL	20 (20–25) <sup>d</sup>	18 (12–24) <sup>b,c</sup>	18 (12–24) <sup>b,c</sup>	24 (16–24) <sup>c,d</sup>
26 mL	20 (15–20) <sup>e</sup>	24 (18–24) <sup>c,d</sup>	19 (18–24) <sup>c,d</sup>	24 (18–24) <sup>d,e</sup>
28 mL	15 (15–20) <sup>e</sup>	24+ (24–24) <sup>d</sup>	24 (20–24) <sup>d,e</sup>	24+ (24+–24+) <sup>e</sup>
30 mL	15 (10–15) <sup>e</sup>	24+ (24+–24+) <sup>d</sup>	24+ (24+–24+) <sup>e</sup>	24+ (24+–24+) <sup>e</sup>

The same letters denote the lack of a significant difference between rows.

Bupivacaine is a widely studied, long-acting, high-quality, cheap LA for brachial plexus block. It is commonly administered because of its strong sensorial block properties but has several disadvantages.<sup>12</sup> Studies have reported that at least 25 to 30 mL of bupivacaine is required to achieve anesthesia.<sup>13,14</sup> However, conflicting results have been reported. In a study that decreased the volume of 0.5% bupivacaine to 1 mL for each nerve,<sup>12</sup> 50% of patients had a successful block and the MEV was 9.6 mL.<sup>6</sup>

In our study, the MEV of 0.5% bupivacaine was 14 mL. Few studies have investigated the MEV of bupivacaine.<sup>6,12</sup> Tran et al.<sup>7</sup> reported that 90% of patients administered 1.5% lidocaine had successful brachial plexus block and the MEV was 30 mL. Although lidocaine and bupivacaine are amino-amide anesthetics, bupivacaine is more potent owing to its higher lipid solubility and may be administered in lower concentrations (usually 0.5% bupivacaine vs. 2% lidocaine).<sup>15</sup> Thus, this comparison should be cautiously considered, and the longer onset time of bupivacaine (median of 40 min in our study) compared with that of lidocaine should be kept in mind, too. Bupivacaine for brachial plexus block reportedly has a block duration of 9 to 12 hours,<sup>16</sup> which agrees with our finding of 10 hours in the 14-mL volume group. However, we found that a greater volume also increased the block duration. Thus, the MEV of bupivacaine may be an important consideration in clinical evaluations of postoperative recovery and pain management.

In the present study, the median time to onset of sensorial block was 40 minutes in the 14-mL group vs. 15 minutes

in the 30-mL group. Our results are greater than those in the literature. Pongraweevan et al.<sup>17</sup> reported a time to onset of 6.68 minutes for 30 mL of 0.5% bupivacaine. Another study reported a median (range) time to onset of 6 (3–12) minutes for 40 mL of 0.5% bupivacaine.<sup>18</sup> However, these studies did not compare different volumes; thus, the evaluation of time to onset may have been less strict than in the present study. Indeed, the evaluation of sensory block in the latter study depended on the patients reporting a “different” (as opposed to the “same”) sensation during the touch test. Pedro et al.<sup>13</sup> reported a time to onset of 5 to 15 minutes for 30 mL of 0.5% bupivacaine administered with the supraclavicular approach; this finding is similar to ours.

A broad range of times to first postoperative analgesic administration has been reported. Liisanantti et al.<sup>19</sup> reported a mean of 17.8 hours after 45 mL of 0.5% bupivacaine, whereas Ozmen et al.<sup>20</sup> reported a mean of 4.4 hours after 20 mL of 0.5% bupivacaine. In the present study, the time to first postoperative analgesic administration was 14 hours after 14 mL of 0.5% bupivacaine, and this time increased to greater than 24 hours with 30 mL. These differences may be due to variations in LA volume and application; however, the pain scoring scales and the value at which additional analgesics were considered necessary could have affected the results. Liisanantti et al.<sup>19</sup> did not use a scoring system to evaluate pain, and Ozmen et al.<sup>20</sup> did not define a specific pain value at which additional analgesics would be administered. In our study, a VAS score greater than 4 indicated that additional analgesics were required.

**Table 4** Associations between anesthetic volume and duration of anesthesia.

Variable	(1)	(2)	(3)	(4)	(5)
(1) Volume, mL	1.00				
(2) Time to onset of successful block, min	–0.89 <sup>a</sup>	1.00			
(3) Time to regression of sensorial block, h	0.80 <sup>a</sup>	–0.55 <sup>a</sup>	1.00		
(4) Time to regression of motor block, h	0.77 <sup>a</sup>	–0.48 <sup>a</sup>	0.90 <sup>a</sup>	1.00	
(5) Time to first postoperative analgesic, h	0.77 <sup>a</sup>	–0.50 <sup>a</sup>	0.90 <sup>a</sup>	0.94 <sup>a</sup>	1.00

Spearman rho values are shown.

<sup>a</sup>  $p < 0.001$

The numbers 1 to 5 represent the different analyzed variables, as seen in the rows of the first column. Correlations are presented with their respective Spearman rho values using those numbers as references of relationships throughout the table. Values of 1.00 are seen as perfect positive correlation when those variables are correlated to themselves, as expected.

We did not observe any procedure-related complications. Studies have reported Horner syndrome (3.2%), phrenic nerve palsy (3%), pneumothorax (1–4%), and hematoma (2–3%), in addition to rarely observed complications such as venous puncture,<sup>21,22</sup> in patients who underwent infraclavicular brachial plexus block. Studies on the complication rates of brachial plexus block techniques mostly report low complication rates, mild complications, and complete recovery (barring rare cases).<sup>14,23,24</sup>

We did not consider the effects of body mass index or type of surgery, which may be limitations. However, the strengths of our study include our use of objective evaluation criteria, blind evaluators, and non-biased patient selection. The lowest effective dose was 14 mL, but because the volume groups were formed by sequentially decreasing the dose of LA by 2 mL from a starting point of 30 mL, successful doses between 12 mL and 14 mL could not be evaluated.

Few studies have determined the MEVs of various LAs administered with various anatomical approaches for USG infraclavicular brachial plexus block.<sup>6,7,12,25</sup> Although the methodologies and results of these studies differ, the aims were similar: to reduce the dose of LA administered for brachial plexus block. We concluded that brachial plexus block can be successfully performed with a low bupivacaine dose, albeit with a long time of onset. When elective surgery requires a brachial plexus block, a low dose of LA may be used without compromising safety. Additional studies with more patients are needed to determine the MEVs of LAs.

## Conclusion

We determined that the MEV of 0.5% bupivacaine for USG lateral sagittal infraclavicular brachial plexus block was 14 mL. However, this low-dose block has a long onset time of 40 (30–45) minutes on average. Future studies should investigate the MEV of low-dose bupivacaine.

## Conflicts of interest

The authors declare no conflicts of interest.

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