Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/kfszek10

MINIMUM EFFECTIVE VOLUME OF BUPIVACAINE 0.25% + LIDNOCAINE 1% WITH EPINEPHRINE 5UG/ML REQUIRED FOR BRACHIAL PLEXUS BLOCK FOR UPPER LIMB SURGERIES.

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ABSTRACT

Supra-clavicular block (SCB) is a highly effective technique for providing analgesia for procedures performed distal to the mid-shaft of the humerus, offering rapid onset, superior quality of analgesia, and fewer complications compared to other regional anesthesia methods. Traditionally, large volumes of local anesthetics (LA) were administered using the peripheral nerve stimulator (PNS)-guided technique, but the introduction of ultrasound (US) guidance has enabled direct visualization of the spread of LA around the brachial plexus, allowing reduced volumes while maintaining block efficacy. Although several studies have reported lower volumes with US-guided SCB, some studies show no significant reduction in volume required for effective blockade in 95% of patients (ED95), with higher volumes sometimes needed. This study aimed to determine the minimum effective anesthetic volume (MEAV) for achieving surgical anesthesia in 95% of patients (MEAV95) using a combination of Lidocaine 1.0% with epinephrine 5 µg/mL and Bupivacaine 0.25% under US guidance. A cross-sectional study was conducted over five months at The Indus Hospital, including 74 patients undergoing elective upper limb surgeries. SCB was performed under US guidance with identification of the brachial plexus, subclavian artery, first rib, and pleura. The total LA volume was divided into three portions, deposited at 6, 3, and 12 o'clock positions around the brachial plexus. Initial LA volume of 30 ml was adjusted by 3 ml per patient according to the Dixon and Massey Up-and-Down Method. Sensory and motor blockade were assessed every five minutes up to 30 minutes. Among 74 patients (42 males, 32 females), a 59.5% success rate was observed. MEAV50 and MEAV95 were calculated as 4.99 ml (95% CI 3.3–6.6) and 21.15 ml (95% CI 12.86–97.1), respectively. Low volumes achieved effective blockade, supporting US-guided SCB efficiency, though multiple

deposition sites and careful needle handling are necessary, and further randomized trials are recommended to validate ED95 estimations.

Keywords: ultrasound-guided, Supra-clavicular block, minimum effective volume, MEAV95

Introduction:

Modern medicine is rapidly evolving, with continuous advancements in surgical techniques and peri- and postoperative patient care, emphasizing patient safety, optimal analgesia, and accelerated recovery [1-3]. In this context, the role of the anesthesiologist has become increasingly critical in ensuring effective pain management while minimizing complications [4-5]. Upper limb surgeries, which were conventionally performed under general anesthesia (GA) with intravenous analgesics [6], have increasingly shifted toward regional anesthesia (RA), particularly brachial plexus (BP) blocks, due to their superior outcomes [7-9]. Studies have demonstrated that RA for upper limb procedures results in shorter recovery times ($p < 0.0001$) and reduced postoperative opioid requirements ($p = 0.0037$), highlighting its efficacy over GA [10-12].

Brachial plexus blocks offer a safe and efficient alternative to GA for a wide range of upper extremity surgeries, with additional benefits including reduced surgical stress response, improved glucose control, decreased tumor recurrence, enhanced patient participation in physiotherapy, and minimized opioid exposure [13-16]. Among the four primary approaches for BP blockade, the supraclavicular approach has gained popularity due to its simplicity and high efficacy, providing anesthesia for procedures distal to the mid-shaft of the humerus with rapid onset, excellent analgesic quality, and minimal complications [17-19].

The integration of ultrasonography into regional anesthesia has further improved the safety and effectiveness of SCB. Real-time visualization of the brachial plexus, subclavian artery, and surrounding structures allows precise needle placement and adjustment, increasing the likelihood of successful blockade despite anatomical variations [20]. Two common techniques for SCB include the peripheral nerve stimulator (PNS) method and ultrasound-guided (US) method. Compared to PNS, US guidance offers several advantages, including higher success rates (95% vs. 85%), more accurate LA deposition, and the potential to reduce the total volume of anesthetic required. For example, studies have shown significant reductions in LA volumes in interscalene blocks (0.9 ml vs. 4.5 ml), axillary blocks (1 ml per nerve), femoral blocks (42% reduction), and sciatic nerve blocks (17 ml) [3]. Reducing LA volume in SCB is clinically important because excessive volumes can result in complications such as unilateral phrenic nerve palsy or Horner's syndrome. Ultrasound guidance also minimizes risks such as pneumothorax by allowing direct visualization of the needle trajectory [12]. Despite reports of reduced LA requirements with US guidance, some studies have indicated that effective blockade in 95% of cases (ED95) may still require high volumes, with one study reporting 43 ml, and there remains insufficient literature regarding the minimum effective volume for US-guided SCB [15].

The rationale of this study is grounded in the need to determine the lowest possible volume of local anesthetic that can provide effective surgical anesthesia while minimizing the risk of adverse events. Traditional SCB techniques often use larger volumes of LA, which may increase the incidence of complications, yet the optimal volume for safe and effective analgesia remains unclear [13]. Therefore, this study aims to identify the minimum effective volume (MEV) of a combined solution of Lidocaine 1.0% with epinephrine 5 µg/mL and Bupivacaine 0.25% required to achieve surgical anesthesia in 95% of patients (MEV95) using US-guided SCB [15].

In this study, minimum effective volume is defined as the volume of combined Lidocaine 1.0% with epinephrine 5 µg/mL and Bupivacaine 0.25% at which surgical anesthesia is achieved. Surgical anesthesia is defined as complete loss of cold sensation (score of 0) with a motor score of 2 or less in the distribution of the radial, ulnar, and median nerves. Successful sensory blockade is defined as complete sensory blockade (score < 2) within 30 minutes of performing SCB. Pain assessment is measured using the Visual Analog Scale (VAS): 0–2 indicates no pain, 3–5 mild pain, 6–7 moderate

pain, and 8–10 severe pain. Motor function is evaluated using the Bromage scale, ranging from 0 (no movement) to 4 (full power). By establishing the MEV95, this study seeks to provide evidence-based guidance for optimizing US-guided SCB, ensuring effective analgesia while minimizing local anesthetic exposure and associated risks.

Materials and Methods

Study Design

This study was designed as a cross-sectional observational study.

Sampling Technique

Consecutive sampling was employed to recruit eligible participants.

Study Setting and Target Population

The study was conducted in the Department of Anesthesia and Critical Care at The Indus Hospital, a free-of-cost tertiary care facility in Karachi, Pakistan. The target population comprised patients scheduled for elective upper limb surgeries below the mid-shaft of the humerus.

Duration of Study

The study was conducted over a period of three to six months following approval from the Institutional Review Board (IRB) and the College of Physicians and Surgeons Pakistan (CPSP), with an additional three months allocated for data analysis and dissertation preparation.

Inclusion Criteria

Patients fulfilling the following criteria were included:

- Age between 16 and 70 years
- ASA physical status I to III
- Elective upper limb surgery below the mid-shaft of the humerus
- Both genders
- Provided written informed consent

Exclusion Criteria

- Patients were excluded if they had:
- Body mass index (BMI) > 35 kg/m²
- Chest or shoulder deformities
- Infection at the injection site
- Pre-existing neurologic disorders
- Known allergy to local anesthetics
- Severe respiratory disease
- Coagulopathy
- Cognitive impairment or active psychiatric illness
- History of bupivacaine allergy
- Pregnancy

Sample Size and Power Calculation

The required sample size was calculated using the WHO sample size calculator. Based on previous literature reporting a 95% MEV of 42 ml ± 52.45 (converted from 95% CI: 42 ml [19–65 ml]) and a margin of error of 0.12, the calculated sample size was 74 patients.

Data Collection Procedure

Following approval from CPSP and IRB, patients scheduled for elective upper limb surgery were identified from preoperative anesthesia assessment notes and final OT lists. The study procedure was

explained to eligible patients in the pre-anesthesia holding area, and written informed consent was obtained. Intravenous access was established, and standard monitoring, including non-invasive blood pressure, electrocardiography, and pulse oximetry, was applied. Sedation and anxiolysis were provided using incremental doses of midazolam (0.01 mg/kg) as required. All blocks were performed by anesthesiologists trained and certified in ultrasound-guided peripheral nerve blocks.

Patient Positioning and Approach

Patients were positioned at a 45-degree incline with the head turned to the contralateral side and a small pillow placed under the head. After aseptic preparation, a sterile-covered ultrasound probe was placed in the supraclavicular fossa in a coronal-oblique plane posterior to the clavicle.

Identification of Structures

The brachial plexus was visualized as a compact hypoechoic structure lateral and cephalad to the subclavian artery, above the first rib. The subclavian artery, first rib, and pleura were identified in all patients.

Local Anesthetic Deposition

The total LA volume was divided into three equal parts, deposited at the 6, 3, and 12 o'clock positions relative to the brachial plexus under direct ultrasound guidance. After skin sterilization with chlorhexidine and local infiltration with 2% lidocaine, an insulated nerve needle was inserted in-plane with the ultrasound beam along the medial border of the probe. The needle was advanced sequentially to the 6, 3, and 12 o'clock positions, with aspiration for 3 seconds before each injection to ensure intravascular placement was avoided.

Dose Adjustment

The initial LA volume was 30 ml (10 ml at each position). Subsequent patient volumes were adjusted by ±3 ml depending on the success or failure of the previous block, in accordance with the Dixon and Massey Up-and-Down Method. Successful blocks prompted a 3 ml decrement, while failed blocks prompted a 3 ml increment, with a minimum volume of 3 ml per deposition site.

Block Evaluation

Sensory and motor blockade were assessed by trained acute pain service nurses at five-minute intervals for 30 minutes following needle withdrawal. Sensory blockade was evaluated using pin-prick testing in the distribution of the median, radial, and ulnar nerves, while motor blockade was assessed using the Bromage scale. Pain intensity was measured using the Visual Analog Scale (VAS).

Data Analysis

Data were analyzed using SPSS version 21.0. Quantitative variables such as age, height, weight, BMI, procedure duration, and LA volume were reported as mean ± standard deviation (SD). Categorical variables, including gender, were reported as frequencies and percentages. Effect modifiers, including age, BMI, procedure duration, and gender, were controlled through stratification, followed by post-stratification t-tests or ANOVA as appropriate. A p-value <0.05 was considered statistically significant.

Results:

A total of 74 patients were included in the study. Out of these patients 42(56.8%) were males while 32 (43.2%) were females. Mean age of the participants at the time of the surgery was 38 years (SD: 13.5). Success rate of 59.5% (n=44) was achieved. No patient suffered any reported complications, including inadvertent puncture of subclavian artery, hematoma formation, pneumothorax, phrenic nerve palsy or horner syndrome. MEAV 50 and 95 was calculated using probit transformation and

logistic regression and found to be 4.99 ml (95%CI 6.6-3.3) and 21.15 ml (95%CI 97.1-12.86) respectively. Other descriptive data are given in table

Table 1: Descriptive Data of different Variables

Total Number of case	**74**
GENDER	
Male n(%)	42(56.8%)
Female n(%)	32(43.2%)
BLOCK OUTCOME	
Successful n(%)	44(59.5%)
Unsuccessful n(%)	30((40.5%)
AGE (years)	
Mean (SD)	37.91(13.56)
Min- max	16-70
HEIGHT (cm)	
Mean (SD)	162.19(10.89)
Min- max	134-183
WEIGHT (Kg)	
Mean (SD)	66.14(14.58)
Min-max	36-100
BMI (Kg/m2)	
Mean (SD)	25.12(5.31)
Min- Max	14.5 – 38.8
DURATION OF SCB PROCEDURE (mins)	
Mean (SD)	8.53(2.79)
Min – max	3.00-14.00
VOLUME OF LOCAL ANESTHETIC (ml)	
Mean (SD)	7.86 (5.47)
Min – max	3-30

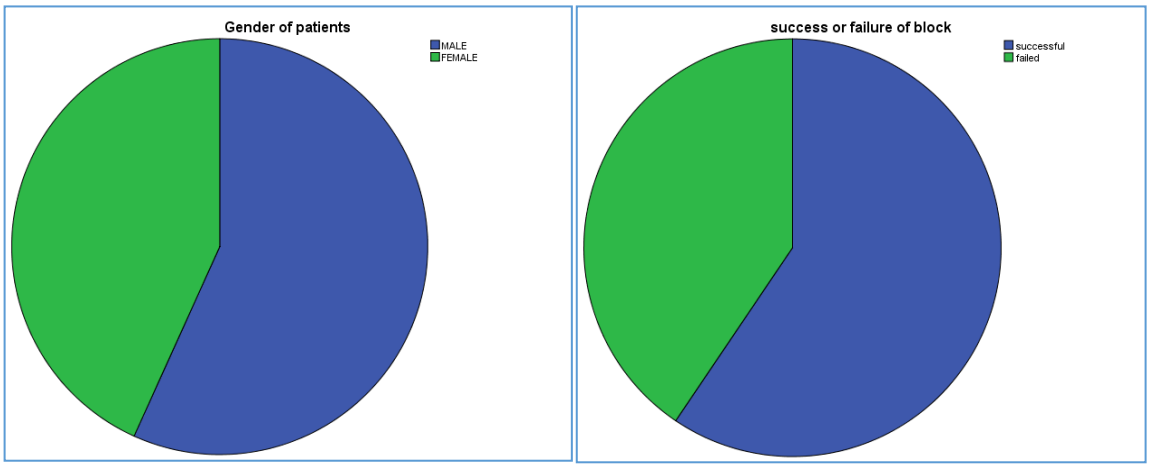

Table 3: Stratification of mean volume of local anesthetic with respect to AGE

GROUPS	Frequency (n)	MEAN	STD.DEVIATION	P-VALUE
Age less than 50 years	60	7.90	5.24	0.910
Age more than 50 years	14	7.71	6.63	

Table 4: Stratification of mean volume of local anesthetic with respect to GENDER

GROUPS	Frequency (n)	MEAN	STD.DEVIATION	P-VALUE
Males	42	8.21	5.70	0.533
Females	32	7.41	5.22	

Table 5: Stratification of mean volume of local anesthetic with respect to BMI

GROUPS	Frequency (n)	MEAN	STD.DEVIATION	P-VALUE
BMI <27.5	53	7.81	5.74	0.895
BMI>27.5	21	8.00	4.87	

Table 6: Stratification of mean volume of local anesthetic with respect to Duration of SCB procedure

GROUPS	Frequency (n)	MEAN	STD.DEVIATION	P-VALUE
Duration <10mins	55	8.56	6.07	0.061
Duration >10mins	19	5.84	2.34	

Supra-clavicular block has proven to be an excellent choice for analgesia in upper limb surgery as this technique has higher success rates and faster onset, with fewer complications. The use of Ultrasound have markedly increased efficacy of regional blocks, for instance, in a meta-analysis done by Abraham and his colleagues, where they reviewed 13 studies that compared US with NS technique, they reported that these studies showed US method yield much higher success rate, with lesser time needed to perform the block and decrease in local anesthetic volumes when compared to NS technique [21]. The decrease in local anesthetic volumes is of particular interest for anesthesiologists as it has shown to markedly reduce complications. Riazi and his team compared lower volumes for interscalene blocks and demonstrated that the incidence of diaphragmatic paralysis was significantly lower in the low-volume group compared with the standard-volume group (45% vs 100%). Along with significant reduction in lung volumes (FVC, FEV1, and PEF) at 30 min post-ISBPB in the standard-volume group when compared with the low-volume group (21.59 vs 20.70 litre/min; 21.23 vs 20.60 litre/min; 22.50 vs 20.83 litre/min). Moreover, decrease in postoperative oxygen saturation

after surgery was significantly more in the standard-volume group (25.85% vs 21.50%, P 0.004) hence demonstrating important clinical benefits of reducing volume of LA [22].

The small volume of local anesthetic for successful block could be explained by a few theories. Firstly, the brachial plexus is most compact and the plexus sheet is smallest at this level, hence a small volume could adequately surround the nerve bundle thereby providing successful block. Secondly through real-time US imaging, deposition of LA can be visualized during injection, enabling the operator to distribute LA uniformly around the target nerve. However, reduction in volume for an effective block has been controversial [24]. Many studies support the reduction in volume for US-SCB. Likewise, in the present study, MEAV 50 and 95 was found to be 4.99 ml (95%CI 6.6-3.3) and 21.15 ml (95%CI 97.1-12.86) respectively. The result of present study is similar to the one done by J.G Song, who found that the MEV95, and MEV 50 of 1.5% mepivacaine for ultrasound-guided supraclavicular block were 17 ml (95% CI, 13-42 ml) and 9 ml (95% CI, 4-12 ml) respectively. However Duggan E and Dughani S were not able to demonstrate this in their studies. Those studies estimated MEV 95, and MEV50 values for local anaesthetic as 42 ml, and 23 ml, respectively.

Duggan E offered a few explanations to why his study failed to support reduction in effective LA volume. Firstly, he suggested that a plexus or bundle of nerves, like divisions of the brachial plexus, had a larger MEAV than a single isolated peripheral nerve; a concept that was also supported by Taboada and his colleagues. Secondly, as demonstrated by Cornish and his team, brachial plexus is contained within a rigid walled tunnel of connective tissue sheet, hence a set minimum volume might be required to adequately fill this tunnel otherwise SCB will not be successful, thus restricting further reduction than the traditional volumes. Furthermore, at the supra-clavicular level, the connective tissue interlaces around the brachial plexus which also may not allow a further decrease in volume [22].

Another reason for the few previous studies to fail to demonstrate reduction in volume was the strict criteria followed in defining a successful block, thus resulting in large MEAV50. Williams and his team(10) assessed the quality of supra-clavicular block using 0.5 mL/kg of bupivacaine 0.5% and lidocaine 2% with epinephrine to a maximum LA volume of 40 mL and noted a 95% success rate using partial or complete sensory block after 30 mins of block performance as criteria for success. However when criterion for success was revised as complete sensory block these authors found a success rate of 55. Although the same strict criteria were followed in this study as used by Duggan and his team, present study was still able to demonstrate decrease in effective LA volumes.

One major factor in determining the volume of local anesthetic is the site at which it is deposited. In conventional technique, the needle is advanced in plane toward the brachial plexus, in a lateral to medial direction. Once the needle is in the sheath, local anesthetic is injected around and in the brachial plexus. In this method, divisions from lower trunk might be spared, and more local anesthetic volume might be required to reach the lower trunk and its divisions. In an effort to overcome this hurdle, Luiz and his colleagues suggested injecting a single bolus at the point where the subclavian artery meets the fist rib, which they called 8 ball corner pocket technique. This technique was thought to be more effective in blockade of the inferior divisions of the brachial plexus, but Duggan did not see reduction in the volume of local anesthetic, despite using corner pocket technique hence failing to prove effectiveness of this technique in reducing volume of LA. Techasuk and his colleague proposed a few other alternative techniques including double injection technique where half of the volume was given in cluster while other half at corner's pocket, and Targeted intra-cluster technique, where half of local anaesthetic volume was deposited at main nerve bundle while remaining were given at small nerves clusters or satellites around the main clusters. Although they found benefits in term of faster procedure time, no significant decrease in volume was reported.

Bigeleisen and his team injected local anaesthetic around the deeper parts of the brachial plexus but injection was performed intra-neurally, which has been feared to produce neurological complications. J.K. Song used the combination of location the needle near the lower trunk and multiple injections with withdrawing the needle and advancing in zigzags to avoid nerve puncture. Similar technique was applied in present study; In addition, the location of the needle tip was confirmed by injected 0.5 ml

of local anesthetic as a test dose to make sure it was not in hypoechoic nodules (in nerves). Moreover to mark the deposition site more objectively, 6'o clock, 3'o clock and 9'o clock positions were chosen to make sure local anaesthetic completely surrounded the nerve bundle, instead of relying on operator's discretion, which might be a factor in reduction of LA volume as reported in this study.

Age is another factor that may influence MEAV. Pavicic studied the effect of age on MEAV and found an almost two-time decrease in LA volume requirements for effective US-SCB in 50% of the elderly patients in comparison with the middle-aged population (potency ratio 1.93, 95% CI 1.16–2.87). They reported MEAV 95 to be 11.1 ml. Similarly, in the study of Paqueron and colleagues, analyzing the influence of age on peripheral nerve blocks, they found 2.5- time longer duration of complete sensory block in the elderly was observed in comparison with young patients indicating that LA agents administered in peripheral nerve blocks have a quite different effect on the elderly population. This difference could be explained by two reasons, at one hand morphological changes of peripheral nerves because of aging may require lesser volume, while on the other hand, there might be increased sensitivity of LA agents in the elderly. Sonographical study of brachial plexus has found that cross sectional area of brachial plexus in elderly is almost reduced to half as compared to young and middle age populations resulting in lesser volumes. Although the range of age in present study was wide from 16 years to 70 years yet no significant difference (P=0.91) in volume of LA required was found in age groups.

Obesity is associated with increase in the difficulty and decreases in success rate of a supraclavicular block. However, Carlo D. Franco still managed to report success rate of 94.7% in 455 cases, despite the increase in difficulty. In present study no significant difference (P=0.81) in LA volume was seen among obese vs non obese group, suggesting the nerve bundle circumference or mass does not vary significantly in obese compared to non-obese population. A study by P.K. Gupta(164), that focused on difference in ED50 in obese versus non obese population reported similar findings, i.e no significant difference in ED 50 between the two groups (8.9(6.2–12.7) vs 10.7 (7.5–15.4)).

Ultrasound has proven to decrease procedure time as demonstrated by Williams and his team, who reported faster procedure time in US as compared to NS (5minutes vs 10 minutes). Moreover, Techasuk demonstrated quicker procedure time with double injection method compared to multiple Targeted cluster injections. However, no study till date had compared difference in procedure time for different local anesthetic volume. Although one might assume that higher volume might increase procedure time, present study failed to find any significant difference (P 0.061), suggesting that procedure time was more dependent on needling technique rather volume of local anesthetic used.

There were few limitation to this study; the use of Dixon and Massey approach to be the most noteworthy. The Dixon and Massey approach is a volume-finding method that aims to calculate the minimum volume that produces a specific outcome in 50% of patients. The method also calculates the CI of such a volume and can only be used in situations where the volume leads to a binary outcome, for example, successful or unsuccessful blocks. The advantages of the up-and-down method include a smaller sample size required to estimate the ED50 and a simple study design. However, there are a few drawbacks with this design such as the wide CI that is insensitive to increasing the sample size. Previous studies using Dixon's up-and-down methodology have also reported a broad 95% CI. Another important limitation of the Dixons up-and down methodology is the inability to accurately determine the ED95, which is of clinical significance rather than ED 50. Considering the S-shape of the probability curves that underlie various regression models, specially logistic regression, the ED95 refers to a much shallower slope compared with the ED50. Hence CIs for ED95, regardless of the calculation method, are therefore wide as compared to the CI of the ED50 estimate(167), which was evident in present study as well where CI for MEAV95 calculated through Probit transformation and logistic regression was between 97.1-12.86. Moreover the use of probit transformation in estimation of ED 50 and ED 95 was criticized by Vagro for inadequate CI. The up-and down methodology of Dixon and Massey also demands that the starting dose should be the minimum dose expected to result in a positive response. Therefore the starting dose of this study was 30ml as it has been documented to effective in 95% of patients.

This study used bupivacaine 0.25% with lidocaine 1% with epinephrine 5ug as adjuvant to the local anesthetics mixture to reduce the Confounding when compared with previous studies who used the same LA mixture (i.e.; 50:50 mixtures of lidocaine 2% and bupivacaine 0.5% with epinephrine). However we did not use any other adjuvant. Since many adjuvants, e.g dexamethasone, clonidine or Dexmedetomidine have shown more prolongation in post operative duration of analgesia, hence it might be possible that such adjuvant may decrease minimum LA volume required for successful block. Therefore further trials are warranted to determine role of these alternative adjuvants in reducing minimum LA volumes.

Lastly, one important limitation to this study is that it did not measure the duration of post operative analgesia up to 12 or 24 hours. However previous studies have not reported any difference in post operative analgesia in low volumes as compared to standard volumes. The study done by Riazi and his team did not find any significant difference between post operative pain relief, quality of sleep or morphine consumption up to 24 hours when they compared low volumes with high volumes in interscalene blocks. Similarly Brenner and his team studied effect of 1ml of bupivicane 0.5% per nerve (4nerves) in axillary brachial plexus block and found excellent post operative analgesia with VAS score less than 4 up to 12 hours. Hence much difference is not expected in case of successful blocks even at low volumes of LA. However further studies are warranted to compare the two groups with respect to duration of block and quality of post operative analgesia.

CONCLUSION

Estimated minimum local anesthetic volume MEAV 95 and MEAV 50 were and 4.99 ml, respectively. However, the location of the needle near the lower trunk of brachial plexus and multiple injections withdrawing the needle should be performed to achieve these results, and very careful injection that requires adequate skills in needle manipulation under ultrasound guidance. Moreover the MEAV95 is estimated through Dixon and Massey up and down method, and like previous studies ,its estimation has wide CI making its reliability doubtful. Large scale studies should be done to determine accurately determine MEAV 95, as it is of clinical relevance instead of MEAV50.

Funding

There is no funding.

Conflict of interest

There is no conflict of interest in this study.

Acknowledgement

Indus Hospital Research Center

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