Equal mixture of 2% lidocaine with adrenaline and 0.5% bupivacaine 20 mL provided faster onset of complete conduction blockade during ultrasound-guided supraclavicular brachial plexus block than 20 mL of 0.5% bupivacaine alone: a randomized double-blinded clinical trial

SriPriya R, Sivashanmugam T, Daniel Rajadurai, S Parthasarathy

ABSTRACT

Introduction Recent evidence has questioned the advantage of local anesthetic (LA) combinations. This study tested the hypothesis that mixing rapid-onset (lidocaine) and long-duration (bupivacaine) LA would provide faster onset of complete conduction blockade (CCB) compared with bupivacaine alone and longer duration of analgesia compared with lidocaine alone during low-volume (20 mL) ultrasound-guided (USG) supraclavicular brachial plexus block (SCBPB).

Methods Sixty-three patients receiving USG-SCBPB were randomly allocated into: group L: 20 mL 2% lidocaine with epinephrine 1:200 000; group B: 20 mL 0.5% bupivacaine; group LB: 20 mL of equi-volume mixture of both drugs. Sensory and motor blockade was recorded on a three point sensory and motor assessment scale at 10 min intervals for up to 40 min and the total composite score (TCS) at each time point was determined. The duration of analgesia was also noted.

Results The mean time to CCB of group LB (16±7 min) was comparable (p>0.05) with group L (14±6 min) and group B (21±8 min) in patients who attained CCB. However, the proportion of patients attaining complete conduction block (TCS=16/16) was significantly lower (p=0.0001) in group B (48%) when compared with group L (95%) and group LB (95%) at the end of 40 min. The median (IQR) duration of postoperative analgesia was longest in group B; 12.2 (12–14.5) hours, followed by group LB 8.3 (7–11) hours and 4 (2.7–4.5) hours in group L.

Conclusion At 20 mL LA volume, equal mixture of lidocaine and bupivacaine provided significantly faster onset of CCB compared with bupivacaine alone and longer duration of postoperative analgesia compared with lidocaine alone but shorter than bupivacaine alone during low-volume USG-SCBPB.

Trial registration number CTRI/2020/11/029359.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ The clinical advantage of mixing two local anesthetics is not established.

WHAT THIS STUDY ADDS

⇒ At 20 mL local anesthetic (LA) volume, equal mixture of lidocaine and bupivacaine provided clinically significant faster onset of complete conduction blockade compared with bupivacaine alone and prolonged analgesia compared with lidocaine alone but shorter than bupivacaine alone during ultrasound-guided (USG) supraclavicular brachial plexus block.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ The pharmacodynamics of LA mixtures during USG low-volume precision blocks might be different—need to be explored.

INTRODUCTION

Mixing of two local anesthetics (LAs) to take advantage of the rapid onset of one agent and prolonged duration of action of another has been practiced since the 1960s.1-4 However, the recent research yields conflicting findings about the clinical advantages of LA mixing. 40 mL equal mixture of Mepivacaine 1.5% (faster-onset, intermediate-duration) with bupivacaine 0.5% (slower-onset, longer-duration) was shown to hasten the onset of conduction blockade in infracavicular brachial plexus block (BPB); however, 30 mL of the same mixture was found to provide no benefit over bupivacaine in the onset of conduction blockade during interscalene BPB (ISB).5-9 In the recent years, an improved understanding of the sonoanatomy of BP elements and injection techniques has enabled us to decrease the LA volume from 30–40 mL to 10–20 mL to provide a successful BP at the supraclavicular area.6-9 In our experience, using bupivacaine alone in such low volume, substantially delayed the onset of complete conduction blockade (CCB). Hence, we designed this study to test the hypothesis that 20 mL equal mixture of 2% lidocaine with epinephrine 1:200 000 and 0.5% bupivacaine would provide faster onset of CCB compared with 20 mL bupivacaine alone and longer duration of analgesia compared with 20 mL lidocaine alone during low-volume (20 mL) ultrasound-guided (USG) supraclavicular BPB (SCBPB).
METHODS
The study protocol was approved by the institutional human ethics committee (MGMC/R/IRC/04/2020/35/HEC/177). Patients aged 18–60 years belonging to American Society of Anesthesiologists (ASA) physical status I and II scheduled for upper extremity bone surgeries, at or below the elbow under SCBPB, were included in the study. Patients who refused to participate, gave a history of allergy to LA drugs, and had evidence of coagulopathy, neurological deficit, infection at supraclavicular fossa, respiratory compromise or difficult sonoanatomy were excluded. A consecutive sampling technique was employed. First patient was recruited on 1 December 2020. All participants submitted a written informed consent before enrollment into the study.

All the blocks were performed in the anesthetic procedure room, approximately 60 min before the planned surgery. 18-gage intravenous access and ASA standard monitoring were established before the BPB. Simple permuted block randomization (7 blocks of nine patients each) was used for group allocation. The randomization sequence was generated by a statistician and hand over in sealed opaque sequentially numbered envelopes. The envelope was opened by an anesthesia resident not involved in the study and prepared the LAs or LA mixtures as per the allocation card. A total of 20 mL of 2% lidocaine HCl with epinephrine 1:200,000 (5 μg/mL) was used in group L. 10 mL of each 2% lidocaine HCl with 1:200,000 epinephrine and 0.5% bupivacaine HCl was used for group LB. A total of 20 mL of 0.5% bupivacaine HCl was used for group B. The study drug was loaded in a 20 mL syringe, connected to a 100 cm pressure monitoring line and handed over to the performer. The performer was not aware of the content of study drug.

Two of the three investigators (SR and ST) who had extensive experience in multipoint subfascial injections performed all the BPBs and took no further part in the study. Patients were positioned with arms by the side and the head turned slightly to the contralateral side, for the block. All the blocks were performed under US guidance and strict aseptic precautions, using a high-frequency linear array transducer (HFL 50, 15–6 MHz) of X-Porte US system (FUJIFILM Sono Site, Bothell, USA). A 25-gage, short-beveled Quinke spinal needle was used to perform the BPB. The needle insertion was either in-plane or out-of-plane depending on the ergonomics achieved. The needle was well introduced into the outermost hyperechoic fascial layer and the tip was positioned within the hyperechoic or hypoechoic circles or paraesthesia. A random multiple site injection was followed. Maximum of 4–5 mL of LA solution was injected at a single site in order to ensure spread of the LA in and around all the elements of brachial plexus, including the corner pocket. The routine performance time for LA injection was 3–5 min. The final needle removal time was noted as ‘time 0’.

The sensory-motor assessment was performed by an independent anesthesiologist who was also blinded to group allocation. Sensory block was assessed on a 3-point qualitative scale (Grade 0, absence of cold and touch sensation; Grade 1, loss of cold but not touch sensation and Grade 2, loss of both cold and touch sensation) using ether-soaked cotton swabs. The distal-most territories of the musculocutaneous nerve (MCN)—lateral forearm, median nerve (MN)—the tip of the middle finger, the ulnar nerve (UN)—the tip little finger and radial nerve (RN)—anatomical snuff box, were tested. A score of 2 in all four nerve territories of the musculocutaneous nerve (MCN)—elbow flexion, MN-thumb opposition, UN-thumb adduction, RN-thumb abduction) was assessed using a 3-point qualitative scale [0—normal motor function (Power 4/5, 5/5), 1—decreased motor function (Power 3/5, 2/5), 2—no motor power (Power 0/5, 1/5)]. A score of 2 in all 4 terminal nerve distribution areas (8/8) was taken as the time for the complete sensory block. Motor blockade of the four-terminal branches (MCN—elbow flexion, MN—thumb opposition, UN—thumb adduction, RN—thumb abduction) was assessed using a 3-point qualitative scale [0—normal motor function (Power 4/5, 5/5), 1—decreased motor function (Power 3/5, 2/5), 2—no motor power (Power 0/5, 1/5)].

Statistical analysis
Sample size estimation
The ‘Statistics and Sample Size’ App (Thai Thanh Truc) was used to calculate the sample size. Time for CCB was the primary outcome variable. In a pilot study on ten patients, we observed that the onset of CCB with drug combination was 19±11 min (mean±SD), while with bupivacaine it was 30±12 min. With a power of 80% and a two-sided type I error rate of 0.05, the minimum sample size required to detect the difference between the two groups (LA mixture vs Bbupivacaine—one pair) was estimated to be 18 per group. Hence, the total sample size of the study was 54 (18×3). To facilitate block randomization and take into account the drop-outs, 63 (21×3) patients were recruited.

Data analysis
SPSS for Windows V.16.0 (SPSS, Chicago, Illinois) was used for statistical analysis. The χ² test was used to compare categorical variables. The normality of continuous variables was tested by the Shapiro–Wilk test. p<0.05 was reported as median (IQR) and compared using the Kruskal–Wallis test. p<0.05 was taken as the threshold of statistical significance.

RESULTS
Seventy patients were evaluated for eligibility, 63 patients were randomly assigned to receive the intervention, and all 63 patients completed the analysis (figure 1). The three study groups were comparable with respect to demographic data, type of surgery performed, and other clinical variables (table 1).
It took approximately 5 min to perform the block. In patients who had a CCB, the mean time to CCB was significantly different between group L and group B (14.6 ± 21.7 min; p = 0.02), whereas the group LB (16.7 min) was comparable (p > 0.05) with other two groups. However, the proportion of patients attaining CCB (TCS = 16/16) was significantly lower (p = 0.0001) in group B (14, 33, 48, 48%) when compared with group L (62, 86, 95, 95%) and group LB (43, 81, 90, 95%) at all four time point intervals. 52% (11/21) of the patients in group B did not attain CCB even at the end of the 40 min observation period (figure 2). TCS against time was used to compare the degree of conduction blockade between groups at different time points. This demonstrated that group LB achieved comparable (p > 0.05) conduction blockade to group L in 20 min, whereas group B took 40 min to reach comparable conduction blockade with group L. However, high variation in TCS even at the end of 40 min suggests that the conduction blockade was more unpredictable in group B (figure 3). The MN and UN took relatively more time for CCB compared with MCN and RN in all three groups (figure 4). The median (IQR) duration of postoperative analgesia was longest in group B (21, 28, 29, 64 min) and the intraoperative nociceptive insult can affect the duration of postoperative analgesia.

The conflicting results from clinical studies evaluating the onset of peripheral nerve blockade with LA mixtures arise from three fundamental differences in the methodologies, namely, the type of nerves assessed (proximal nerves arising from mantle fascia, subfascia/extra fascial, targeted intracluster and selective truncal analgesia) was longest in group B; 12.2 (12–14.5) R S, et al. Reg Anesth Pain Med 2023;0:1–6. doi:10.1136/rapm-2023-104542

DISCUSSION
In this randomized, double blinded clinical trial we found, 20 mL of bupivacaine–lidocaine mixture significantly increased the proportion of patients who experienced CCB within the first 40 min of observation (95% vs 48%; p = 0.0001) compared with bupivacaine alone, and extended the duration of postoperative analgesia (8.3 vs 4 hours; p = 0.0001) compared with lidocaine alone during USG-SCBPB.

As the final needle tip position and injection techniques like subfascial/extra fascial, targeted intracluster and selective truncal analgesia (8.3 vs 4 hours; p = 0.0001) compared with lidocaine alone during USG-SCBPB.
fibers/distal nerves arising from core fibers), the definition of a successful block (sensory onset/motor onset/time to readiness for surgery/CCB) and the volume/concentration of LA administered.

Gadsen et al compared the onset of sensory blockade in the AN territory (a proximal nerve) following ISB and concluded that there was no significant difference between the LA mixture and bupivacaine.\(^5\) However, according to the same study, the sensory block in the UN region (a distal nerve) was substantially lower in bupivacaine group compared with the mixture (13 vs 26%; \(p=0.03\)) even an hour after the procedure. Even though the ulnar sparing is a well-known fact during ISB, since the performer and the injection techniques were same, the difference in the incidence of UN sparing between the two groups of ISB can only be attributed to the pharmacodynamic difference of LA mixture over bupivacaine. Even in our study, a higher percentage of patients had achieved CCB of the proximal nerves (MCN, RN) than the distal nerves (UN, MN) at the various time points in all three groups. The gap was very prominent in group B, where at the end of 40 min, 100% of the patients had achieved CCB of MCN and RN but only 48% had achieved the same for the UN and MN (figure 4). Various laboratory investigations have demonstrated that highly lipid-soluble drugs like bupivacaine enter the membrane faster with greater efficacy, however, this benefit is negated by their avid non-specific binding to adventitia, perineurium, and superficial fascicles (mantle fibers). This limits their diffusion across different tissue barriers. Lidocaine on the other hand is one-tenth as lipophilic as bupivacaine (by octanal-to-buffer partition coefficient), and 2.5 times more permeant through the perineural sheath.\(^{12,13}\) Thus, the slow onset of bupivacaine became evident at distal nerves (core fibers) as opposed to proximal nerves (mantle fibers).

The spectrum of conduction blockade following PNB ranges from normal sensory and motor function on one end to the CCB (complete loss of sensation (anesthesia) and motor paralysis (power 0/5, 1/5)) at the other end. Between the two extremes, the onset of sensory block, the onset of motor block, time to readiness for surgery, and surgical anesthesia are various endpoints requiring progressively more soakage time. The soakage time is primarily required for the intraneural diffusion and blockade of all types of nerve fibers.\(^{14}\) A portion of the injected drug may, however, be lost due to extraneural diffusion. The pharmacodynamic difference between lidocaine and bupivacaine becomes very evident when we compare the final point in the conduction blockade spectrum, especially in the larger-diameter nerves. Cuvinillon et al demonstrated a faster onset of CCB with a mixture of lidocaine and bupivacaine compared with bupivacaine alone during both femoral and sciatic nerve blocks.\(^{15}\) Similarly, in our study, when we compared the progress of conduction blockade through TCS, we can appreciate significant degree of conduction blockade even at the end of 10 min in the bupivacaine group. However, to reach the CCB in all patients, it took beyond 40 min. Furthermore, that the TCS variation was much higher at all-time intervals makes bupivacaine more unpredictable for

![Figure 3](http://rapm.bmj.com/)

**Figure 3** Total composite score at different time intervals is represented as mean±SD. *group L vs group B; \(p<0.05\). #group LB vs group B and group L; \(p<0.05\).

![Figure 4](http://rapm.bmj.com/)

**Figure 4** Kaplan-Meier plot of the proportion of patients with complete conduction block of the four terminal nerves by the time shown in all three groups. Group-L; \(p=0.36\), group LB; \(p=0.06\), group B; \(p<0.001\). CCB, complete conduction blockade.

![Figure 5](http://rapm.bmj.com/)

**Figure 5** Kaplan-Meier plot of the proportion of patients reporting pain by the time shown. Group L vs LB; \(p<0.001\), group LB vs B; \(p<0.001\).
CONCLUSION

Clinical research looking at the dynamics of LA mixtures has produced contradictory results, due to methodological differences. Clinically significant pharmacodynamic variations are discernible when LA dose close to MELAV and MEC is accurately deposited within the Brachial Plexus sheath, and CCB is determined. At 20 mL local anesthetic volume, the equal mixture of lidocaine and bupivacaine provided significantly faster onset of CCB compared with bupivacaine alone and longer duration of postoperative analgesia compared with lidocaine alone but shorter than bupivacaine alone during USG-SCBPB.

REFERENCES


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### Details of Principal Investigator

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<td>Professor</td>
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<tr>
<td>Affiliation</td>
<td>MGMCR, Puducherry</td>
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<tr>
<td>Address</td>
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</tr>
<tr>
<td>Phone</td>
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<td>Fax</td>
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<tr>
<td>Email</td>
<td><a href="mailto:docsripriya@gmail.com">docsripriya@gmail.com</a></td>
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2. History of bleeding disorders
3. Local infection at the site of block
4. Pre-existing neurological deficit
5. Cardio-Respiratory compromise.
6. Known allergy to local anesthetic drug.
7. Patients in whom the supraclavicular sono-anatomy is not clear.

Method of Generating Random Sequence
Permuted block randomization, variable

Method of Concealment
Sequentially numbered, sealed, opaque envelopes

Blinding/Masking
Participant, Investigator and Outcome Assessor Blinded

Primary Outcome
Outcome: to compare time to complete conduction block in the four terminal nerve areas
Timepoints: 10, 20, 30, 40 minutes

Secondary Outcome
Outcome: to compare the duration of analgesia in the three groups
Timepoints: 10, 20, 30, 40 minutes

Target Sample Size
Total Sample Size: 63
Sample Size from India: 63
Final Enrollment numbers achieved (Total): 0
Final Enrollment numbers achieved (India): 0

Phase of Trial
Phase 1

Date of First Enrollment (India)
01/12/2020

Date of First Enrollment (Global)
No Date Specified

Estimated Duration of Trial
Years: 0
Months: 6
Days: 0

Recruitment Status of Trial (Global)
Not Applicable

Recruitment Status of Trial (India)
Completed

Publication Details
There are no publications yet. nil.

Brief Summary
In this study one group of patients will be receiving block with a drug that is fast acting. One group of patients will be receiving block with a drug that takes some more time to begin acting. Yet another group will receive a combination of the two drugs. You will have an equal chance of being included in any of the groups. After the injection is done, we will test you at 10 minute intervals to get information on how much time it takes to produce complete loss of sensation and complete loss of motor power. After that, the surgery will begin. After the surgery is over, we will continue to follow up till you first perceive pain.
To determine the latency of three local anaesthetic solutions during ultrasound guided supraclavicular brachial plexus block for forearm bone surgeries – A double blind randomized control trial.

DR. R. SRIPRIYA DNB (Anaes)
PROFESSOR
DEPARTMENT OF ANAESTHESIOLOGY
MGMCRI
PRINCIPLE INVESTIGATOR

DR. R. SRIPRIYA  DNB (Anaes)
Designation: Professor
Specialty: Anaesthesiology
Phone Number: 9365815939
email: docsripriya@gmail.com

COINVESTIGATORS

Dr. T. SIVASHANMUGAM. MD, FRCP, DNB, PDCC
Professor
Department of Anaesthesiology
094425 05567
drsiva95@gmail.com
1 INTRODUCTION

The onset of complete conduction blockade following supraclavicular brachial plexus block depends on two major factors namely the proximity of injected drug to the neural elements and the drug characteristics. Proximity to the neural elements depends on the guidance (landmark, nerve stimulator, ultrasound) used (1). Consistent success with ultrasound guided multipoint sub-fascial injection of SCBP has been previously demonstrated.

Among the drug characteristics, the type of local anaesthetic (rapid onset-short acting vs slow onset-long acting), volume and concentration of LA are the important drug characteristics influencing onset. Combination of local anesthetics is used frequently to compensate for the delayed onset of one agent (bupivacaine) and the short duration of action of the other agent (Lignocaine) (3,4). Miller has cautioned on the use of maximum doses of two LA in a mixture as the toxicity of such combinations are additive (5).

Clinical studies evaluating the efficacy of such combinations provided variable results due to the differences in guidance device, injection techniques, local anesthetic drug as well as the clinical end points used for defining success. Jeff Gadsden et al have observed that, for ultrasound guided interscalene block, a combination of mepivacaine 1.5% and bupivacaine 0.5% resulted in a block onset similar to either anaesthetic alone (6). However, in our clinical experience, we have observed that the onset of action of SCBPB is delayed with bupivacaine when compared to drug combinations.

Hence, we designed this study to determine the effect of lignocaine- bupivacaine combination with either drug given alone on block onset of complete conduction blockade and duration of analgesia during Ultrasound Guided Supraclavicular Brachial Plexus Block.

2 AIMS AND OBJECTIVES

1. **Aim**: To assess the onset of complete conduction blockade and Duration of Analgesia following SCBPB using three different LA solutions. 20 ml of equivolume mixture of 0.5% bupivacaine + 2% lignocaine (2.5 mcg/ml adrenaline), 20 ml 0.5% bupivacaine and 20 ml of 2% lignocaine (5 mcg/ml adrenaline).

2. **Objectives:**
a. To compare the time to complete sensory block in each of 4 major nerve distribution areas: Median, Radial, Ulnar, Musculocutaneous nerves on an qualitative scale of 0, 1, 2 in the three groups.

b. To compare the time to complete Motor Block in each of 4 major nerve distribution areas: Medial, Radial, Ulnar, Musculocutaneous nerves on an qualitative scale of 0, 1, 2 in the three groups.

c. To compare the Duration of Analgesia in the three groups.

3 REVIEW OF LITERATURE

1) Two different techniques of injecting local anaesthetic drugs under ultrasound guidance for supraclavicular Brachial Plexus Block was compared by Sivashanmugam et al. They performed a randomised comparative study in 32 patients undergoing upper extremity surgery. A 1:1 mixture of local anaesthetics (2% lignocaine with adrenaline and 0.5% bupivacaine) 25 ml was injected subfascially or extrafascially to the brachial plexus sheath. They assessed the Block Onset time and duration of post operative analgesia. Their study concluded that subfascial injection provided faster onset (7 ± 3) min than extrafascial (20 ± 10) min and longer duration of analgesia subfascial (9.3 ± 1.4) and extrafascial (6.1 ± 1.4) hours.

2) That mixing of two types of local anaesthetics (faster onset with intermediate duration and slower onset with long duration) would reduce the peripheral nerve block onset by 20% or more than using long acting local anaesthetics was stated by Laur JJ et al. They performed a randomised triple blinded study in 3 study groups in 93 patients (GROUP 1 - 1.5% mepivacaine with epinephrine, GROUP 2 - 1.5% mepivacaine with epinephrine and 0.5% bupivacaine, GROUP 3 - 0.5% bupivacaine alone for Infraclavicular block. Their study concluded that 1.5% mepivacaine with epinephrine and 0.5% bupivacaine produced faster onset 17(12-21) min than 0.5% bupivacaine alone 21(12-24) min in Landmark Guided Infraclavicular Block.
3) Whether addition of 2% Lignocaine to 0.5% bupivacaine provided a decreased block onset time and drug effect time when compared with 0.5% bupivacaine alone in landmark guided Lateral Sagittal infraclavicular block was investigated by Ozgur OZMEN et al. The study was carried out in 120 patients undergoing upper extremity surgery who were randomly divided into 3 groups each group containing 40 patients. Group B received 20ml of 0.5% bupivacaine, Group B+L received 10ml of 0.5% bupivacaine + 10ml of 2% lignocaine and Group L received 20ml of 2% lignocaine. Their study concluded that the block onset time is very long in Group B (9.7 + 1.86) min than other two groups [Group B+L 4.0 + 1.31 min , Group L 4.4 + 1.03 min ]. Group B+L produced prolonged duration of analgesic (6.1 + 2.21) hours than Group B (4.4 + 1.21) hours & Group L (2.6 + 0.62) hours.

4) A study to know whether mixing of two local anaesthetic agents and by increasing their concentration would provide early onset of action and long duration of analgesia in landmark guided supraclavicular brachial plexus block was conducted by Raizada et al. The study was performed in 3 study groups, each group containing 20 patients. Group 1 - received 30 ml of 1% Lignocaine with Adrenaline, Group 2 - received 10 ml of 1.5% lignocaine and 20 ml of 0.25% Bupivacaine, Group 3 - received 10 ml of 2% lignocaine and 20 ml of 0.5% bupivacaine. Out of the above three groups Group 2 (13.91 + 5.21 min) and Group 3 (11.25 + 5.79 min) had faster onset of action than Group 1 (21.17 + 4.19 min) and long duration of block: Group 1 - 59.2 + 33.2 min > Group 2 - 486.17 + 109.3 min < Group 3 - 515.9 + 138.4 min. Their study concluded that addition of lignocaine to bupivacaine provided early onset and the combination of 2% lignocaine and 0.5% bupivacaine was found to be the best choice for long and emergency operative procedures.

5) That mixture of short acting and long acting local anaesthetics are used in daily practice but there is lack of information over the advantages of such mixture was proposed by JeffGadsden et al. Therefore they performed a study in 64 patients undergoing arthroscopic shoulder surgery in 3 random groups receiving (30ml of 1.5% mepivacaine, 30 ml of 0.5% bupivacaine, mixture of 15ml of 0.5% bupivacaine and 15ml of 1.5% Mepivacaine) to study latency of block onset and duration of analgesia in ultrasound guided Interscalene block. Their study revealed that, under ultrasound guidance the onset of block for the drug mixture 1.5% mepivacaine with 0.5% bupivacaine (11.3 + 5.3 min) was longer either local anaesthetics 1.5% mepivacaine (8.7 + 4.3 min) &
0.5% bupivacaine (10.0 + 5.1 min) alone. Therefore, mixture of the two local anaesthetic
drugs didn't provide any significant change in onset of action. Moreover the duration of analgesia was high in 0.5% Bupivacaine (14.0 + 6.2 hours) than mixture of 1.5% mepivacaine with 0.5% bupivacaine (10.3 + 4.9 hours).

4 RESEARCH HYPOTHESIS

A mixture of lignocaine and bupivacaine provides quicker onset when compared to bupivacaine given alone and prolonged analgesia when compared to lignocaine given alone.

5 SUBJECTS AND METHODS

After obtaining IRC and Ethical committee approval the study will be conducted in Mahatma Gandhi Medical College and Research.

Study population
Patients undergoing elective or emergency upper limb bone surgeries in MGMCRI will form our study population.

Inclusion criteria:
Patients belonging to the age group 18-60 years with ASA grade I and grade II undergoing elective or emergency procedure for upper limb bone surgeries at or below the elbow.

Exclusion criteria:
1. Patient refusal for the block. Patients refusing the block will be administered general anaesthesia.
2. History of bleeding disorders
3. Local infection at the site of block
4. Pre-existing neurological deficit
5. Cardio-Respiratory compromise.
6. Known allergy to local anesthetic drug.
7. Patients in whom the supraclavicular sono-anatomy is not clear.
Sample size

“Statistics and Sample Size” App (version 5.0 developed by Thai Thanh Truc) was used to calculate the sample size. In a pilot study in ten patients, we observed that the onset of complete conduction block with drug combination was $19 \pm 11$ minutes, while with bupivacaine it was $30 \pm 12$ minutes. With an alpha error of 0.05 and power of 80%, the minimum sample size was estimated to be 18 in each group. To take into account the drop-outs, 63 patients from the study population meeting the inclusion criteria will be recruited.

All consecutive patients posted for upper extremity surgery will be screened for recruitment—continuous sampling.

Patients will be Randomised to any one of the three study groups:

- **Group LB**: Patients receiving 10ml 0.5% bupivacaine + 10 ml 2% lignocaine with adrenaline pre-mixture.
- **Group L**: Patients receiving 20 ml 2% lignocaine with adrenaline premixture.
- **Group B**: Patients receiving 20 ml 0.5% bupivacaine.

Randomization will be done using block randomization technique. Each block will contain 9 envelopes, 3 belonging to each group. Patients were randomized to one of the three study groups: lignocaine- bupivacaine (Group LB), bupivacaine (Group B) or lignocaine (Group L) by drawing sealed envelopes that contained a card with the group name written in it. A resident of anesthesia, who was not involved in the study, will generate the envelopes.

All the blocks will be performed in the procedure room under standard monitoring (electrocardiography, pulseoximetry and non-invasive blood pressure). An 18-gauge IV line will be secured. An IV sedation of 2mg midazolam will be given before the ultrasound procedure. The patient will be positioned with the arms by the side. All blocks will be performed under ultrasound guidance by using high frequency linear probe (HFL50) by one of the two investigators. Patients will be randomly allocated into anyone of the groups by selecting a sealed envelope contain the allocated group.

The drug preparation will be performed by an independent anesthesiology resident blinded to the study. For the bupivacaine group- Group B, 20 ml of 0.5% bupivacaine will be
used for BPB. For the lignocaine-bupivacaine group – Group LB, a combination of 10 ml 2% lignocaine with adrenaline and 10 ml 0.5% bupivacaine will be used for BPB.

For Group L, 20 ml of lignocaine with adrenaline mixture will be used. The study drug will be loaded in 20 ml syringe connected to a 100-centimeter pressure monitoring line and 25-gauge spinal needle.

The brachial plexus will be scanned close to the subclavian artery as a bunch of grapes (Multiple small hypoechoic nodules embedded in a hyper echoic area and encircled by a hyper echoic line). The study drug will be injected subfascial as described previously by the investigators\(^1\). Adequate spread of local anesthetics will be confirmed by USG imaging. If necessary, the needle will be repositioned for adequate spread. The person performing the block will take no further part in data collection.

**Assessment**

After a satisfactory drug deposition, the Final Needle removal will be noted as block time. Since then, the neurological assessment will be done by an Observer blinded to group allocation, every 10 min till 40 minutes.

Sensory Blockade will be assessed on a three-point Qualitative Scale for perseverance of cold sensation to Ether-soaked cotton.

0 - perceives both touch and temperature
1 - perceives only the touch but not the temperature
2 - perceives neither touch nor temperature

Sensory Blockade will be assessed in the territories of Musculocutaneous nerve (MCN) - Lateral forearm, Median Nerve (MN) – Tip of Middle Finger, Ulnar Nerve (UN) – Little Finger and Radial Nerve (RN) – Anatomical snuff box. Score of 2 in all the 4 nerve distribution area will be taken as **time for complete sensory block**.

Motor Blockade will be assessed on a 3 point Qualitative Scale.

0 - Normal Motor Function (Power 4/5, 5/5)
1 - Decreased Motor Function (Power 3/5, 2/5)
2 - No Motor Power (Power 0/5, 1/5)

for the Four Terminal Branches (Elbow Flexion - Musculocutaneous Nerve, Thumb Opposition - Median Nerve, Thumb Adduction - Ulnar Nerve, Thumb Abduction- Radial Nerve). Score of 2 in all the 4 nerve distribution area will be taken as **time for complete motor block**.
After starting the surgery if the patient feels discomfort at the surgical site another supplementation of 1mcg/kg Fentanyl will be given intravenously. Block will be considered failed if the patient complains of pain or requires more than 2mcg/kg Fentanyl. Further anesthetic management will be decided by the attending Anesthesiologist.

Inside the operating room, patients will be sedated for comfort before the start of surgery using intravenous midazolam 1 mg and fentanyl 1 µg/kg. Block will be considered a failure if the patients complained of pain during any stage of surgery or required any form of rescue analgesic interventions. Post-operatively, patients will be instructed to inform when they perceive pain at the surgical site and receive Inj.Acetaminophen 1 gm and ketorolac 30 mg intravenously and subsequently put on regular oral analgesics as per departmental acute pain service protocol. The time gap from Time 0 to the first perception of pain by the patient will be taken as the duration of analgesia. 24-hours later, the patients will be questioned for the presence of paresthesia, dysesthesia, or motor weakness in the operated limb.

5.1 FLOW-CHART TO SUMMARIZE THE SEQUENCE

OFEVENTS

Patients undergoing surgery in MGCRI

Pre anesthetic evaluation

\[
\text{Inclusion criteria: ASA 1 and 2 patients of both sex between the age of 18 to 60 years, forearm bone surgeries.}\n\]

\[
\text{Exclusion criteria: h/o LA allergy, coagulopathy, difficult sonoanatomy, baseline neurological deficit, infection at the site of block, respiratory compromise.}\n\]

Premedication with T. Ranitine 150 mg PO, T. Metoclopramide 10 mg PO, T. Alprazolam 0.5mg PO on the night before surgery and on the day morning
Permutated block randomization using sealed envelope technique.

- **Group L**
  - (2% lignocaine with 5mcg/cc Adrenaline 20 ml)

- **Group B**
  - (0.5% bupivacaine 20 ml)
  - **Group LB**
    - (2% lignocaine with

Post surgery

1. Time to first analgesic requirement. Testing in the four major nerve distributions @ 10, 20, 30 & 40
### 5.2 STUDY TERMINATION

Study will be terminated once sample size is obtained

### 6 STUDY VARIABLES

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<td>Chi square test</td>
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7 REFERENCES


2. Laur, John J, Emine Ozgur Bayman, Peter J. Foldes, and Richard W Rosenquist. “Triple-Blind Randomized Clinical Trial of Time until Sensory Change Using 1.5% Mepivacaine with Epinephrine, 0.5% Bupivacaine, or an Equal Mixture of Both for Infraclavicular Block.” Regional Anesthesia and Pain Medicine 2012;37:28–33.


8 PRELIMINARY WORK DONE ALREADY

Pilot study on 10 patients.

9 ETHICAL ISSUES

This study involves humans and requires frequent testing of sensory and motor blockade.

Only temperature and light touch is used for sensory assessment.

In case of surgery exceeding block duration, general anesthesia will be administered.

The study falls in the “more than minimal risk” category. Combination of local anaesthetics used in the present study, is regularly used for peripheral nerve blocks.
10 INFORMED CONSENT PROCEDURE

During the preanaesthetic visit, the procedure will be explained to the patient. They will be informed that there are three arms in the study and they will have an equal chance of entering into either arm. This will be explained in their own language and consent will be obtained for including them in the study.

11 QUALITY CONTROL

Name of Officer designated by the department for quality control:
Dr. VR Hemanth Kumar
Professor & Head
Department of anaesthesiology
9003550553
drvrhk@gmail.com

12 SPONSORSHIPS

NIL
13 INVESTIGATORS DECLARATION

This is to certify that the protocol entitled “To determine the latency of three local anaesthetic solutions during ultrasound guided supraclavicular brachial plexus block- A double blind randomized control trial.” was reviewed by us for submission to the SBV Institutional Ethics Committee and certified that this protocol represents an accurate and complete description of the proposed research. We have read the ICMR guidelines, ICP-GCP guidelines/CPCSEA guidelines/and other applicable guidelines and undertake to ensure that the rights and welfare of the study subjects are protected.

The study will be performed as per the approved protocol only. If any deviation is warranted, the same will be presented to the ethical committee and permission will be sought. We assure that the study will be terminated immediately in case of any unforeseen adverse consequences and we will inform the same to the ethical committee immediately.

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<tr>
<td>Investigator</td>
<td>Dr. Sripriya. R</td>
<td>Professor, Dept. of Anesthesiology</td>
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<tr>
<td>Co-Investigator</td>
<td>Dr. T. Sivashanmugam</td>
<td>Professor, Dept. of Anesthesiology</td>
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**Patient/Participant Information Sheet (PIS)**

(Information for Participants of the Study)

We welcome you and thank you for having accepted our request to consider whether you can participate in our study. This sheet contains the details of the study, the possible risks, discomfort and benefits for the participants are also given. You can read and understand by yourself; if you wish, we are ready to read and explain the same to you.

If you do not understand anything or if you want any more details we are ready to provide the details.

1. **What is the title of the Research Project?**

   "To determine the latency of three local anaesthetic solutions for ultrasound guided supraclavicular brachial plexus block – A double blind randomized control trial."

2. **Who/where is this study being conducted?**

   This study is being conducted by Dr. SRIPRIYA. R, professor, department of anaesthesiology, M GMCRI

3. **What is the purpose of the study?**

   Different types of drugs are used around nerves for blocking pain during regional anaesthesia. A few of them start acting fast, but provide short duration of pain relief. A few of these drugs start acting late, but provide long duration of pain relief. By combining them, we get the advantages of either drug used alone. In this study we want to find out the onset of action when a combination of these drugs is used and the duration of pain relief provided by combining them for supraclavicular brachial plexus block. The procedure will be done under ultrasound guidance.

4. **Procedure/Methods of the study (in brief, simple non-technical terms)**

   In this study one group of patients will be receiving block with a drug that is fast acting. One group of patients will be receiving block with a drug that takes some more time to begin acting. Yet another group will receive a combination of the two drugs. You will have an equal chance of being included in any of the groups. After the injection is done, we will test you at 10 minute intervals to get information on how much time it takes to produce complete loss of sensation and complete loss of sensation.
motor power. After that, the surgery will begin. After the surgery is over, we will continue to follow up till you first perceive pain.

5. **How long you are expected to participate in this study?**

   We will be visiting you after the surgery is over to get information on when you are beginning to first perceive pain. Once you perceive pain, the time will be noted and we will give you medicines for pain relief. After that the study ends.

6. **Why I am being considered as one of the participant?**

   You have been chosen as you are undergoing surgery for forearm bone fracture and this block will give you pain relief both during the surgery and even after the surgery is over.

7. **Should I definitely have to take part in this study?**

   No. If you do not wish to participate you will not be included in this study. Also you will continue to get the medical treatment without any prejudice.

8. **If I am participating in this study, what are my responsibilities? (Responsibility of the individual as a participants)**

   Being a participants in this study your responsibility are :1. To cooperate during preanesthetic checkup 2. To cooperate when the block action is being checked 3. To inform us when you first perceive pain after surgery is over.

9. **Are there any benefits for me/Public?**

   The results of the study may benefit future patients. This study will give us information on whether there is any use in combining these drugs.

10. **Will there be any discomfort / risks to me?**

    No risks. But some discomferts may be there. You may have mild pain on the needle insertion. We will be giving medicines at the needle prick site to reduce it. Risk will be the same as for any block.

11. **Will by participating in this study, my personal details will be kept confidentially?**

    Your participation in the study and the study records relating to you will be kept confidential throughout the study and thereafter. Your personal identity will not be revealed in case of publication in any journal or analysis of your results, nor will it be
shared with anyone. The study records relating to you will be preserved for a period of three (if academic Research)/ five years (if clinical trial) for analysis and follow up.

12. Will I be paid for participating in the Study?
No, you will not be paid for participating in the study.

13. Can I withdraw from this study at any time during the study period?
Your participation in the study is purely voluntary. You are free to withdraw from the study at any time without assigning any reason. Your withdrawal from the study would in no way affect the medical care or other benefits which you are otherwise entitled to receive from the Institute.

14. Possible current and future uses of the biological material to be generated from the research and if the material is likely to be used for secondary purposes or would be shared with others, for which we seek your permission prior to the study inclusion?
Not applicable.

15. Possible current and future uses of the data to be generated from the research and if the data is likely to be used for secondary purposes or would be shared with others, for which we seek your permission prior to the study inclusion?
The data collected from you may be utilized for further analysis in future, if needed. All the data obtained from you will be used only for research purposes. It will not be used for any secondary purpose nor will it be shared with others. In case of analysis of your data in any publication in any journal, your identification will not be revealed.

16. Will I be informed of this study’s results and the findings?
Yes, on your request the results of the study and its findings you will be informed.

17. Provision of free treatment for research related injury.
Not applicable. The procedure and drug used in the study is used routinely for anaesthetic management of patients with fractures of upper limb. Hence no research related injury is involved in the study.
18. Compensation to the participant for death or disability arising out of foreseeable and unforeseeable risks attributable to the study.

Not applicable. The procedure and drug used in the study is used routinely for anaesthetic management of patients with fractures of upper limb. Hence no research related injury is involved in the study.

Address and mobile number of the Principal Investigator (PI) and Co-PI, if any:

Dr Sripriya.R, Professor, Dept of anaesthesiology, MGCRI
9365815939.

Dr Sivashanmugam. T, Professor, Dept of anaesthesiology, MGCRI
9442505567

Address and telephone number of the IHEC office, MGCRI

Office of Institutional Human Ethics Committee, 1st floor college block (Adjacent to dept. of Pathology), MGCRI, Puducherry 607 402. Phone No.: 0413- 2616700 (Extn No.: 754)

Signature of the Participant     Signature of the Investigators
MAHATMA GANDHI MEDICAL COLLEGE AND RESEARCH INSTITUTE
PUDUCHERRY

FORM FOR GETTING INFORMED CONSENT FOR THOSE PARTICIPATING IN THE RESEARCH PROJECT

Name of the Research Project

“To determine the latency of three local anaesthetic solutions for ultrasound guided supraclavicular brachial plexus block – A double blind randomized control trial.”

I ____________________ have been informed about the details of the study in own language.

I have understood the details about the study.

I know the possible risks and benefits for me, by taking part in the study.

I understand that I can withdraw from the study at any point of time and even then, I will continue to get the medical treatment as usual.

I understand that I will not get any payment for taking part in this study.

I will not object if the results of this study are getting published in any medical journals, provided my personal identity is not reviewed.

I know what I am supposed to do by taking part in this study and I assure that I will give my full co-operation for this study.

I nominate --------------------- (name) (mention the relation) to be my dependant to receive compensation if any.

Signature/Thumb impression of the participant (Name/Address/Occupation/Monthly income)

__________________________________          __________________________________

Signature/Thumb impression of the witness (Name/Address)

__________________________________ __________________________________

Name & Signature of the investigator

__________________________________
**Clinical Trial Details (PDF Generation Date :- Tue, 21 Mar 2023 08:29:02 GMT)**

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<tbody>
<tr>
<td>&gt; Mahatma Gandhi Mediical College and research Institute, Pilliyarkuppam, Pondicherry 607402</td>
<td></td>
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</table>

### Primary Sponsor

**Name**: nil  
**Address**: NA  
**Type of Sponsor**: Other [NA]

### Details of Secondary Sponsor

**Name**: NIL  
**Address**: NIL

### Countries of Recruitment

**List of Countries**: India

### Sites of Study

<table>
<thead>
<tr>
<th>Name of Principal Investigator</th>
<th>Name of Site</th>
<th>Site Address</th>
<th>Phone/Fax/Email</th>
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<tbody>
<tr>
<td>sripriya R</td>
<td>MGCRI</td>
<td>Department of anaesthesiology, 2nd floor, OT complex Pondicherry PONDICHERRY</td>
<td>9365815939 <a href="mailto:docsripriya@gmail.com">docsripriya@gmail.com</a></td>
</tr>
</tbody>
</table>

### Details of Ethics Committee

**Name of Committee**: Institutional human ethics committee  
**Approval Status**: Approved  
**Date of Approval**: 25/09/2020  
**Is Independent Ethics Committee?**: No

### Regulatory Clearance Status from DCGI

**Status**: Not Applicable  
**Date**: No Date Specified

### Health Condition / Problems Studied

<table>
<thead>
<tr>
<th>Health Type</th>
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<tr>
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### Intervention / Comparator Agent

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<th>Name</th>
<th>Details</th>
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<tr>
<td>Intervention</td>
<td>three local anaesthetics for supraclavicular brachial plexus block</td>
<td>Group LB: Patients receiving 10ml 0.5% bupivacaine + 10 ml 2% lignocaine with adrenaline pre-mixture.</td>
</tr>
<tr>
<td>Comparator Agent</td>
<td>local anesthetic drugs</td>
<td>Group L: Patients receiving 20 ml 2% lignocaine with adrenaline premixture. Group B: Patients receiving 20 ml 0.5% bupivacaine.</td>
</tr>
</tbody>
</table>

### Inclusion Criteria

| Age From | 18.00 Year(s) |
| Age To | 60.00 Year(s) |
| Gender | Both |

### Exclusion Criteria

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<tr>
<td>1. Patient refusal for the block. Patients refusing the block will be administered general anaesthesia.</td>
<td></td>
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</tbody>
</table>
In this study one group of patients will be receiving block with a drug that is fast acting. One group of patients will be receiving block with a drug that takes some more time to begin acting. Yet an other group will receive a combination of the two drugs. You will have an equal chance of being included in any of the groups. After the injection is done, we will test you at 10 minute intervals to get information on how much time it takes to produce complete loss of sensation and complete loss of motor power. After that, the surgery will begin. After the surgery is over, we will continue to follow up till you first perceive pain.
To determine the latency of three local anaesthetic solutions during ultrasound guided supraclavicular brachial plexus block for forearm bone surgeries – A double blind randomized control trial.

DR. R. SRIPRIYA  DNB (Anaes)
PROFESSOR
DEPARTMENT OF ANAESTHESIOLOGY
MGMCRI
PRINCIPLE INVESTIGATOR

DR. R. SRIPRIYA  DNB (Anaes)
Designation: Professor
Specialty: Anaesthesiology
Phone Number: 9365815939
email: docsripriya@gmail.com

COINVESTIGATORS

Dr. T. SIVASHANMUGAM. MD, FRCP, DNB, PDCC
Professor
Department of Anaesthesiology
094425 05567
drsiva95@gmail.com
1 INTRODUCTION

The onset of complete conduction blockade following supraclavicular brachial plexus block depends on two major factors namely the proximity of injected drug to the neural elements and the drug characteristics. Proximity to the neural elements depends on the guidance (landmark, nerve stimulator, ultrasound) used (1). Consistent success with ultrasound guided multipoint sub-fascial injection of SCBP has been previously demonstrated.

Among the drug characteristics, the type of local anaesthetic (rapid onset-short acting vs slow onset-long acting), volume and concentration of LA are the important drug characteristics influencing onset. Combination of local anesthetics is used frequently to compensate for the delayed onset of one agent (bupivacaine) and the short duration of action of the other agent (Lignocaine) (3,4). Miller has cautioned on the use of maximum doses of two LA in a mixture as the toxicity of such combinations are additive (5).

Clinical studies evaluating the efficacy of such combinations provided variable results due to the differences in guidance device, injection techniques, local anesthetic drug as well as the clinical end points used for defining success. Jeff Gadsden et al have observed that, for ultrasound guided interscalene block, a combination of mepivacaine 1.5% and bupivacaine 0.5% resulted in a block onset similar to either anaesthetic alone (6). However, in our clinical experience, we have observed that the onset of action of SCBPB is delayed with bupivacaine when compared to drug combinations.

Hence, we designed this study to determine the effect of lignocaine-bupivacaine combination with either drug given alone on block onset of complete conduction blockade and duration of analgesia during Ultrasound Guided Supraclavicular Brachial Plexus Block.

2 AIMS AND OBJECTIVES

1. **Aim**: To assess the onset of complete conduction blockade and Duration of Analgesia following SCBPB using three different LA solutions. 20 ml of equivolume mixture of 0.5% bupivacaine + 2% lignocaine (2.5 mcg/ml adrenaline), 20 ml 0.5% bupivacaine and 20 ml of 2% lignocaine (5 mcg/ml adrenaline).

2. **Objectives:**
a. To compare the time to complete sensory block in each of 4 major nerve distribution areas: Median, Radial, Ulnar, Musculocutaneous nerves on an qualitative scale of 0, 1, 2 in the three groups.
b. To compare the time to complete Motor Block in each of 4 major nerve distribution areas: Medial, Radial, Ulnar, Musculocutaneous nerves on an qualitative scale of 0, 1, 2 in the three groups.
c. To compare the Duration of Analgesia in the three groups.

3 REVIEW OF LITERATURE

1) Two different techniques of injecting local anaesthetic drugs under ultrasound guidance for supraclavicular Brachial Plexus Block was compared by Sivashanmugam et al. They performed a randomised comparative study in 32 patients undergoing upper extremity surgery. A 1:1 mixture of local anaesthetics (2% lignocaine with adrenaline and 0.5% bupivacaine) 25 ml was injected subfascially or extrafascially to the brachial plexus sheath. They assessed the Block Onset time and duration of post operative analgesia. Their study concluded that subfascial injection provided faster onset (7 +3) min than extrafascial (20 + 10 ) min and longer duration of analgesia subfascial (9.3 + 1.4 ) and extrafascial (6.1 + 1.4) hours.

2) That mixing of two types of local anaesthetics (faster onset with intermediate duration and slower onset with long duration )would reduce the peripheral nerve block onset by 20% or more than using long acting local anaesthetics was stated by Laur JJ et al. They performed a randomised triple blinded study in 3 study groups in 93 patients (GROUP 1- 1.5% mepivacaine with epinephrine, GROUP 2 - 1.5% mepivacaine with epinephrine and 0.5% bupivacaine, GROUP 3 - 0.5% bupivacaine alone for Infraclavicular block. Their study concluded that 1.5% mepivacaine with epinephrine and 0.5% bupivacaine produced faster onset 17(12-21) min than 0.5% bupivacaine alone 21(12-24) min in Landmark Guided Infraclavicular Block.
3) Whether addition of 2% Lignocaine to 0.5% bupivacaine provided a decreased block onset time and drug effect time when compared with 0.5% bupivacaine alone in landmark guided Lateral Sagittal infraclavicular block was investigated by Ozgur OZMEN et al. The study was carried out in 120 patients undergoing upper extremity surgery who were randomly divided into 3 groups each group containing 40 patients. Group B received 20ml of 0.5% bupivacaine, Group B+L received 10ml of 0.5% bupivacaine + 10ml of 2% lignocaine and Group L received 20ml of 2% lignocaine. Their study concluded that the block onset time is very long in Group B (9.7 ± 1.86)min than other two groups [ Group B+L 4.0±1.31 min , Group L 4.4±1.03 min ]. Group B+L produced prolonged duration of analgesic (6.1 ± 2.21)hours than Group B (4.4 ± 1.21)hours & Group L (2.6 ± 0.62)hours.

4) A study to know whether mixing of two local anaesthetic agents and by increasing their concentration would provide early onset of action and long duration of analgesia in landmark guided supraclavicular brachial plexus block was conducted by Raizada et al. The study was performed in 3 study groups, each group containing 20 patients. Group 1 - received 30 ml of 1% Lignocaine with Adrenaline, Group 2 - received 10 ml of 1.5% lignocaine and 20 ml of 0.25% Bupivacaine, Group 3 - received 10 ml of 2% lignocaine and 20 ml of 0.5% bupivacaine. Out of the above three groups Group 2 (13.91±5.21min) and Group 3 (11.25±5.79 min) had faster onset of action than Group 1 (21.17+4.19 min) and long duration of block: Group 1 - 59.2+33.2 min > Group 2 - 486.17+109.3 min < Group 3 - 515.9+138.4 min. Their study concluded that addition of lignocaine to bupivacaine provided early onset and the combination of 2% lignocaine and 0.5% bupivacaine was found to be the best choice for long and emergency operative procedures.

5) That mixture of short acting and long acting local anaesthetics are used in daily practice but there is lack of information over the advantages of such mixture was proposed by JeffGadsden et al. Therefore they performed a study in 64 patients undergoing arthroscopic shoulder surgery in 3 random groups receiving (30ml of 1.5% mepivacaine, 30 ml of 0.5% bupivacaine, mixture of 15ml of 0.5% bupivacaine and 15ml of 1.5% Mepivacaine) to study latency of block onset and duration of analgesia in ultrasound guided Interscalene block. Their study revealed that, under ultrasound guidance the onset of block for the drug mixture 1.5% mepivacaine with 0.5% bupivacaine (11.3±5.3min) was longer either local anaesthetics 1.5 % mepivacaine (8.7 ± 4.3 min) &
0.5% bupivacaine (10.0 + 5.1 min) alone. Therefore, mixture of the two local anaesthetic drugs didn't provide any significant change in onset of action. Moreover the duration of analgesia was high in 0.5% Bupivacaine (14.0 + 6.2 hours) than mixture of 1.5% mepivacaine with 0.5% bupivacaine (10.3 + 4.9 hours).

4 RESEARCH HYPOTHESIS

A mixture of lignocaine and bupivacaine provides quicker onset when compared to bupivacaine given alone and prolonged analgesia when compared to lignocaine given alone.

5 SUBJECTS AND METHODS

After obtaining IRC and Ethical committee approval the study will be conducted in Mahatma Gandhi Medical College and Research.

Study population
Patients undergoing elective or emergency upper limb bone surgeries in MGMCRI will form our study population.

Inclusion criteria:
Patients belonging to the age group 18-60 years with ASA grade I and grade II undergoing elective or emergency procedure for upper limb bone surgeries at or below the elbow.

Exclusion criteria:
1. Patient refusal for the block. Patients refusing the block will be administered general anaesthesia.
2. History of bleeding disorders
3. Local infection at the site of block
4. Pre-existing neurological deficit
5. Cardio-Respiratory compromise.
6. Known allergy to local anesthetic drug.
7. Patients in whom the supraclavicular sono-anatomy is not clear.
Sample size

“Statistics and Sample Size” App (version 5.0 developed by Thai Thanh Truc) was used to calculate the sample size. In a pilot study in ten patients, we observed that the onset of complete conduction block with drug combination was 19±11 minutes, while with bupivacaine it was 30±12 minutes. With an alpha error of 0.05 and power of 80%, the minimum sample size was estimated to be 18 in each group. To take into account the drop-outs, 63 patients from the study population meeting the inclusion criteria will be recruited.

All consecutive patients posted for upper extremity surgery will be screened for recruitment—continuous sampling.

Patients will be Randomised to any one of the three study groups:

- **Group LB**: Patients receiving 10ml 0.5% bupivacaine + 10ml 2% lignocaine with adrenaline pre-mixture.
- **Group L**: Patients receiving 20ml 2% lignocaine with adrenaline premixture.
- **Group B**: Patients receiving 20ml 0.5% bupivacaine.

Randomization will be done using block randomization technique. Each block will contain 9 envelopes, 3 belonging to each group. Patients were randomized to one of the three study groups: lignocaine-bupivacaine (Group LB), bupivacaine (Group B) or lignocaine (Group L) by drawing sealed envelopes that contained a card with the group name written in it. A resident of anesthesia, who was not involved in the study, will generate the envelopes.

All the blocks will be performed in the procedure room under standard monitoring (electrocardiography, pulseoximetry and non-invasive blood pressure). An 18-gauge IV line will be secured. An IV sedation of 2mg midazolam will be given before the ultrasound procedure. The patient will be positioned with the arms by the side. All blocks will be performed under ultrasound guidance by using high frequency linear probe (HFL50) by one of the two investigators. Patients will be randomly allocated into any one of the groups by selecting a sealed envelope contain the allocated group.

The drug preparation will be performed by an independent anesthesiology resident blinded to the study. For the bupivacaine group- Group B, 20ml of 0.5% bupivacaine will be
used for BPB. For the lignocaine-bupivacaine group – Group LB, a combination of 10 ml 2% lignocaine with adrenaline and 10 ml 0.5% bupivacaine will be used for BPB.

For Group L, 20 ml of lignocaine with adrenaline mixture will be used. The study drug will be loaded in 20 ml syringe connected to a 100-centimeter pressure monitoring line and 25-gauge spinal needle.

The brachial plexus will be scanned close to the subclavian artery as a bunch of grapes (Multiple small hypoechoic nodules embedded in a hyper echoic area and encircled by a hyper echoic line). The study drug will be injected subfascial as described previously by the investigators. Adequate spread of local anesthetics will be confirmed by USG imaging. If necessary, the needle will be repositioned for adequate spread. The person performing the block will take no further part in data collection.

Assessment

After a satisfactory drug deposition, the Final Needle removal will be noted as block time. Since then, the neurological assessment will be done by an Observer blinded to group allocation, every 10 min till 40 minutes.

Sensory Blockade will be assessed on a three-point Qualitative Scale for perseverance of cold sensation to Ether-soaked cotton.

0 - perceives both touch and temperature
1 - perceives only the touch but not the temperature
2 - perceives neither touch nor temperature

Sensory Blockade will be assessed in the territories of Musculocutaneous nerve (MCN) - Lateral forearm, Median Nerve (MN) – Tip of Middle Finger, Ulnar Nerve (UN) – Little Finger and Radial Nerve (RN) – Anatomical snuff box. Score of 2 in all the 4 nerve distribution area will be taken as time for complete sensory block.

Motor Blockade will be assessed on a 3 point Qualitative Scale.

0 - Normal Motor Function (Power 4/5, 5/5)
1 - Decreased Motor Function (Power 3/5, 2/5)
2 - No Motor Power (Power 0/5, 1/5)

for the Four Terminal Branches (Elbow Flexion - Musculocutaneous Nerve, Thumb Opposition - Median Nerve, Thumb Adduction - Ulnar Nerve, Thumb Abduction - Radial Nerve). Score of 2 in all the 4 nerve distribution area will be taken as time for complete motor block.
After starting the surgery if the patient feels discomfort at the surgical site another supplementation of 1mcg/kg Fentanyl will be given intravenously. Block will be considered failed if the patient complains of pain or requires more than 2mcg/kg Fentanyl. Further anesthetic management will be decided by the attending Anesthesiologist.

Inside the operating room, patients will be sedated for comfort before the start of surgery using intravenous midazolam 1 mg and fentanyl 1 μg/m/kg. Block will be considered a failure if the patients complained of pain during any stage of surgery or required any form of rescue analgesic interventions. Post-operatively, patients will be instructed to inform when they perceive pain at the surgical site and receive Inj.Aacetaminophen 1 gm and ketorolac 30 mg intravenously and subsequently put on regular oral analgesics as per departmental acute pain service protocol. The time gap from Time 0 to the first perception of pain by the patient will be taken as the duration of analgesia. 24-hours later, the patients will be questioned for the presence of paresthesia, dysesthesia, or motor weakness in the operated limb.

5.1 FLOW-CHART TO SUMMARIZE THE SEQUENCE OF EVENTS

Patients undergoing surgery in MGMCRI

Pre anesthetic evaluation

Inclusion criteria: ASA 1 and 2 patients of both sex between the age of 18 to 60 years, forearm bone surgeries.
Exclusion criteria: h/o LA allergy, coagulopathy, difficult sonoanatomy, baseline neurological deficit, infection at the site of block, respiratory compromise.

Premedication with T. Ranitine 150 mg PO, T. Metoclopramide 10 mg PO, T. Alprazolam 0.5mg PO on the night before surgery and on the day morning
Permutated block randomization using sealed envelope technique.

**Group L**
(2% lignocaine with 5mcg/cc Adrenaline 20 ml)

**Group B**
(0.5% bupivacaine 20 ml)

**Group LB**
(2% lignocaine with

1. Time to first analgesic requirement. Testing in the four major nerve distributions @ 10, 20, 30 & 40
5.2 STUDYTERMINATION

Study will be terminated once sample size is obtained

6 STUDYVARIABLES

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<th>Scale of measurement (Quantitative / qualitative)</th>
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<th>Statistical test to be used</th>
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<td>Duration of analgesia</td>
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<td>% of patients with complete conduction block at 10, 20 and 30 minutes</td>
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<td>Complications (if any)</td>
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<td>Chi square test</td>
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7 REFERENCES

2. Laur, John J, Emine Ozgur Bayman, Peter J. Foldes, and Richard W Rosenquist. “Triple-Blind Randomized Clinical Trial of Time until Sensory Change Using 1.5% Mepivacaine with Epinephrine, 0.5% Bupivacaine, or an Equal Mixture of Both for Infraclavicular Block.” Regional Anesthesia and Pain Medicine 2012;37: 28–33.

8 PRELIMINARY WORK DONE ALREADY
Pilot study on 10 patients.

9 ETHICAL ISSUES
This study involves humans and requires frequent testing of sensory and motor blockade. Only temperature and light touch is used for sensory assessment.
In case of surgery exceeding block duration, general anesthesia will be administered.
The study falls in the “more than minimal risk” category. Combination of local anaesthetics used in the present study, is regularly used for peripheral nerve blocks.
10 INFORMED CONSENT PROCEDURE

During the preanaesthetic visit, the procedure will be explained to the patient. They will be informed that there are three arms in the study and they will have an equal chance of entering into either arm. This will be explained in their own language and consent will be obtained for including them in the study.

11 QUALITY CONTROL

Name of Officer designated by the department for quality control:
Dr. VR Hemanth Kumar
Professor & Head
Department of anaesthesiology
9003550553
drvrhk@gmail.com

12 SPONSORSHIPS

NIL
13 INVESTIGATORS DECLARATION

This is to certify that the protocol entitled “To determine the latency of three local anaesthetic solutions during ultrasound guided supraclavicular brachial plexus block- A double blind randomized control trial.” was reviewed by us for submission to the SBV Institutional Ethics Committee and certified that this protocol represents an accurate and complete description of the proposed research. We have read the ICMR guidelines, ICP-GCP guidelines/CPCSEA guidelines/and other applicable guidelines and undertake to ensure that the rights and welfare of the study subjects are protected.

The study will be performed as per the approved protocol only. If any deviation is warranted, the same will be presented to the ethical committee and permission will be sought. We assure that the study will be terminated immediately in case of any unforeseen adverse consequences and we will inform the same to the ethical committee immediately.

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<th>Name</th>
<th>Designation</th>
<th>Signature</th>
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</thead>
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<tr>
<td>Investigator</td>
<td>Dr. Sripriya. R</td>
<td>Professor, Dept. of Anesthesiology</td>
<td></td>
</tr>
<tr>
<td>Co-Investigator</td>
<td>Dr. T. Sivashanmugam</td>
<td>Professor, Dept. of Anesthesiology</td>
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</tbody>
</table>
Patient/Participant Information Sheet (PIS)

(Information for Participants of the Study)

We welcome you and thank you for having accepted our request to consider whether you can participate in our study. This sheet contains the details of the study, the possible risks, discomfort and benefits for the participants are also given. You can read and understand by yourself; if you wish, we are ready to read and explain the same to you.

If you do not understand anything or if you want any more details we are ready to provide the details.

1. What is the title of the Research Project?

"To determine the latency of three local anaesthetic solutions for ultrasound guided supraclavicular brachial plexus block – A double blind randomized control trial."

2. Who /where is this study being conducted?

This study is being conducted by Dr. SRIPRIYA. R, professor, department of anaesthesiology, MGMCR

3. What is the purpose of the study?

Different types of drugs are used around nerves for blocking pain during regional anaesthesia. A few of them start acting fast, but provide short duration of pain relief. A few of these drugs start acting late, but provide long duration of pain relief. By combining them, we get the advantages of either drug used alone. In this study we want to find out the onset of action when a combination of these drugs is used and the duration of pain relief provided by combining them for supraclavicular brachial plexus block. The procedure will be done under ultrasound guidance.

4. Procedure/Methods of the study (in brief, simple non-technical terms)

In this study one group of patients will be receiving block with a drug that is fast acting. One group of patients will be receiving block with a drug that takes some more time to begin acting. Yet another group will receive a combination of the two drugs. You will have an equal chance of being included in any of the groups. After the injection is done, we will test you at 10 minute intervals to get information on how much time it takes to produce complete loss of sensation and complete loss of
motor power. After that, the surgery will begin. After the surgery is over, we will continue to follow up till you first perceive pain.

5. How long you are expected to participate in this study?
We will be visiting you after the surgery is over to get information on when you are beginning to first perceive pain. Once you perceive pain, the time will be noted and we will give you medicines for pain relief. After that the study ends.

6. Why I am being considered as one of the participant?
You have been chosen as you are undergoing surgery for forearm bone fracture and this block will give you pain relief both during the surgery and even after the surgery is over.

7. Should I definitely have to take part in this study?
No. If you do not wish to participate you will not be included in this study. Also you will continue to get the medical treatment without any prejudice.

8. If I am participating in this study, what are my responsibilities? (Responsibility of the individual as a participants)
Being a participants in this study your responsibility are:1. To cooperate during preanesthetic checkup 2. To cooperate when the block action is being checked 3. To inform us when you first perceive pain after surgery is over.

9. Are there any benefits for me/Public?
The results of the study may benefit future patients. This study will give us information on whether there is any use in combining these drugs.

10. Will there be any discomfort / risks to me?
No risks. But some discomforts may be there. You may have mild pain on the needle insertion. We will be giving medicines at the needle prick site to reduce it. Risk will be the same as for any block.

11. Will by participating in this study, my personal details will be kept confidentially?
Your participation in the study and the study records relating to you will be kept confidential throughout the study and thereafter. Your personal identity will not be revealed in case of publication in any journal or analysis of your results, nor will it be
shared with anyone. The study records relating to you will be preserved for a period of three (if academic Research)/ five years (if clinical trial) for analysis and follow up.

12. Will I be paid for participating in the Study?
   No. you will not be paid for participating in the study.

13. Can I withdraw from this study at any time during the study period?
   Your participation in the study is purely voluntary. You are free to withdraw from the study at any time without assigning any reason. Your withdrawal from the study would in no way affect the medical care or other benefits which you are otherwise entitled to receive from the Institute.

14. Possible current and future uses of the biological material to be generated from the research and if the material is likely to be used for secondary purposes or would be shared with others, for which we seek your permission prior to the study inclusion?
   Not applicable.

15. Possible current and future uses of the data to be generated from the research and if the data is likely to be used for secondary purposes or would be shared with others, for which we seek your permission prior to the study inclusion?
   The data collected from you may be utilized for further analysis in future, if needed. All the data obtained from you will be used only for research purposes. It will not be used for any secondary purpose nor will it be shared with others. In case of analysis of your data in any publication in any journal, your identification will not be revealed.

16. Will I be informed of this study’s results and the findings?
   Yes, on your request the results of the study and its findings you will be informed.

17. Provision of free treatment for research related injury.
   Not applicable. The procedure and drug used in the study is used routinely for anaesthetic management of patients with fractures of upper limb. Hence no research related injury is involved in the study.
18. **Compensation to the participant for death or disability arising out of foreseeable and unforeseeable risks attributable to the study.**

Not applicable. The procedure and drug used in the study is used routinely for anaesthetic management of patients with fractures of upper limb. Hence no research related injury is involved in the study.

**Address and mobile number of the Principal Investigator (PI) and Co-PI, if any:**

Dr Sripriya.R, Professor, Dept of anaesthesiology, M GMCRI  
9365815939.

Dr Sivashanmugam. T, Professor, Dept of anaesthesiology, M GMCRI  
9442505567

**Address and telephone number of the IHEC office, M GMCRI**

Office of Institutional Human Ethics Committee, 1st floor college block (Adjacent to dept. of Pathology), M GMCRI, Puducherry 607 402. Phone No.: 0413- 2616700 (Extn No.: 754)

Signature of the Participant  
Signature of the Investigators
MAHATMA GANDHI MEDICAL COLLEGE AND RESEARCH INSTITUTE
PUDUCHERRY

FORM FOR GETTING INFORMED CONSENT FOR THOSE PARTICIPATING IN THE RESEARCH PROJECT

Name of the Research Project

“To determine the latency of three local anaesthetic solutions for ultrasound guided supraclavicular brachial plexus block – A double blind randomized control trial.”

I _______________ have been informed about the details of the study in own language.

I have understood the details about the study.

I know the possible risks and benefits for me, by taking part in the study.

I understand that I can withdraw from the study at any point of time and even then, I will continue to get the medical treatment as usual.

I understand that I will not get any payment for taking part in this study.

I will not object if the results of this study are getting published in any medical journals, provided my personal identity is not reviewed.

I know what I am supposed to do by taking part in this study and I assure that I will give my full co-operation for this study.

I nominate --------------------- (name) (mention the relation) to be my dependant to receive compensation if any.

Signature/Thumb impression of the participant (Name/Address/Occupation/Monthly income)

__________________________________          __________________________________

__________________________________

Signature/Thumb impression of the witness (Name/Address)

__________________________________

__________________________________

Name & Signature of the investigator

__________________________________