COMPARATIVE STUDY OF THE EFFECTS OF 0.5% ROPIVACAINE AND 0.5% LEVOBUPIVACAINE IN ULTRASOUND GUIDED BRACHIAL PLEXUS BLOCK IN PATIENTS UNDERGOING UPPER LIMB SURGERIES - A PROSPECTIVE RANDOMISED DOUBLE BLINDED STUDY -

A DISSERTATION SUBMITTED IN PARTIAL FULFILMENT OF THE REQUIREMENT FOR THE M. D. DEGREE (BRANCH X) ANAESTHESIOLOGY EXAMINATION OF THE TAMIL NADU DR. M. G. R. MEDICAL UNIVERSITY, TO BE CONDUCTED IN APRIL 2017

DECLARATION

I hereby declare that this dissertation titled **'Prospective Randomised Double Blinded Study Comparing the Effects of 0.5% Ropivacaine and 0.5% Levobupivacaine in Ultrasound Guided Supraclavicular Brachial Plexus Block in Patients Undergoing Upper Limb Surgeries'** was prepared by me in partial fulfilment of requirement of the regulations for the award of degree MD Anaesthesia of The Tamil Nadu Dr. M. G. R. University, Chennai. This has not formed the basis for the award of any degree to me before and I have not submitted this to any other university previously.

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Vellore

September 2016

CERTIFICATE

This is to certify that the dissertation entitled **'Prospective Randomized Double Blinded Study Comparing the Effects of 0.5% Ropivacaine and 0.5% Levobupivacaine in Ultrasound Guided Supraclavicular Brachial Plexus Block in Patients Undergoing Upper Limb Surgeries'** is a bonafide work of **Dr. Deepthy D Pillai,** towards the M. D. Branch –X (Anaesthesiology) Degree Examination of the Tamil Nadu Dr. M. G. R. University, Chennai, to be conducted in April 2017.

Dr. Anna B Pulimood

Principal

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Christian Medical College, Vellore

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Tamil Nadu - 632004

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This is to certify that the dissertation entitled **'Prospective Randomized Double Blinded Study Comparing the Effects of 0.5% Ropivacaine and 0.5% Levobupivacaine in Ultrasound Guided Supraclavicular Brachial Plexus Block in Patients Undergoing Upper Limb Surgeries'** is a bonafide work of **Dr. Deepthy D Pillai,** under my supervision in the Department of Anaesthesia, Christian Medical College, Vellore in partial fulfilment of the requirements for the M. D Branch –X (Anaesthesiology) Degree Examination of the Tamil Nadu Dr. M. G. R. University, Chennai, to be held in April 2017 and no part of thereof has been submitted for any other degree.

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A Randomized controlled trial comparing the effect of supraclavicular brachial plexus block using 0.5% levobupivacaine and 0.5% ropivacaine in patients undergoing upper limb surgeries.
Dr. Deepthy D Pillai (Emp. No. 29432), PG Registrar, Anaesthesia, Dr. Kalyana Chakravarthy, Anesthesia, Dr. Riya Jose, Anesthesia, Ms. Tunny Sebastian, Biostatistics

Ref: IRB Min No: 9497 [INTERVEN] dated 24.06.2015

Dear Dr. Deepthy D Pillai

I enclose the following documents:-

1. Institutional Review Board approval 2. Agreement

Could you please sign the agreement and send it to Dr. Nihal Thomas, Addl. Vice Principal (Research), so that the grant money can be released.

With best wishes,

Dr. Nihal Thomas
Secretary (Ethics Committee)
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Dear Dr. Deepthy D Pillai ,

The Institutional Review Board (Silver, Research and Ethics Committee) of the Christian Medical College, Vellore, reviewed and discussed your project titled "A Randomized controlled trial comparing the effect of supraclavicular brachial plexus block using 0.5% levobupivacaine and 0.5% ropivacaine in patients undergoing upper limb surgeries." on June 24th 2015.

The Committee reviewed the following documents:

1. IRB Application format
2. Data Collection proforma
3. Patient Information Sheet and Informed Consent Form (English, Tamil, Hindi, Bengali, Telugu)
4. Cvs of Drs. Deepthy D Pillai, Kalyana Chakravarthy, Riya Jose, Ms. Tunny Sebastian
5. No of documents 1 - 4

The following Institutional Review Board (Silver, Research & Ethics Committee) members were present at the meeting held on June 24th 2015, at 9.45 am in the CREST/SACN Conference Room Christian Medical College, Bagayam, Vellore 632002.

2/5

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We approve the project to be conducted as presented.

IRB Min No: 9497 [INTERVEN] dated 24.06.2015

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The Institutional Ethics Committee expects to be informed about the progress of the project, any **adverse events** occurring in the course of the project, any **amendments in the protocol and the patient information / informed consent**. On completion of the study you are expected to submit a copy of the **final report**. Respective forms can be downloaded from the following link: http://172.16.11.136/Research/IRB_Polices.html in the CMC Intranet and in the CMC website link address: http://www.cmch-vellore.edu/static/research/Index.html.

The study will need to be submitted to a three monthly **Data Safety Monitoring Board** (DSMB) review with duly filled in form found in the link http://172.16.11.136/Research/IRB_Polices.html

The trial need to be registered with **Clinical Trial Registry India** (CTRI) http://ctri.nic.in before commencing.

Kindly provide the total number of patients enrolled in your study and the total number of withdrawals for the study entitled: "A Randomized controlled trial comparing the effect of supraclavicular brachial plexus block using 0.5% levobupivacaine and 0.5% ropivacaine in patients undergoing upper limb surgeries." on a monthly basis. Please send copies of this to the Research Office (research@cmcvellore.ac.in)

Fluid Grant Allocation:

A sum of 19,800/- INR (Rupees Nineteen Thousand Eight hundred only) will be granted for 1 Year and out of which a maximum of Rs 5,000/- can be spent for stationery, printing, Xeroxing and computer charges (if computers used are within the institution)

Yours sincerely,

Dr. Nihal Thomas
Secretary (Ethics Committee)
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I also wish to thank my family for the constant support and encouragement in all my endeavours.

Finally and most importantly, I would like to express my sincere gratitude to all the patients who participated in this study.

Abstract

Title: Prospective Randomized Double Blinded Study Comparing the Effects of 0.5% Ropivacaine and 0.5% Levobupivacaine in Ultrasound Guided Supraclavicular Brachial Plexus Block in Patients Undergoing Upper Limb Surgeries

Department: Anaesthesia

Name of Candidate: Dr. Deepthy D Pillai

Degree & Subject: M. D. Anaesthesia

Name of Guide: Dr. Sajan Philip George

Context: Regional anaesthesia and in particular brachial plexus block, is very useful for patients undergoing upper limb surgeries. It offers sympathetic blockade, better postoperative analgesia and fewer side-effects compared to general anaesthesia. Supraclavicular approach provides a denser block to upper arm elbow and forearm. We propose to compare the effects of 0.5% Levobupivacaine with 0.5% Ropivacaine in terms of onset and duration of sensory and motor blockade and duration and effectiveness of post-operative analgesic effect

Aims: To compare the onset and duration of sensory and motor blockade and post-operative analgesic effect between 0.5% Levobupivacaine and 0.5% Ropivacaine in supraclavicular brachial plexus block in patients undergoing upper limb orthopaedic surgeries.

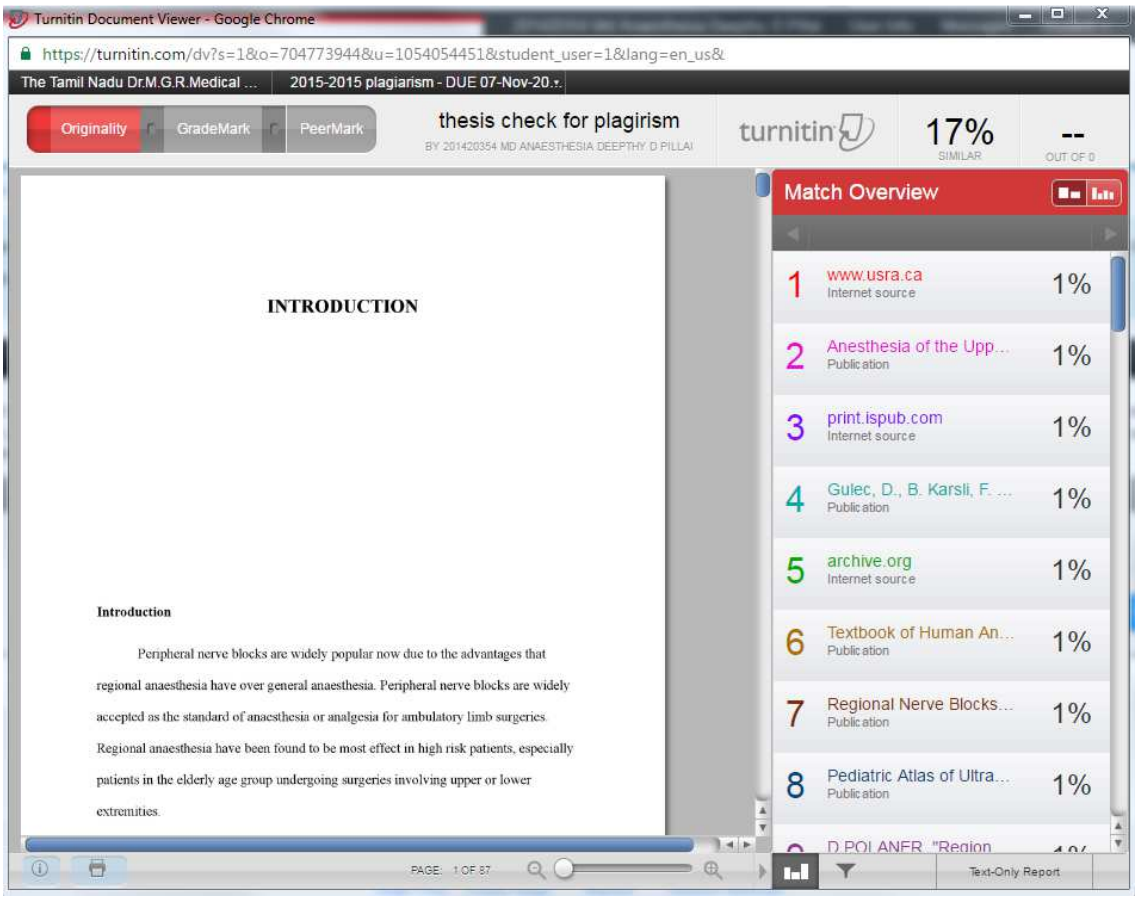
Study design: Prospective randomized double-blind study.

Materials and Method: After obtaining approval from the institutional ethics committee and informed consent, 80 consecutive orthopaedic patients for upper limb surgeries were included in the study. Patients were randomized into two arms based on computer generated random numbers. One arm received 25 ml 0.5% Levobupivacaine and other arm received 25 ml of 0.5% Ropivacaine under ultrasound guidance. Baseline hemodynamic parameters were recorded before the procedure. End of injection was taken as time 0, thereafter patients were monitored 5, 10, 15, 20, 25 and 30 minutes. Post operatively VAS scores were monitored 3,6,12 and 24 hourly and rescue analgesic injection Diclofenac 75 mg IV was given when VAS score was more than or equal to 4.

Conclusion: The onset of sensory and motor blockade and the duration of post op analgesia between 0.5% Ropivacaine and 0.5% Levobupivacaine were comparable.

Keywords: Ultrasound guided supraclavicular block, Ropivacaine, Levobupivacaine. Upper limb surgeries, brachial plexus block, post-operative pain.

Turnitin Certificate



Contents

INTRODUCTION

Introduction

Peripheral nerve blocks are widely popular now due to the advantages that regional anaesthesia has over general anaesthesia. Peripheral nerve blocks are widely accepted as the standard of anaesthesia or analgesia for ambulatory limb surgeries. Regional anaesthesia have been found to be most effect in high risk patients, especially patients in the elderly age group undergoing surgeries involving upper or lower extremities.

Patients with comorbidities such as cardiovascular diseases, chronic lung disease, metabolic diseases, neuropathies and/or immunosuppressive states, when undergoing general anaesthesia, face challenges like changes in haemodynamic stress response and potential for drug interaction due to polypharmacy. These patients would benefit from regional anaesthesia, especially for ambulatory limb surgeries.

Regional anaesthesia can be a good alternative to general anaesthesia with the advent of accessories such as peripheral nerve stimulator and ultrasound. All the disadvantages of a block by a blind technique have been overcome with nerve stimulation and ultrasound guidance. The added advantages of visualization of the nerve plexus have helped in administration of the drug with more precision, obtaining better quality of the nerve block, shortening the latency and minimizing the amount of drug needed for the block. It has also resulted in decreased complications such as vessel puncture and injury to pleura.

Nerve stimulation was earlier considered as the gold standard for neuronal blockade, with its ability to predict the spread of drug to the proximity of the nerve. However, the neuronal sparing which was seen with this technique was probably due

to non-uniform distribution of sensory and motor fascicles in a compound nerve. This meant that the technique was relatively insensitive but very specific.

Ultrasound overcame this shortcoming by providing direct visualization of the nerve. Combining nerve stimulator and ultrasound proved to be more accurate and reliable. Ultrasound guided nerve blocks provided visual guidance to needle position and, hence, more successful and safer blocks.

Newer local anaesthetics with minimal cardiovascular effects and longer duration of action have been developed. This study aims to compare the onset of motor and sensory blockade and the duration post-operative pain relief between Ropivacaine and Levobupivacaine. Levobupivacaine compared to Ropivacaine is a new local anaesthetic agent.

AIMS AND OBJECTIVES

Aims and Objectives

- **Aims**:

  To study the effect of 0.5% Ropivacaine and 0.5% Levobupivacaine in supraclavicular brachial plexus block in patients undergoing upper limb surgeries.

- **Objectives:**

  1. Primary Objective: To compare the onset of motor and sensory blockade of 0.5% Levobupivacaine and 0.5% Ropivacaine.
  2. Secondary Objective: To compare the duration of post-operative analgesia of 0.5% Levobupivacaine with 0.5% Ropivacaine

Null Hypothesis

There is no difference in the onset of motor and sensory blockade and in the duration of post-operative analgesia between 0.5% Levobupivacaine and 0.5% Ropivacaine when used in ultrasound guided supraclavicular brachial plexus block for patients undergoing upper limb surgeries.

REVIEW OF LITERATURE

Review of literature

1. ANATOMY OF BRACHIAL PLEXUS

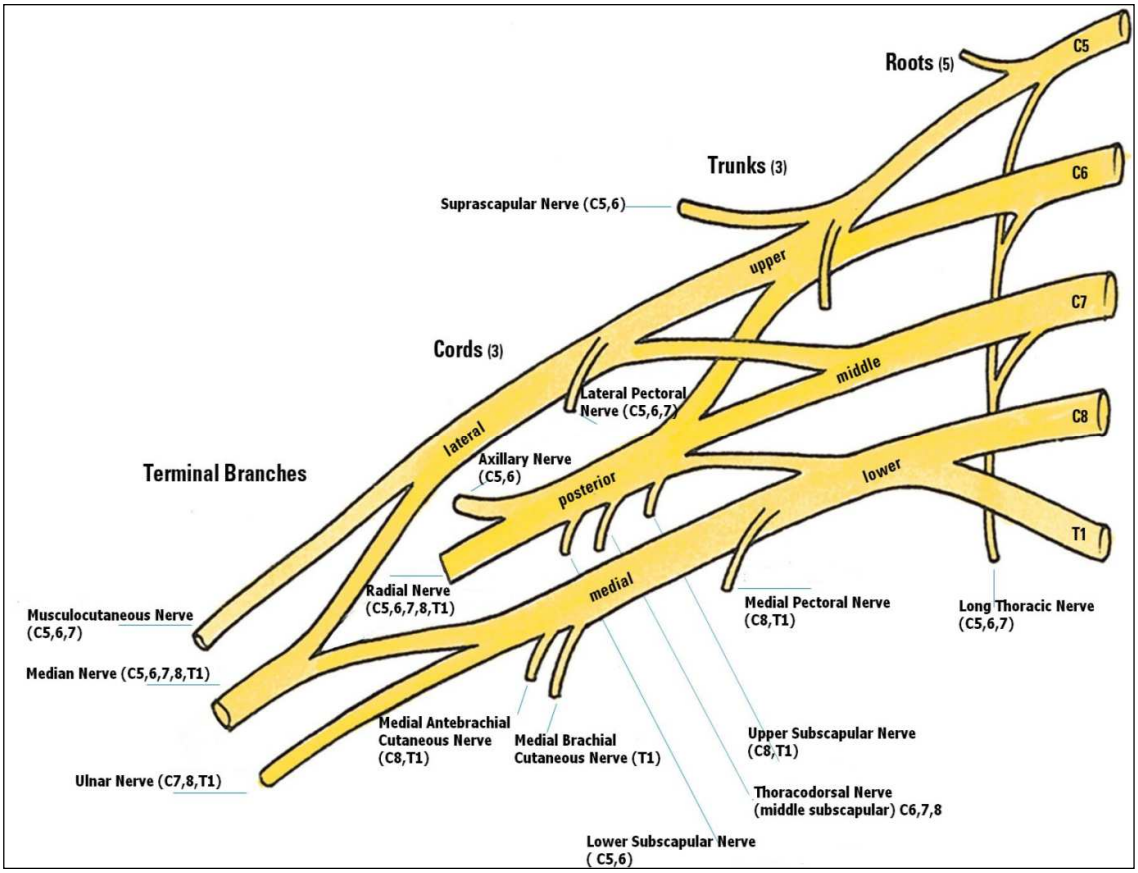


Figure 1: Anatomy of Brachial Plexus [1]

BRACHIAL PLEXUS FORMATION:

The first thoracic nerve unites with the ventral rami of lower 4 cervical nerve to form the brachial plexus. C4 or T2 also contribute frequently for the formation of brachial plexus. When the contribution from C4 is more and T2 is absent, the plexus will have a more cephalad position and is known as pre fixed while if the contribution from T2 is more it is known as post fixed and will have a more caudal position. An anomalous first rib or a cervical rib is usually associated with these positions. [2]

The brachial plexus can be divided into Roots, Trunks, Divisions, Cords and Branches.

- ROOTS:

  The roots represent the anterior primary divisions of lower four cervical and first thoracic nerves. They emerge from the intervertebral foramina and above the first rib they fuse to form the trunks. [3]

- TRUNKS:

  The roots fuse above the first rib to form the trunks of brachial plexus. C5 and C6 form the upper trunk by uniting at the lateral border of scalenus medius. The lower trunk is formed by C8 and T1 roots behind the scalenus anterior muscle. The middle trunk is formed by the C7 root alone.

- DIVISIONS:

  Each trunk divides into anterior and posterior division under the clavicle after they pass over the first rib.

- CORDS:

  Under the clavicle the anterior and posterior divisions of each trunk reunite to form the cords. There are 3 cords named according to their relation to the axillary artery. The anterior division of upper and middle trunk join to form the lateral cord and it lies lateral to the axillary artery. The anterior division of the lower trunk forms the medial cord which descends medial to the axillary artery. The posterior divisions from all three trunks unite and form the posterior cord, which initially lies above the axillary artery and later descends behind the artery. The posterior cord gives rise to nerves that supply the extensor surface of the upper limb while the medial and lateral cords supply the flexor surface.

- MAJOR TERMINAL NERVES:

The cords either give off a major branch to the upper extremity or contribute for its formation and then terminate as a major branch. The medial cord gives rise to medial head median nerve and terminates as the ulnar nerve while the lateral cord gives rise to lateral head of median nerve and terminates as the musculocutaneous nerve. The major branch from the posterior cord is the axillary nerve and it continues as the radial nerve. In summary, brachial plexus is formed by the union of 5 nerve roots (C5-T1) and terminates in 5 major nerves namely radial nerve, ulnar nerve, axillary nerve and musculocutaneous nerve.

DISTRIBUTION OF BRACHIAL PLEXUS

Brachial plexus can be broadly divided into those branches that arise from above the clavicle known as supraclavicular branches and those that arise from below the clavicle known as infraclavicular branches. [2]

- **Supraclavicular Branches**

A. FROM ROOTS:

1) Nerves to scaleni and longus colli – C5, C6, C7, C8

They arise from lower cervical ventral rami almost immediately after emerging from the intervertebral foramina after receiving the respective sympathetic nerve contributions.

They supply;

- Longus collis muscle (C2-C7)
- Anterior scalene muscle (C4-C6)
- Middle scalene muscle (C6-C8)
- Posterior scalene muscle (C6-C8)
- Scalenus minimus muscle (C7-C8)

2) Branch to phrenic nerve – C5

Anterior to the scalenus anterior muscle a branch arising from the fifth cervical nerve joins the phrenic nerve.

3) Dorsal scapular nerve – C5

It arises from the ventral ramus of the fifth cervical nerve and passes behind the levator scapulae muscle after piercing the scalenus medius muscle. It ends in the rhomboids muscle.

It supplies:

- Levator scapulae muscle C3-C5
- Rhomboid minor muscle C5, Rhomboid major muscle C5
- Scalenus minimus muscle (C7-C8)

4) Long thoracic nerve – C5, C6, C7

Long thoracic nerve arises mainly from C5 and C6 nerve roots. C7 contributes for its formation 42% of the cases. It pierces the scalenus medius muscle and unites lateral to it. It descends dorsal to the brachial plexus and first part of axillary artery.

B. FROM TRUNKS:

1) Nerve to subclavius –C5, 6

The subclavius muscle is supplied by this nerve. The nerve arises mainly from C5 and C6 nerve roots. The nerve lies anterior to the brachial plexus and to the third part of subclavian artery. The accessory phrenic nerve sometimes arises from this nerve.

2) Suprascapular nerve-C5, 6

The nerve arises from the upper trunk of the brachial plexus mainly from its superior aspect. It courses laterally and deep to 2 main muscles namely trapezius and omohyoid and then enters the supraspinatus fossa through the suprascapular notch.

It supplies 2 main muscles, the supraspinatus C5 and the infraspinatus muscle C5-6. It sometimes gives off a sensory branch to the shoulder joint. It pierces the

deltoid muscle and supplies within the territory of the axillary nerve, the skin of the proximal one third of arm.

- **Infraclavicular Branches**

They comprise all of the motor and sensory nerves to the upper extremity. Apart from some exceptions, there are no branches arising from the divisions of plexus; rest of the branches are from the three cords. These branches arise from the cords but their fibres can be traced up to spinal nerves.

A. LATERAL CORD:

1) Lateral pectoral nerve- C5, C6 and C7

It is bigger than the medial pectoral nerve. It pierces the clavipectoral fascia and supplies the pectoralis major muscle. It lies superficial to the first part of axillary vein and artery in its course. It also supplies some fibres to the pectoralis minor muscle by sending a ramus to the medial pectoral nerve. It supplies- Pectoralis major muscle (C5-T1)

2) Musculocutaneous nerve – C5, C6, C7

The musculocutaneous nerve is the major terminal branch of the lateral cord. After giving off the lateral head to median nerve, it leaves the plexus and enters the coracobrachialis muscle. It courses through axilla in coracobrachialis muscle and descends obliquely and later between triceps and brachialis, sending motor fibres to the two muscles. Lateral to the tendon of biceps it pierces the deep fascia and continues as the lateral cutaneous nerve of the forearm below the elbow.

It supplies - Coracobrachialis muscle (C6, 7), Biceps muscle (C5, 6), Brachialis muscle (C5, 6).

These are powerful flexor muscles of the forearm, paralysis of which causes inability to flex, supinate and abduct the forearm. The arm hangs in medial rotation, in which forearm is extended and pronated – "Erb's paralysis". The skin over the anterolateral surface of the forearm is supplied by the lateral cutaneous branch of the musculocutaneous nerve.

3) Lateral head of median nerve

Median nerve: C6, 7, 8 T1 (Labourer's nerve)

The median nerve is comprised of lateral and medial head .The lateral head arises from the lateral cord of brachial plexus and the medial head from the medial cord. The lateral and medial head unite on the ventral surface of the third part of axillary artery. It lies lateral to the brachial artery in the arm and becomes anterior to it near the insertion of the coracobrachialis muscle. The median nerve then descends medial to the brachial artery to the cubital fossa where it lies posterior to bisceps aponeurosis and brachialis muscle. It crosses lateral to ulnar artery as it enters the forearm between the 2 heads of pronator teres muscle. It then goes behind the tendinous bridge formed between the two heads of flexor digitorum superficialis and descends anterior to flexor digitorum profundus and posterior to superficialis muscle. The nerve lies superficial approximately 5 cm from the flexor retinaculum between the flexor digitorum superficialis and carpi radialis muscle. It enters the palm after passing deep to the flexor retinaculum and terminates in muscular and cutaneous branches.

Muscular branches:

- Flexor digitorum profundus

- Flexor pollicis longus
- Pronator quadratus
- Pronator teres
- Flexor digitorum superficialis.
- Flexor carpi radialis
- Opponens pollicis
- Abductor pollicis brevis
- Flexor pollicis brevis
- Lumbricals

Cutaneous branches:

The sensory supply is by the palmar cutaneous branches that supply the skin over lateral three and half fingers and also the skin over the dorsal aspect of the same fingers. It may sometimes supply the area innervated by the radial nerve and provide sensory supply to dorsal surface of the entire thumb and first three fingers as far as metacarpophalangeal joint .It may also supply the area innervated by ulnar nerve, and may provide sensory innervation of entire ring finger.

Median nerve can be injured in the forearm. It occurs proximal to its muscular and cutaneous branches thereby all digits losses flexion of the second phalange .The flexion of terminal phalange of the index and middle finger is lost. The flexion of terminal phalanges of the other 2 fingers may be possible by the interossei. The thumb cannot be opposed or abducted, nor flexed at its interphalangeal joint. Sensation in the area of distribution is lost. Paralysis of

intrinsic pollicis muscles and unopposed action of the extensor pollicis longus produces an ape like deformity of the hand. [5]

Injury in the mid-forearm may cause only weakness in flexion of the index ("pointing index") finger, as the branch to flexor digitorum superficialis arise above this level.

Injury proximal to flexor retinaculum causes inability to oppose the thumb. Any condition resulting in reduction in the space below the flexor retinaculum cause pressure on the nerve in the carpal tunnel, between flexor retinaculum and the carpal bones, resulting in pain and slight sensory impairment in the digits supplied and sometimes slight wasting of the thenar muscles is called "carpal tunnel syndrome". [6]

B. MEDIAL CORD:

1) Medial head of median Nerve C8, T1

It forms the median nerve by uniting with the lateral head of median nerve.

2) Medial pectoral nerve C8, T1

The nerve initially travels between the axillary vein and artery. The lateral pectoral nerve and medial pectoral nerve then forms a loop around the artery and enters the pectoralis minor muscle to supply it. Some fibres pass inferiorly to end in pectoralis major. It supplies pectoralis minor muscle C8, T1.

3) Medial cutaneous nerve of the arm C8, T1

This nerve exits axillary sheath high up in the axilla and supplies the medial aspect of the upper arm up to the medial epicondyle.

4) Medial cutaneous nerve of the forearm C8, T1

It supplies the skin over biceps muscle till the elbow. In the arm it is medial with respect to the brachial artery. It divides into 2 branches: Anterior large branch and posterior branch which supplies the skin over the entire medial part of forearm till wrist.

5) Ulnar nerve (C7) C8, T1 (Musician's nerve)

It descends medial to the axillary artery till almost the mid-part of forearm. It lies parallel to and between the median nerve and the medial cutaneous nerve of the forearm. Then it angles dorsally and laterally to descend in the groove on the medial head of the triceps. Then it travels behind the medial epicondyle of humerus where it is covered only by skin and fascia ("Fussy bone") and passes down the ulnar side of the forearm to the hand, dividing into superficial and deep terminal branches.

Muscular branches supply:

- Flexor carpi ulnaris C8, T1
- Ulnar head of flexor digitorum profundus – C8, T1
- Abductor digiti minimi - C8, T1
- Flexor digiti minimi brevis - C8, T1
- Abductor pollicis - C8, T1
- Palmar interossei - C8, T1
- Dorsal interossei - C8, T1

Cutaneous branches:

Cutaneous branches supply the skin of the little finger and the medial half of the hand and ring finger. Occasionally, it may encroach on the area usually served by the median nerve in palmar aspect and the area served by radial nerve in the dorsal aspect.

C. POSTERIOR CORD

1) Upper subscapular nerve (C5, 6)

It is smaller than the inferior, enters the subscapularis. It supplies the subscapularis muscle.

2) Lower subscapular nerve (C5, 6)

It supplies the lower portion of subscapularis muscle and terminates in teres major muscle. It supplies – Subscapularis, Teres major muscle

3) Thoracodorsal nerve (C6, 8)

It arises between the two subscapular nerves, courses along the posterior wall of the axilla with subscapular artery and terminates in latissimus dorsi.

4) Axillary (circumflex humeral) nerve (C6, 8)

Axillary nerve divides into anterior and posterior branches. The deltoid receives supply from the anterior branch of the axillary nerve (C5-6). It also supplies skin over the lower part of the deltoid muscle. The teres minor muscle is supplied by the posterior branch of the axillary nerve. The posterior aspect of the deltoid receives cutaneous supply from posterior branch of axillary nerve. The posterior branch continues as the upper lateral cutaneous nerve of arm. The

cutaneous supply to lower part of deltoid and upper part of triceps is from this muscle. Shoulder joint receives an articular branch from this nerve.

5) Radial nerve (C5, 6, 7, 8)

It is the largest branch of the brachial plexus, is the terminal continuation of the posterior cord. It descends behind the third part of the axillary artery. With the profunda artery, it inclines dorsally between the long and medial head of the triceps then passes obliquely across the back of the humerus in the spiral groove and then reaches the lower anterior side of the forearm where its terminal branches arise.

Muscular branches supply:

- Triceps brachi – C7, 8
- Supinator – C6
- Extensor carpi radialis brevis – C6, 7
- Abductor pollicis longus – C6, 7
- Extensor pollicis longus - C6,-8
- Extensor indicis - C6,-8
- Extensor pollicis brevis - C6, 7
- Brachioradialis – C5, 6
- Extensor carpi radialis longus - C6, 7
- Extensor carpi ulnaris - C6-8
- Extensor digitorum - C6-8
- Extensor digiti minimi - C6-8

Sensory supply via, the dorsal cutaneous nerve of posterolateral aspect of the upper arm; dorsal cutaneous nerve of the forearm, supplying the posterior aspect of the forearm as far as the wrist and the superficial terminal branches supply the dorsal aspect of the entire thumb and dorsal aspect of the index, middle and radial half of the ring finger as far as the distal interphalangeal joint. Occasionally radial nerve may encroach upon the areas supplied by the ulnar and median nerve.

Articular branches supply the carpal, distal radioulnar, some intercarpal and intermetacarpal joints. Digital branches supply the metacarpophalangeal and proximal interphalangeal joints.

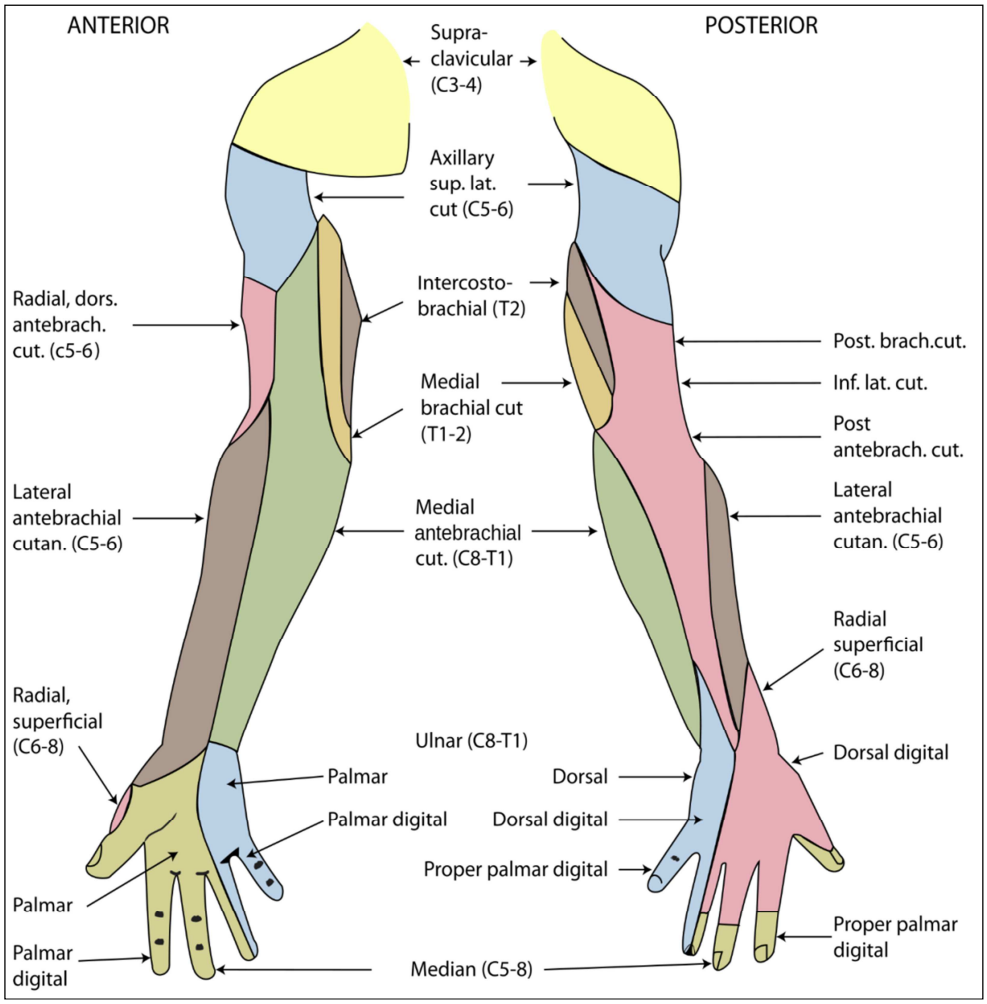


Figure 2: Cutaneous Distribution of Brachial Plexus Nerves [7]

The segmental preganglionic sympathetic contributions are variable, but generally extend more caudally. The highest contribution is usually T2 with T1 contributing only rarely, while lowest may be as far as T8, T9 or even T10.The post ganglionic contributions are from grey rami communicates from the sympathetic chain.

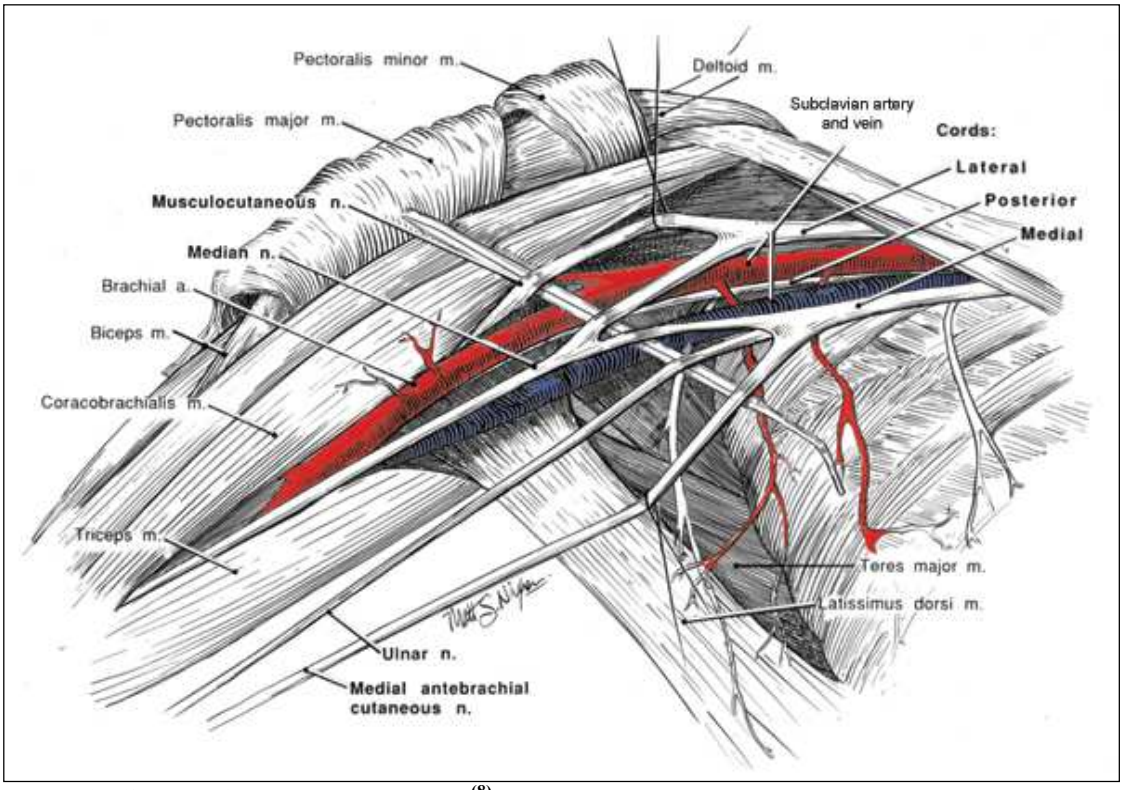


Figure 3: Course of the Brachial Plexus [8]

Brachial plexus in its course from the transverse process of the cervical vertebra to the first rib it is found to lie between the middle and anterior scalene muscle and covered by the fascia of the 2 muscles.

2. BRACHIAL PLEXUS BLOCK HISTORY

The first brachial plexus block was performed by William Stewart Halsted in 1885. [9] Halsted exposed the nerve roots surgically under local infiltration and injected each of them with a small amount of dilute cocaine (0.1%) interneurally under direct vision. Only about 0.5 ml of local anaesthetic was required to produce complete anaesthesia.

In 1897, George Crile used a similar technique in which the plexus was exposed under local anaesthesia. Just behind the sternomastoid muscle, cocaine was injected into the nerve trunks under direct vision which was done as a therapeutic measure in a 12 year old boy who developed tetanic spasms following a compound fracture of the forearm; later the technique was used to provide anaesthesia for upper arm surgeries.

- **Evolution of Supraclavicular Brachial Plexus Block**

In 1911-1912, Kulenkampff described the first percutaneous supraclavicular approach. He pointed out that above the clavicle the plexus lies under the skin as it passes over the first rib and is accessible to a percutaneous technique.[9] The midpoint of clavicle and the subclavian artery provided a constant landmark, most frequently at the point where external jugular vein intersects the clavicle. He performed his first attempt on himself and used 5 ml of Novocaine; later he increased it to 10 ml and was able to obtain complete anaesthesia. Direction of the needle was backwards, inwards and downwards. He emphasized that the purpose of the technique was not to hit the rib but to find the trunks by eliciting paraesthesia. He said that the first rib just prevented pleural penetration. He used a 4 cm needle.

Labat in 1922 advocated injection at three separate points which failed to elicit paresthesia by Kulenkampff's method; first injection, beneath the deep fascia in the direction of the first rib, second towards the Chassaignac's tubercle and third towards the lateral margin of the first rib behind the clavicle (5 ml with each injection).

In 1926, Livingston carried out Kulenkampff's technique without the production of paraesthesia as soon as the deep cervical fascia had been penetrated. 30 ml of 2% procaine was injected. He wrote that the plexus and the artery are separated from the surrounding structures by a fascial investment. In 1940, Patrick chose to lay down a "wall of anaesthetic" through which the plexus must pass in its course over the first rib, where 60-70 ml of solution was being injected during 5-6 insertions. This technique became the "standard technique of supraclavicular block, subsequently referred to by many as the "classical supraclavicular technique". In 1942 Knight modified Patrick's technique by making the three injections through three separate needle insertions, parallel to one another. For the first time he utilized a directly caudal direction of needle insertion.

In 1944, Murphey used a single injection technique and used lateral border of anterior scalene muscle as the landmark and direction of needle insertion caudal as with Knight's technique, not medial or dorsal, as with most other techniques.

In 1949, Bonica and Moore utilized both Kulenkampff's and Patrick's technique; the classical landmarks, direction of needle insertion and elicitation of paraesthesia prior to first injection were followed. This was followed by laying down of a wall of anaesthetic solution by "walking the rib" and making multiple injections during each withdrawal of the needle.

In 1958, Lookman, fully realized the potential of the fascial sheath around the plexus. He carefully dissected the plexus and said that the plexus lies in a closed compartment. He said this space lies between the anterior and middle scalene muscles and is pyramidal in shape, with its apex pointing upwards and medially towards the extent of the fourth cervical vertebra. The proper placement of needle was not verified.

Fortin and Tremblay advocated the use of a short needle which was long enough to reach the plexus but too short to reach the lung, in an attempt to minimize the threat of pneumothorax.

In 1964, Winnie after numerous anatomical dissections showed that the relation of the plexus and the subclavian artery to the midpoint of the first rib is not constant. He showed that there is a constant relationship between brachial plexus, 1st rib and the middle and anterior scalene muscle. He inserted needle between the two muscles in the direction of the space between them. Once paraesthesia is obtained, a single injection is made into the space.

In 1928, Von Perthes located the brachial plexus by means of electrical stimulation. He used an induction apparatus as a current source and transmitted it through a nickel needle insulated with lacquer. It was not widely accepted due to lack of a polished technique. In 1955, Pearson located motor nerves by means of electrical stimulation using insulated needles. In 1969 Wright devised the Block-Aid monitor which made the use of nerve stimulators more feasible. All the early reports of the use of Peripheral Nerve Stimulator (PNS) for regional anaesthesia noted the use of insulated needles. In 1973, worrying that such needles might alter the feel of the

tissues or that the insulation might peel off, Montgomery and colleagues tried using the conventional non insulated needles.

Proximal muscle groups are paralysed earlier than the occurrence of sensory loss or sympathetic block. De Jong in 1977 explained that this phenomenon is the result of anaesthesia developing in the mantle fibres earlier than core fibres.

Yasuda and co-workers in 1980 had 98% success rate using the stimulator for supraclavicular block but again made no comparison with others techniques. Lanz et al in 1983 attempted to study the effectiveness of blockade with various techniques, but they concluded that the approach to be used should depend upon the site of operation.

3. TECHNIQUES OF SUPRACLAVICULAR BRACHIAL PLEXUS BLOCK

The supraclavicular brachial plexus block can be performed by the following techniques:

- Ultrasound Guided Nerve Block
- Peripheral Nerve Stimulator Guided Block
- Landmark Technique/Blind Approach
- Combination Of Ultrasound And Peripheral Nerve Stimulator

A) ULTRASOUND GUIDED NERVE BLOCK

First nerve blocks using ultrasound was performed in 1978. Earlier reports that were published focused mainly on ultrasound guided brachial plexus block by supraclavicular, infraclavicular, axillary and interscalene technique. Now studies on ultrasound guided femoral, sciatic and stellate ganglion blocks are quite promising. Ultrasound guidance was found to be useful for visualising epidural space and facilitating neuraxial blockade in children, obese individuals and parturient. [(10)]

The earlier used method of peripheral nerve blockade was dependant on surface anatomy and certain landmarks. This leads more than 20% failure rate of regional anaesthesia technique. Failure of block can be due to improper needle placement or inadequate spread of local anaesthetic agent. This method uses multiple attempts to get a satisfied result and hence can lead to operator frustration, patient discomfort, unnecessary waste of theatre time and unwanted complications. Landmark technique is particularly difficult in obese patients.

Anatomical variations of brachial plexus can be easily picked up by ultrasound due to its real time images with less patient discomfort in contrast to conventional methods resulting in repeated needle pricks in an attempt to find the plexus with more patient discomfort. Ultrasound is the most apt tool for peripheral nerve blocks as compared to MRI or CT because it is portable, less expensive, user friendly, less radiation exposure and above all provides real time image guidance for peripheral nerve blocks.

- **ULTRASOUND**

Characteristics of Ultrasound

Ultrasound can be described as a form of mechanical sound energy. It produces alternate areas of compression i.e. high pressure and rarefaction i.e. low pressure as it travels through a conducting medium in the form of a longitudinal wave form. The ultrasound wave frequency is generally above 20,000 Hz. Ultrasound that is used for medical purposes have their frequency between 2.5-1.5 MHz. The hearing range for human beings is 20-20,000 Hz.

Generation of an ultrasound wave

When an electric field is applied to the array of piezoelectric crystals located on the surface of the transducer, it produces an ultrasound wave. The electrical stimulation produce mechanical distortion of the piezoelectric crystals and the resulting vibrations produce sound waves which is mechanical energy.

An ultrasound wave is produced from each of these piezoelectric crystals and hence an ultrasound beam is produced by the summation of all these waves.

Generation of ultrasound waves are in the form of pulses and each of these contain 2 or 3 sound cycles.

Pulse length

The pulse length (PL) refers to the distance travelled by each pulse. Waves that have short pulse length help in improving the axial resolution of ultrasound. The damping materials present in the transducer cannot reduce pulse length to less than 2 or 3 sound cycles.

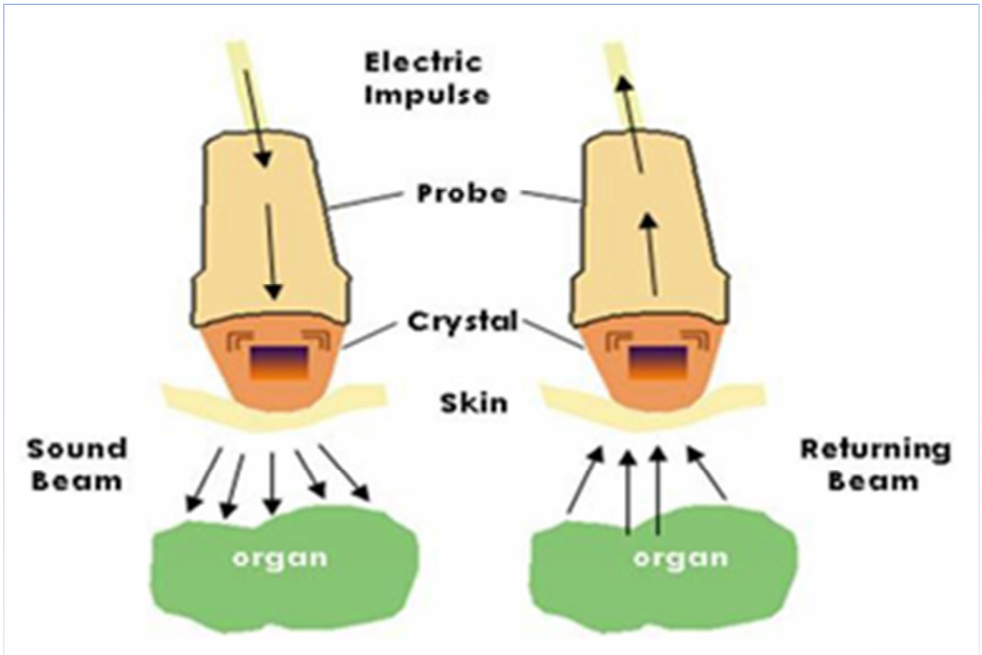


Figure 4: Generation of Ultrasound Image [10]

There are three main modes for an ultrasound. They are Amplitude or A mode, Brightness or B mode and Motion or M mode.

Among the three modes, the B mode is most commonly used for ultrasound guided regional anaesthesia.

There are 5 basic components of an ultrasound scanner that are required for generation, display and storage of an ultrasound image.

1. A pulser energises the crystals by applying voltage of high amplitude.
2. A transducer helps in converting to electrical to mechanical energy and the reverse.
3. A receiver helps in detecting signals and also amplifies weak signals.
4. Ultrasound is depicted in variety of modes by the display.
5. Memory stores the ultrasound video display.

Ultrasound tissue interaction

As the ultrasound beam travels through tissue layers, the amplitude of the original signal becomes attenuated as the depth of penetration increases.

Attenuation can be defined as the loss of energy due to absorption, scattering of ultrasound waves at tissue interface and reflection.

Most of the attenuation in soft tissues is caused by absorption. Absorption can result in the production of heat. 'Decibels per centimetre of tissue' is used to measure attenuation and there is an attenuation coefficient for each tissue type. A higher attenuation coefficient means there is a greater reduction in the intensity of the ultrasound wave by that particular tissue.

Attenuation depends on two things namely the frequency of the ultrasound wave and the distance travelled. Higher the frequency of ultrasound wave, higher will be the attenuation and lesser will be the wave penetration.

It is possible to decrease the attenuation by increasing signal intensity of the returning echo. The degree of this receiving amplification is known as gain. Increasing the gain will amplify only the returning signal and not the transmit signal.

Table 1: Tissue Echogenicity [10]

Tissue	Ultrasound Appearance
Veins	Compressible and appear anechoic
Arteries	Pulsatile and appear anechoic
Fat	Mainly hypoechoic with irregular hyperechoic lines.
Muscles	A hypoechoic background with hyperechoic lines.
Tendons	Mostly hyperechoic
Bone	They have hypoechoic shadow in the hyperechoic lines.
Nerves	Hypoechoic or hyperechoic based on location.

Reflection and scattering of the ultrasound waves can also result in attenuation and hence decrease in its intensity. The degree of reflection is determined by the difference in the acoustic impendence of the two tissue at the interface .This is known as acoustic mismatch. The resistance offered by a tissue for the passage of ultrasound waves is known as its acoustic impedance. More the acoustic impedance mismatch greater will be the reflection of ultrasound waves.

Ultrasound Transducers and Manipulation

Ultrasound transducers consist of piezoelectric crystals that emit and receive high-frequency sound waves by interconverting electrical and mechanical energy. Linear-array transducers have a high scan line density and therefore produce the best image quality. These transducers, in particular the high-frequency broad band linear probes, have proven the most useful for nerve imaging. Images from linear arrays are displayed in rectangular format. When a linear transducer is needed but the space at the block site is small, a compact linear ("hockey stick") transducer can be very useful. Peripheral nerves can be viewed in short axis or long axis. [11]

A trapezoidal shaped ultrasound image is produced by curvilinear array transducer. These transducers are useful when there is limited working room in the anatomic site for the block (e.g., the infraclavicular region). These probes are easier to work with and provide a broader image.

The terms generally used during ultrasound manipulation are as follows:

- **Sliding Movement:** Nerve identification is made easy by sliding the transducer probe along the direction of the nerve using the short axis.
- **Tilting (side-to-side):** The brightness of nerves in the echo image varies with the degree of tilt of the transducer. A good image can be obtained by optimising the angle of tilt.
- **Compression:** Confirmation of venous structures is done by compression. Compression helps to provide better contact of the transducer probe with the skin surface and also helps in bringing structures closer to the transducer.

- **Rocking:** Rocking is useful when the working space is limited. It is done to improve the visibility of the needle tip and the anatomic structures.
- **Rotation:** Some rotation of the probe will produce true short-axis views rather than oblique or long-axis views.

Ultrasound imaging of nerves

High resolution ultrasound imaging helps to detect the fascicles of peripheral nerves. Nerves with few fascicles like the cervical ventral rami appear monofascicular on ultrasound scans. For distinguishing between nerves and tendons based on their echo texture the ultrasound frequencies of 10 MHz or more is required.

Ultrasound Guided Supraclavicular Brachial Plexus Blockade

Ultrasound guidance for supraclavicular brachial plexus is very popular now days. The supraclavicular approach for brachial plexus is more sought out as the nerve visibility is better especially because the divisions of the brachial plexus are located approx. 20 to 30 mm from the skin and appear very compact. [13][14][15]
Ultrasound provides better visualization and hence complications like vascular puncture and pneumothorax are less likely to occur.

In one of the most commonly used technique for ultrasound guided supraclavicular block patient is made to lie in the supine position with the head turned to the side opposite to the side of block. The operator stands at the head end of the patient or on patient's side depending on his or her comfort.

The ultrasound probe used is a compact linear transducer. It provides more space for the operator for giving the block. Commonly used is the Sonosite-HMR

Ultrasound Machine available with HFL 38/6-13 MHz transducer and 38 mm linear array probe.

Technique

Patient is made to lie in the supine position with head turned to the side opposite to side of block. After adequate cleaning and draping the side to be blocked and preparing the ultrasound probe, a 38 mm linear high frequency 10-15 MHz probe is placed on the supraclavicular fossa. Fine adjustments are made on the depth, focus and gain to get a good image.

The trunks or divisions of the brachial plexus are visualised in the short axis view.

The nerves in the supraclavicular fossa under ultrasound appear as oval or round hypo echoic structures. The nerve lies posterior and lateral to the subclavian artery and above the first rib. The most important thing is to locate the subclavian artery first by systematic scanning of the supraclavicular fossa from medial to lateral side. The anterior scalene muscle can also be visualised. Insertion is on the first rib between two vessels. The subclavian vein lies medial to the artery.

In the 'in plane approach' of needle insertion a 10 cm 22 G insulated stimulating needle is inserted on the outer or lateral end of the ultrasound probe after the skin is infiltrated with local anaesthetic. The needle is inserted in the same plane as the ultrasound beam along the long axis of the probe. This technique allows the real-time visualisation of the needle tip and hence can ensure the proper injection of the drug as well as prevent unwanted complications **(16).**

B) PERIPHERAL NERVE STIMULATOR GUIDED BLOCK

Electrophysiology

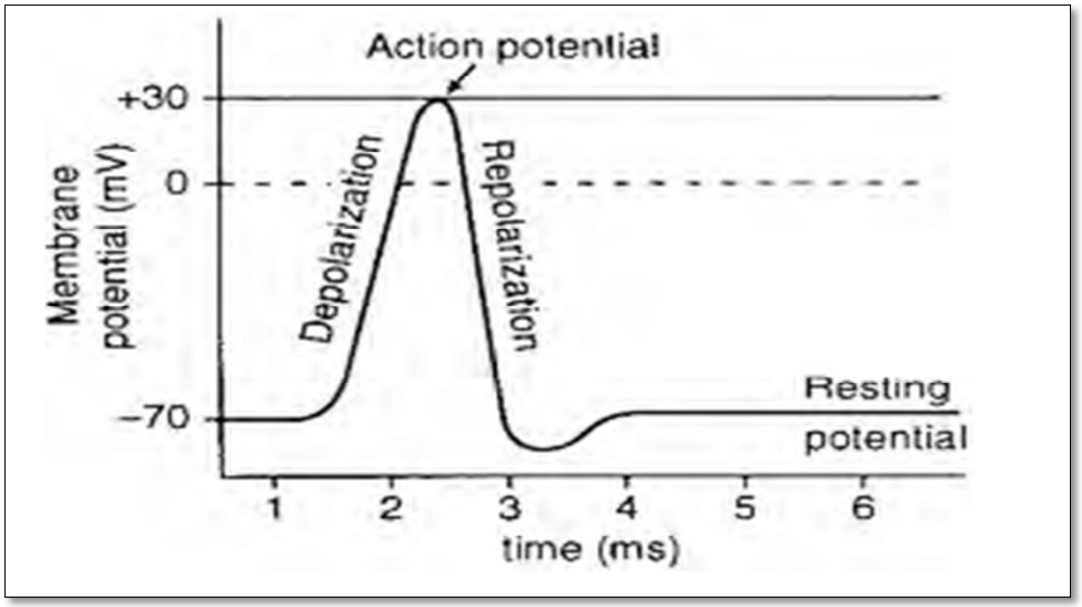


Figure 5: Nerve Action potential [17]

Like other cells in our body the electric potential inside a neuronal cell body is negative. This is known as the resting membrane potential and is about -70 mv. A neuron when stimulated brings about a change in the ion permeability of the neuronal cell membrane which lasts for a short time. There is increase in conductance of sodium channels with change in permeability. A strong stimulus can depolarize the neuronal cell membrane and produce an action potential which propagates along the nerve and stimulates the muscle resulting in contraction of the muscle. If the stimulus is not strong or applied only for a very short time then it fails to produce an action potential. A nerve action potential is shown in Figure 5.

- Rheobase

The minimum amount of current required to produce an action potential is known as rheobase. Below this level an impulse cannot be produced by the current even if it is applied for a long duration.

- Chronaxie

Chronaxie refers to the time for which the current should be applied in order to initiate an impulse. The current applied should be twice the rheobase. The excitability of different tissues can be described with help of chronaxie.

Table 2: Chronaxie of Different Nerves

Nerves	**Chronaxie time in millisecond**
Unmyelinated C fiber	0.40
Myelinated Aδ fiber	0. 17
Myelinated Aα fiber	05-0.10

Threshold current can be defined as the minimum current that is required to produce a motor response. A current value of 0.2-0.7 mA is sufficient to provide a successful block. The distance of the needle from the nerve cannot be determined by the value of current used to produce a motor response. Even when the stimulating needle is in close proximity to the target nerve it possible that there could be no motor response with current intensity as high as 1.5 mA. This has been demonstrated with help of ultrasound.

Nerve stimulators produce a constant current between the anode and cathode which is independent of the impedance of the tissue that surrounds the nerve fibre. The output of current can vary from .01 mA to 5 mA. The output of the current can be changed by the knob present in the peripheral nerve stimulator.

- Distance

$E = K (Q / r^2)$ is known as the coulomb's law. In the above equation E is the intensity of the stimulus, K is the constant and Q gives the minimum current from the tip of the stimulating needle and r is the distance between the source of the current and the target nerve. As per the equation the stimulating current Q is directly proportional to r^2, where 'r' is the distance of the needle from the target nerve. Hence when the needle is in close proximity to the target the amount of current required to produce a motor response is less and vice versa. So when the distance of the needle from the target nerve is decreased from 4 mm to 1 mm the current intensity becomes one by sixteenth its original intensity.

- Polarity

The stimulating needle is kept as the cathode i.e. needle is negative, to which the nerve stimulator is connected. It is ideal to keep the stimulating needle as the cathode rather than anode as the latter would make the nerve hyperpolarised and in turn increase the intensity of the current required to produce a response.

- Frequency

The ideal frequency for nerve stimulation in peripheral nerve blockade is 1 to 2 Hz. A more frequent stimulation of the nerve will increase the patient discomfort and a

less frequency of stimulation might increase the risk of intraneural placement between the current stimuli.

- Stimulating needles

Stimulating needles are of two types insulated and non-insulated. Currently only insulated needles are used. The whole shaft of an insulated needle is insulated except for its tip.

Uninsulated needles or the bare stimulating needles have flow of current occurring along the entire shaft of the needle while in an insulated needle the current flow is only at the tip. Hence a higher intensity of current is required in case of an uninsulated needle for stimulation. There is increase in the accuracy and ease of identification of the target nerve when an insulated needle is used. When the distance from the target nerve fibre is increased there is an increase in the intensity of the stimulating current for an insulated needle. Needles are available in different lengths ranging from 25-150 mm. Needle gauge range from 20 to 25 G. The length of the needle required for nerve stimulation depends on the site where nerve blockade is performed and the type of nerve that is being blocked. There are many markings on the stimulating needle that helps determining the depth of the needle under the skin. For continuous blockade of nerves it is possible to insert catheters to a desired location through an insulated needle with a Tuohy tip or by catheter over needle method. Another type of catheters that can be used is stimulating catheters. These emit current from their tip that would in turn help in locating the final position of the tip of the stimulating needle.

Using a Nerve Stimulator for a Peripheral Nerve Block

Check the equipment prior to performing the nerve block. The nerve stimulator is set at a current of 1-2 mA, pulse duration of 0.1 milliseconds and frequency of 2 hertz. With the help of ECG electrodes the anode is connected to the patient and the cathode i.e. the stimulating needle is connected to the peripheral nerve stimulator. The flexible tubing of the nerve stimulator is connected to the syringe containing the local anaesthetic agent and it is flushed with it in order to prevent the injection of air bubbles into field while performing the block. The operator has to make sure the circuit is complete before performing the nerve block. Some nerve stimulators have flashing lights or audible sounds that indicate that the circuit is complete. The needle is advanced till the desired motor response ie muscle twitch is obtained. Once the motor response is obtained the current is reduced to a point where there is complete absence of motor response. The current intensity is noted and 0.2 mA to 0.5 mA is considered the ideal range.

If motor response is obtained when the current intensity is less than 0.2 mA, then intraneural placement of the needle is indicated. Hence, the needle should be withdrawn and repositioned immediately.

After locating the nerve with the stimulating needle aspirate with help of syringe in order to rule to prevent intravascular injection of local anaesthetic agent. Once aspiration is negative local anaesthetic is injected in 5 ml increments without changing the position of the needle tip. The motor response disappears when 0.5 to 1 ml of local anaesthetic agent is injected. Intraneural placement of the needle can be identified by failure of disappearance of the motor response this is because when the needle is

placed correctly there is disappearance of motor response after injection of a small volume of local anaesthetic agent. This is known as the 'Raj Test' and the disappearance of motor response is explained by the increase in electrical conductivity around the stimulating needle tip when electrically conducting solutions like normal saline or local anaesthetic is injected. This causes a decrease in the current density around nerve fibre and leads to disappearance of twitch or motor response. Another method to know intraneural placement is the increase in resistance felt during the injection of drug or saline.

When an intraneural placement is suspected the needle tip is immediately withdrawn and placed correctly under ultrasound guidance.

C) LANDMARK TECHNIQUE OR BLIND APPROACH

Anatomic landmarks are important in the performance of supraclavicular block using this technique. Over the first rib the three trunks are found to be clustered. They lie posterior in relation to the subclavian artery and can be easily appreciated in a thin patient. [11]

The patient is made to lie in supine position with the head facing the opposite side. The arm on the same side is adducted and the hand is extended as far as possible towards the ipsilateral knee. In the classic technique, the operator marks the posterior belly of sternocleidomastoid muscle and midpoint of clavicle.

After skin preparation using antiseptic solution a 22 gauge 4 cm needle is introduced by the anaesthetist in a caudad direction slightly medial and posterior till paraesthesia is obtained or till the first rib is encountered. If the first rib is till subclavian artery or plexus is encountered. If the subclavian artery is encountered then

the needle is withdrawn and introduced posterolaterally which would result in paraesthesia as plexus is reached. Once the plexus is identified 20-30 ml of local anaesthetic is injected in 3 ml increments. Aspiration is done after injecting every 3 ml in order to prevent intra-arterial injection of local anaesthetic.

The rib is usually encountered at a depth of 3-4 cm. In an obese patient or if there is distortion of anatomy or hematoma the depth may vary.

The modified plumb bob technique involves almost the same technique except that the needle entry point is at the lateral border of the sternocleidomastoid muscle.

D) COMBINATION OF ULTRASOUND & PERIPHERAL NERVE STIMULATOR

This involves combination of both ultrasound guided imaging of the plexus and use of peripheral nerve stimulator to elicit motor response. It improves the precision of nerve block and helps in reducing complications like pneumothorax and intra-arterial injection of local anaesthetic. This technique also enables in reducing the amount of local anaesthetic solution used to provide the nerve block.

- **Contraindications**

Contraindications to peripheral nerve blocks can be divided into absolute and relative contraindications. [11]

ABSOLUTE CONTRAINDICATIONS:

1. Patient refusal
2. Infection at the site of injection: Infection at the injection is an absolute contraindication as insertion of needle can spread the infection. In addition local anaesthetics do not work in acidotic environment.
3. An allergy to local anaesthetics. If the patient had a true allergic reaction to a local anaesthetic, it is essential to identify the local anaesthetic agent. Ester local anaesthetics have a greater incidence of allergic reactions, due to their metabolism to Para Amino Benzoic Acid (PABA). Amide local anaesthetics have a very low incidence of allergic reactions.
4. Diaphragmatic paralysis on the contralateral side.

RELATIVE CONTRAINDICATIONS:

1. Paediatric, combative, and/or demented patients.
2. Bleeding disorder. Hematoma formation result of bleeding disorders can lead to ischaemic nerve damage. In case of peripheral nerve blocks for extremities can cause tourniquet syndrome and, hence, ischaemic damage.
3. Pre-existing peripheral neuropathies- there is a possibility it can lead to permanent nerve damage. Hence, careful documentation of sensory and motor deficits should be done prior to the administering peripheral nerve block.

- **Complications**

Even though the block appears to be difficult especially in obese individuals, complications associated with supraclavicular block are few. Pneumothorax appears to be a major complication associated with this block and is more prone to occur with landmark technique than with ultrasound guided method. Supraclavicular block is best avoided in uncooperative patients or in those patients with respiratory distress.

Other complications include phrenic nerve block (40% to 60%), Horner's syndrome, and neuropathy. Phrenic nerve block and cervical sympathectomy need only reassurance of the patient. Permanent nerve damage is possible, but very rare.

4. DRUGS

A) ROPIVACAINE

It is a new local anaesthetic agent with prolonged duration of action belonging to the amino amide group. Ropivacaine along with bupivacaine and mepivacaine belong to the pipecoloxylidides group of local anaesthetics. It was found that the propyl derivatives of pipecoloxylidides are less cardio toxic than butyl group. [19]

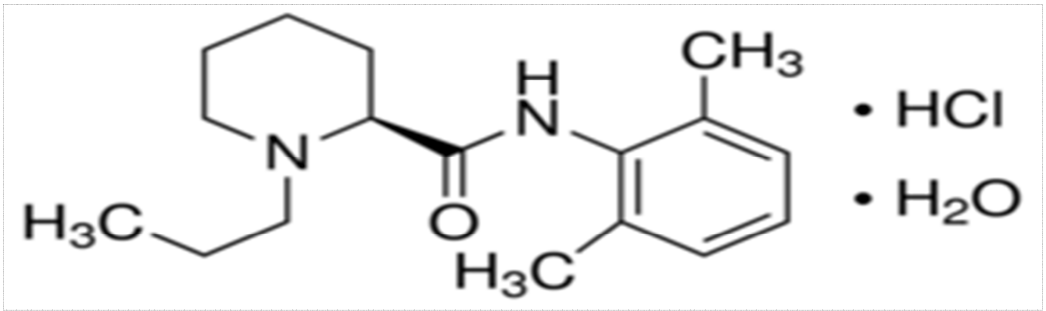


Figure 6: Chemical Structure of Ropivacaine [19]

Chemical Structure

Ropivacaine is chemically known as S-(-) propyl-2', 6'-pipecoloxylidide hydrochloride monohydrate. The drug is a white crystalline powder with a molecular weight of 328.89.

Physical Properties

Ropivacaine has a pKa similar to that of bupivacaine (8.1) and mepivacaine. Ropivacaine has minimal lipid % solubility. Ropivacaine is preservative free and is available in 2 mg/ml (0.2%), 5 mg/ml (0.5%), 7.5 mg/ml (0.75%) and 10 mg/ml (1%) concentrations. The specific gravity of Ropivacaine is 1.002 to 1.005 at 25 degree C.

Mechanism of Action

Ropivacaine mainly blocks the conduction of nerve impulses and also the propagation of nerve impulse by blocking the sodium channels in the nerve cell membrane. Pain impulses are mainly transmitted by small myelinated A fibres and unmyelinated C fibres whereas large A fibres transmit mainly motor impulses. The C fibres are blocked at the same rate by all local anaesthetics while the rate of blockade of A fibres depend on the physiochemical properties like pKa and lipid solubility. Even though the pKa of Ropivacaine and bupivacaine are similar Ropivacaine is less lipid soluble than bupivacaine and, hence, it takes more time to block A fibres than bupivacaine. Ropivacaine has less motor blockade than bupivacaine. The order of loss of nerve function is pain, temperature, touch, proprioception and skeletal muscle tone.

Pharmacokinetics

a. <u>Absorption and distribution:</u>

The plasma concentration of Ropivacaine depends mainly on the total dose of the drug administered, the mode of administration and also on haemodynamic state of the patient along with vascularity of the site of administration.

Ropivacaine is 94% bound to the plasma protein alpha 1 acid glycoprotein .On intravenous administration the pharmacokinetics of Ropivacaine is linear and dose dependant up to 80 mg while on epidural administration the absorption is complete and biphasic. The mean half-life of the initial phase is 14 minutes and this followed by slower phase of 4.2 hours. Ropivacaine rapidly crosses the placenta on epidural administration but the plasma concentration of Ropivacaine is found to be lower in the foetus as the alpha 1 acid glycoprotein is more in the mother.

b. Metabolism and excretion :

Ropivacaine is mainly metabolised by aromatic hydroxylation and N-dealkylation both of which happens in the liver. Aromatic hydroxylation by cytochrome p4590A1 enzyme produces 3 hydroxy Ropivacaine. N-dealkylation to -pipecoloxylidide is done by cytochrome 3A4. The main pathway of excretion is via the kidneys. After intravenous administration 86% of the drug is excreted via the kidneys. The mean half-life of Ropivacaine is 1.8 (+/- 0.7) hour after intravenous administration and 4.2 (+/- 1) hour after epidural administration.

c. Potency

The potency of local anaesthetic depends mainly on its lipid solubility. Ropivacaine is found to be equipotent to bupivacaine at higher doses and at lower concentration it is found to be less potent than Levobupivacaine and bupivacaine.

Pharmacodynamics

Ropivacaine is found to have less cardio toxicity as compared to bupivacaine is mainly due to its lower lipid solubility and stereo selective properties. Ropivacaine is found to have antibacterial activity especially against staphylococcus aureus, pseudomonas and E.coli. Ropivacaine is found to inhibit platelet aggregation especially in concentration used for epidural administration.

Dosage and Clinical Application

a. For major or minor nerve blocks : 0.2-0.5% concentration of Ropivacaine can be used .10-100 mg or 5-10 ml can be used for minor blocks and 250 mg or 30-

40 ml can be used for major nerve blocks. For ultrasound guided blocks the dose is less.

b. Epidural anesthesia: 0.2-0.75% Ropivacaine can be used .Volume of drug can range from 15-30 ml.
c. Spinal anesthesia: 0.5-0.75% can be used. 2-3 ml or 15-20 mg is used
d. For infiltration 0.2-0.5% Ropivacaine can be used 0.3 mg /kg is the maximum dose that can be used.

Adverse Effects

These include injection site reaction and pain. The main cardiovascular effects of Ropivacaine include vasovagal attack postural hypotension and syncope. Ropivacaine do not cause excitatory symptoms of central nervous system toxicity owing to its depressant effects in the medulla. It can cause tinnitus, hearing abnormalities, hypomagnesaemia, and neonatal jaundice.

Drug Interaction

Drugs like theophylline and imipramine are found to increase the dose of Ropivacaine via competitive inhibition as these drugs are also metabolised by CYP1A2.

Ropivacaine should be used in caution with other amide type local anaesthetics as the toxic effects of these drugs are additive.

B) LEVOBUPIVACAINE

Levobupivacaine is an amide local anaesthetic. It is the L (-) isomer of the commonly used local anaesthetic bupivacaine. [20]

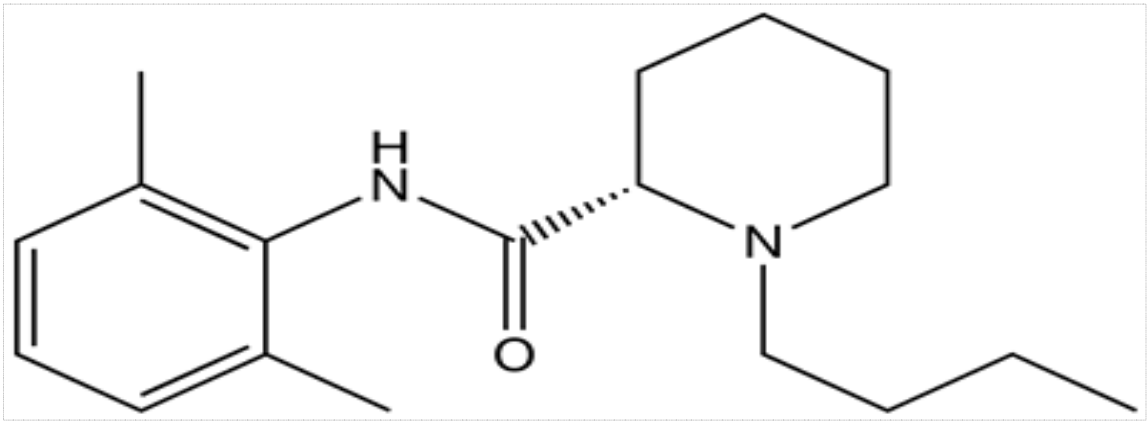


Figure 7: Chemical Structure of Levobupivacaine [20]

Structure and Physical Properties

Levobupivacaine is an amide local anaesthetic and a pure S (-)-enantiomer of bupivacaine with a pKa of 8.1. The amino group can exists either in the tertiary form or in the quaternary form based on the pH of the drug. The quaternary form is more water soluble.

Mechanism of Action and Pharmacokinetics

Levobupivacaine exerts its mechanism of action by reversible binding to the intracellular portion of the sodium channels and hence preventing sodium influx and depolarisation .The onset of action varies according to the diameter of the nerve of the nerve fibre, presence of myelin sheath and conduction velocity. [20]

The onset and duration of action of Levobupivacaine varies depending on the route of administration as its absorption is dependent on the vascularity of the tissue. Levobupivacaine administered via epidural space shows biphasic absorption-i.e. rapid absorption of small quantity of the drug followed by slow absorption of the remaining drug. The peak concentration is reached within 30 minutes after epidural administration of Levobupivacaine. The absorption of Levobupivacaine via epidural space gets affected with age as the initial rapid phase of absorption is shorter in elderly (>70 years of age). The spread of analgesia is found to be higher by 3 dermatomes in elderly. Hence dose adjustment is required in elderly individuals.

The volume of distribution of Levobupivacaine following intravenous administration is 66.91+/-18.23 litres. The half-life of Levobupivacaine is 3.3 hours and the rate of clearance following intravenous administration is 39.06+/-13.29 l/hour.

Levobupivacaine is highly protein bound compared to racemic bupivacaine almost 97% of the drug is bound to alpha 1 acid glycoprotein.

Levobupivacaine is mainly metabolized in the liver by CYP3A4 and CYP1A2 to inactive metabolites desbutyl Levobupivacaine and 3 hydroxy Levobupivacaine. 3 hydroxy Levobupivacaine further metabolised to glucoronide and sulphate conjugates.

Dosage of Levobupivacaine

Table 3: Dosage of Levobupivacaine.[20]

Surgical Anaesthesia	**Percentage concentration of drug**	**Dosage**
Epidural Anesthesia – Surgical procedure.	0.5 – 0.75	10 -20 ml of the solution, 375 mg is the maximum dose used.
Peripheral Nerve Block	0.25 – 0.5	10-40 ml can be used .Maximum dose is 150 mg.
Spinal Anesthesia-Surgical procedure	0.5	2- 3 ml .Maximum dose used is 15 mg.
Local Infiltration : Adults	0.25	2-60 ml can be used for local infiltration
Pain Management	**Concentration of the drug in percentage**	**Dosage**
Epidural for labour analgesia.	0.125	4-10 ml/ hour (5-12.5 mg/h)

Adverse Effects:

Levobupivacaine compared to bupivacaine has relatively less cardio toxicity and is hence is preferred for peripheral nerve blocks. The nonspecific side effects include headache hypotension, nausea, vomiting and dizziness. Levobupivacaine has a good safety profile with a safety margin of 1.3 which means the toxic effects of the drug is not evident until the concentration is more than 30% in the blood.

5. ASSESSMENT OF POSTOPERATIVE ANALGESIA

a) Visual Analogue Scale

It is also known as numeric rating scale .It is more sensitive for assessing acute pain especially postoperative pain. This scale is based on the patient's subjective feeling of pain. The scale ranges from no pain (score of 0) and worst pain (score of 100). A higher score indicates greater severity of pain.

The pain scoring as per VAS scoring is as follows:

- No pain (0-4 mm)
- Mild pain (5-44 mm),
- Moderate pain (45-74 mm)
- Severe pain (75-100 mm) [21]

VAS takes less than one minute to complete .Patient is asked to draw a line perpendicular to the VAS line that represents the pain intensity at that moment.
The score is then determined by measuring the distance between the no pain mark in the VAS scale and patients mark.

b) Numeric Rating Scale:

It is a numeric variant of the VAS score and it is a unidimensional measure of severity of pain. It is an 11 point scale –with 0 representing no pain and 10 representing very severe pain. Higher the scores more severe is the pain. NRS takes less than one minute to complete and is very useful for assessment of post-operative pain especially in elderly and those with motor impairment. [4]

MATERIAL AND METHODOLOGY

Materials and Methodology

Source of data: Christian Medical College, Vellore

Key Criteria

Inclusion Criteria:

1) Patients aged 18-70 years scheduled for upper limb surgeries
2) ASA 1-2 Patients

Exclusion Criteria:

1) Patients who refused to be part of the study.
2) Patients with significant coagulopathies.
3) Patients with psychiatric history.
4) Patients allergic to amide local anaesthetic
5) Pregnant patients
6) Patients with weight less than 50 kg
7) Diaphragmatic Paralysis

Method of randomization:

Block randomization method was used. The computer generated random codes were used for allotting the patient into the two groups.

Method of allocation concealment:

Sealed and opaque envelopes were used.

Blinding and masking:

Principle investigator and the co-investigator were blinded.

METHODS

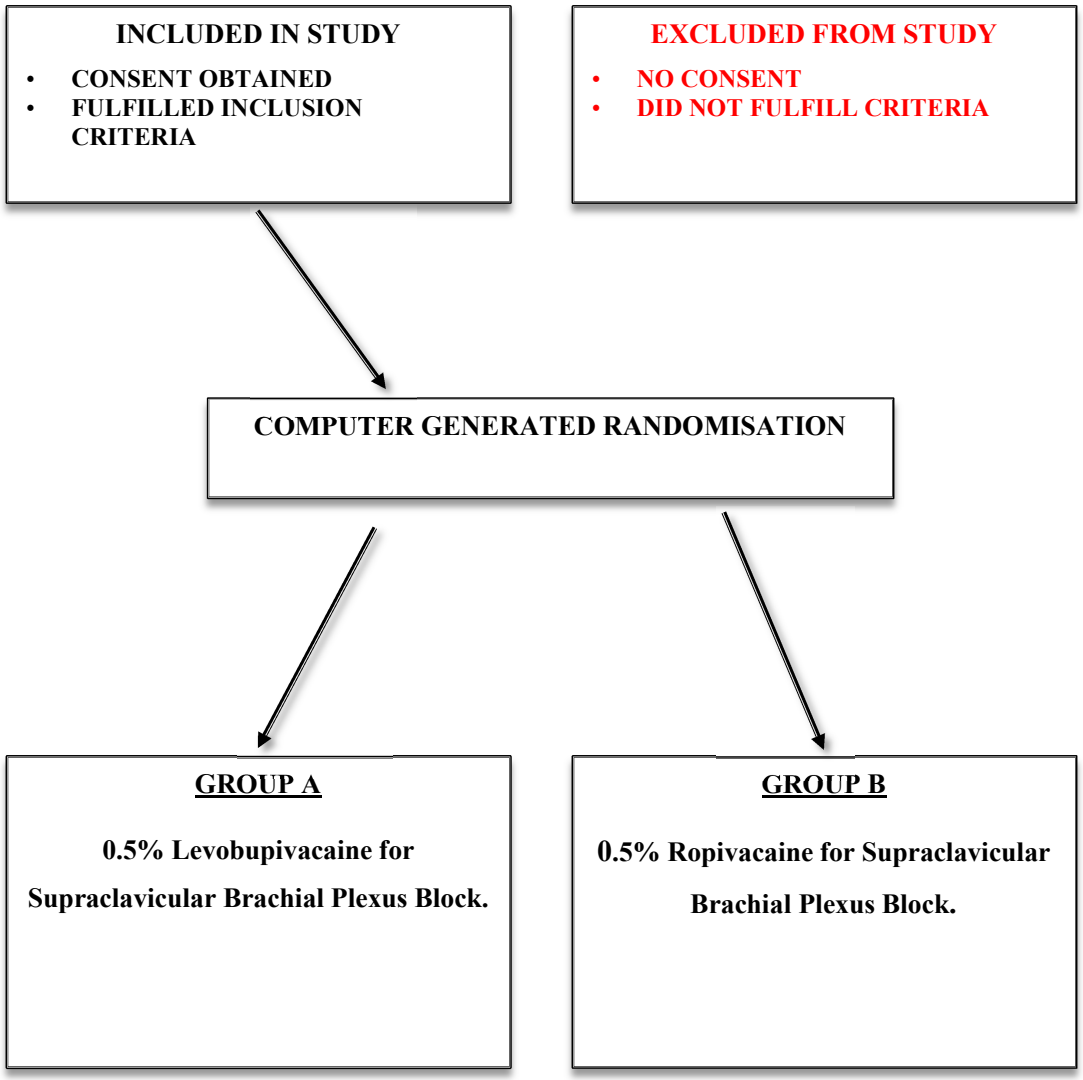
All consenting patients posted for upper limb surgery in the age group 18 to 70 years and fulfilling the inclusion criteria were enrolled for the study. Documents providing information on the proposed study and form for obtaining consent (Consent Form) were provided to the patient in the pre-anaesthesia clinic. Patients were premedicated with Tab Diazepam 5 mg (for patients weighing less than 50 kg); Tab Diazepam 10 mg (for patients weighing more than 50 kg) and Tab Ranitidine 150 mg. Standard fasting orders as per ASA guidelines were followed. In the operating room, an intravenous peripheral access was obtained in the opposite limb and pulse oximetry, non-invasive blood pressure and ECG leads were applied.

Patients allocated, randomly, into two (2) groups based on computer generated block randomization. Group A received 25 ml of 0.5% levobupivacaine and Group B received 25 ml of 0.5% ropivacaine in the supraclavicular brachial plexus block. In each group, supraclavicular brachial plexus block was performed under ultrasound guidance following routine aseptic precautions.

The end of injection of the drug was taken as “time 0”. Patients were evaluated for the onset of motor and sensory blockade every 5, 10, 15, 20, 25 and 30 minutes before the surgery and postoperatively for 3 hours, 6 hours, 12 hours and 24 hours for the duration of post-operative analgesia.

Patients were assessed for sensory blockade by touching the corresponding dermatomes with blunt end of a 26 gauge needle. The palmar surface of index and little fingers were used to test the median and ulnar nerve in the hand respectively. The dorsal surface of thumb was used to test the radial nerve. Motor blockade was

assessed by asking patients to move the thumb wherein grade "0" represented normal movement of thumb i.e. patient was able to touch the pulp of little finger with pulp of thumb, grade "1" represented partial blockade i.e. patient was able to touch pulp of index finger with pulp of thumb and grade "2" was complete blockade i.e. lateral pinch (thumb to lateral aspect of index finger). Postoperatively, pain was assessed using the numeric rating scale (NRS), according to which "0" represented no pain and "10" meant worst possible pain. Post operatively, when NRS was equal to or more than 4, Inj. Diclofenac 75 mg IM was given as rescue analgesic.



Sample size:

The sample size was calculated using n Master 2.0 software. To test the significant difference between the two groups (primary and secondary outcomes), the minimum required number of cases were approximately 31 in each group. **So the total number of subjects needed for this study was 62.**

Table 4: Sample size estimation

Two Means - Hypothesis testing for two means			
	Sensory Block	**Verbal Numeric Rating Scale**	**Postoperative Analgesia**
Standard deviation in group I	2.9	3.14	285
Standard deviation in group II	2.6	1.15	247
Mean difference	2.4	2.28	190
Effect size	0.87	1.06	0.71
Alpha error (%)	5	5	5
Power (1- beta) %	80	80	80
1 or 2 sided	2	2	2
Required sample size per group	21	17	31

The expected mean and standard deviation values were taken from the literature: Cline et al (2004) and Mageswaran and Choy (2011).

STATISTICAL ANALYSIS

Statistical Analysis

The data was analysed using the software SPSS 16.0. The mean and standard deviation was used to describe the outcome measures such as sensory block duration, visual numerical rating scale and postoperative analgesia. The statistical significance between the two groups was analysed using independent samples t test. For non-normal data alternate descriptive statistics such as median was used to describe the observations and the non-parametric test - Mann Whitney U test - was used for testing the significant difference between the two groups. The results were presented using error plots, box plots and histogram plots also. Chi-square test with continuity correction was used to test the significant difference in distribution of treatments among the different categories of age, gender and ASA grades.

RESULTS

Results

A total of 40 patients were recruited in this study between September 2015 and February 2016, with 20 patients in each Group. Group A received 0.5% Levobupivacaine and Group B received 0.5 % Ropivacaine by means of ultrasound guided supraclavicular nerve block. Due to time constraints the sample size 62 could not be reached.

Table 5: Baseline Characteristics

Variables	Group A		Group B		p Value
	N	%	N	%	
Age Group (years)					
18-35	8	40	10	50	0.790
36-50	9	45	7	35	
51-75	3	15	3	15	
Gender					
Male	16	80	17	85	>0.999
Female	4	20	3	15	
ASA					
Grade 1	17	85	14	70	0.449
Grade 2	3	15	6	30	

Demographic Data

The baseline data comparing gender, age and ASA status between Group A and Group B are tabulated below.

- **Gender**

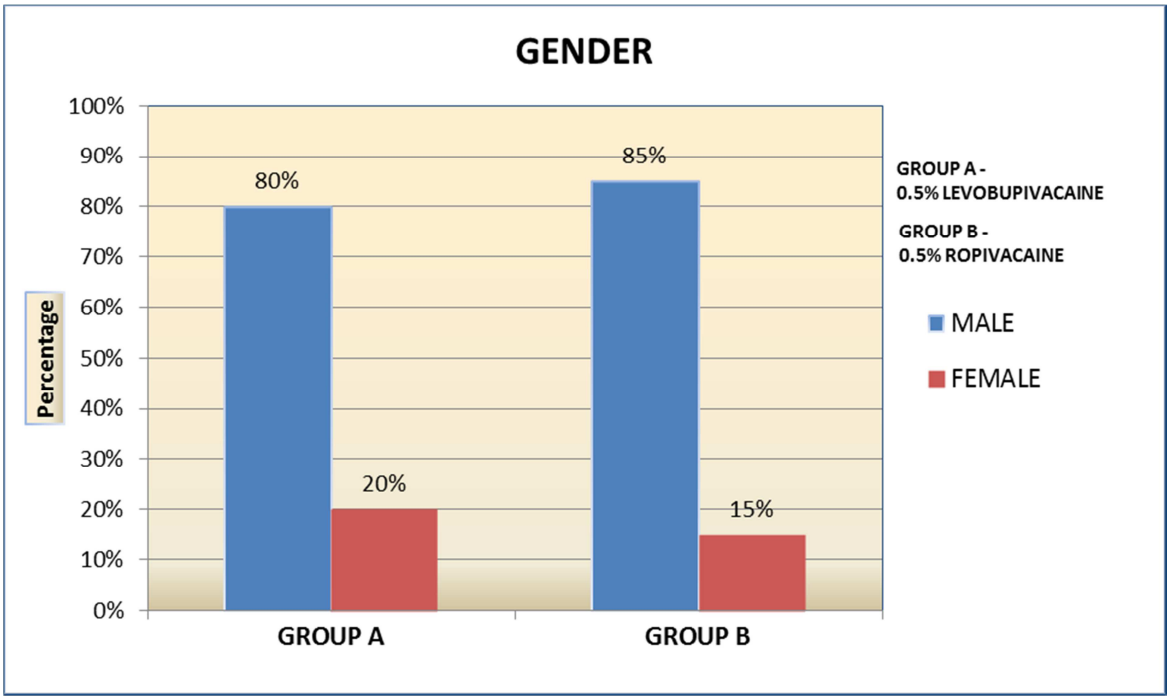


Figure 8: Comparison of Gender Distribution between Group A and Group B patients.

Eighty percent of patients in Group A (0.5% levobupivacaine) were males and eighty five percent of patient in Group B (0.5% ropivacaine) were males. There is no significant difference in the gender distribution between the two groups.

- **Age**

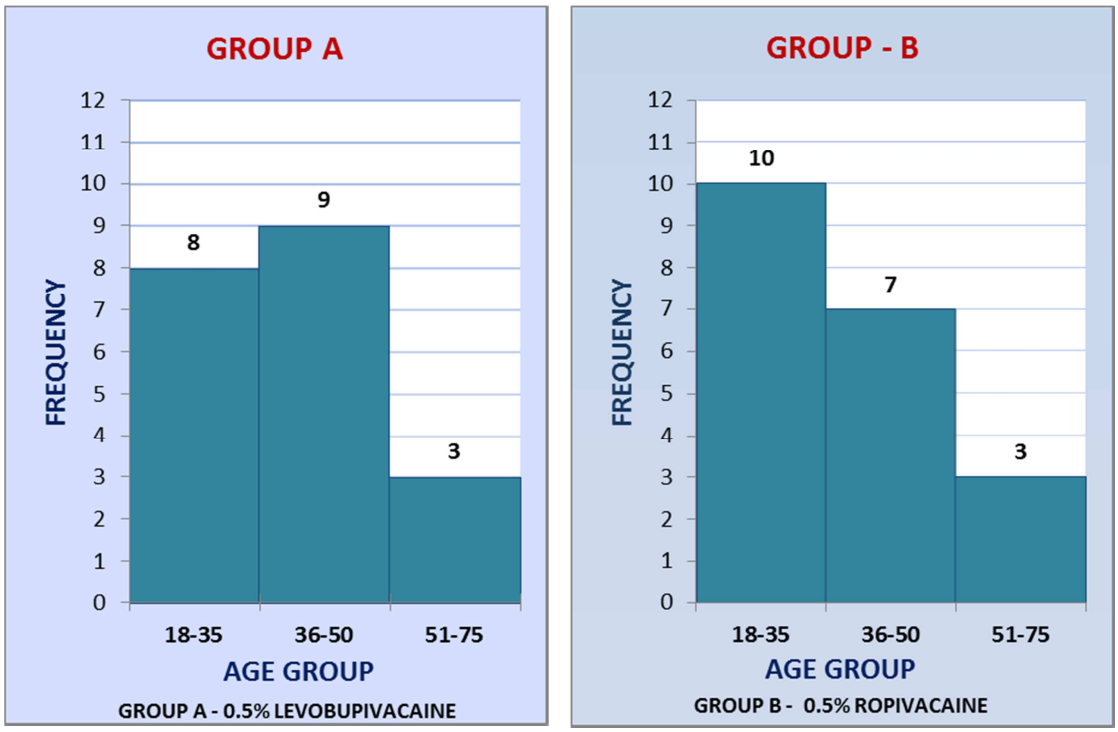


Figure 9: Comparison of Age between Group A and Group B patients

The above histogram depicts age distribution of patients in Group A and Group B. The mean age of patients in Group A (0.5% Levobupivacaine) is 38.5 years and Group B (0.5% Ropivacaine) is 35.75 years.

- **ASA Status**

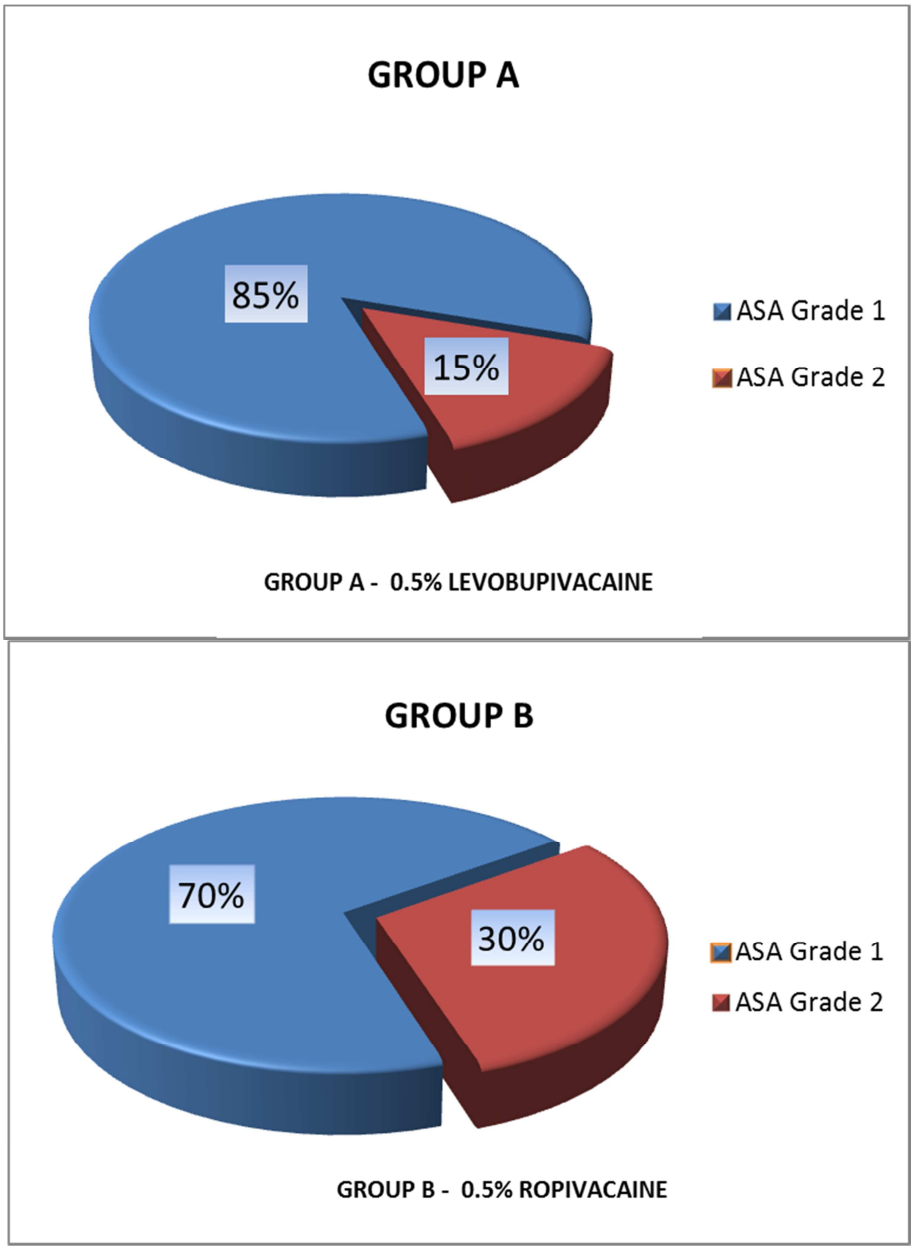


Figure 10: Comparison of ASA status between Group A and Group B patients.

The above pie diagrams compare the ASA status between Group A and Group B patients. Eighty five percent of Group A (0.5% Levobupivacaine) patients belonged to ASA 1 compared to seventy percent of patients in Group B (0.5% Ropivacaine).

Primary and Secondary Outcome

Table 6: Comparison of primary and secondary outcomes between Group A (0.5% Levobupivacaine) and Group B (0.5% Ropivacaine).

VARIABLES	GROUP A 0.5% LEVOBUPIVACAINE		GROUP B 0.5% ROPIVACAINE		p value
	Median	ICR (q1-q3)	Median	ICR*	
Time of onset of sensory block (minutes)	10	10 - 15	10	5 - 10	0.123
Time of onset of motor block (minutes)	10	5 - 15	15	5 - 18.75	0.310
Duration of post-op analgesia (minutes)	745	510 - 1420	735	551.25 - 1548.75	0.588

ICR= INTERQUARTILE

- **Onset of Sensory Block**

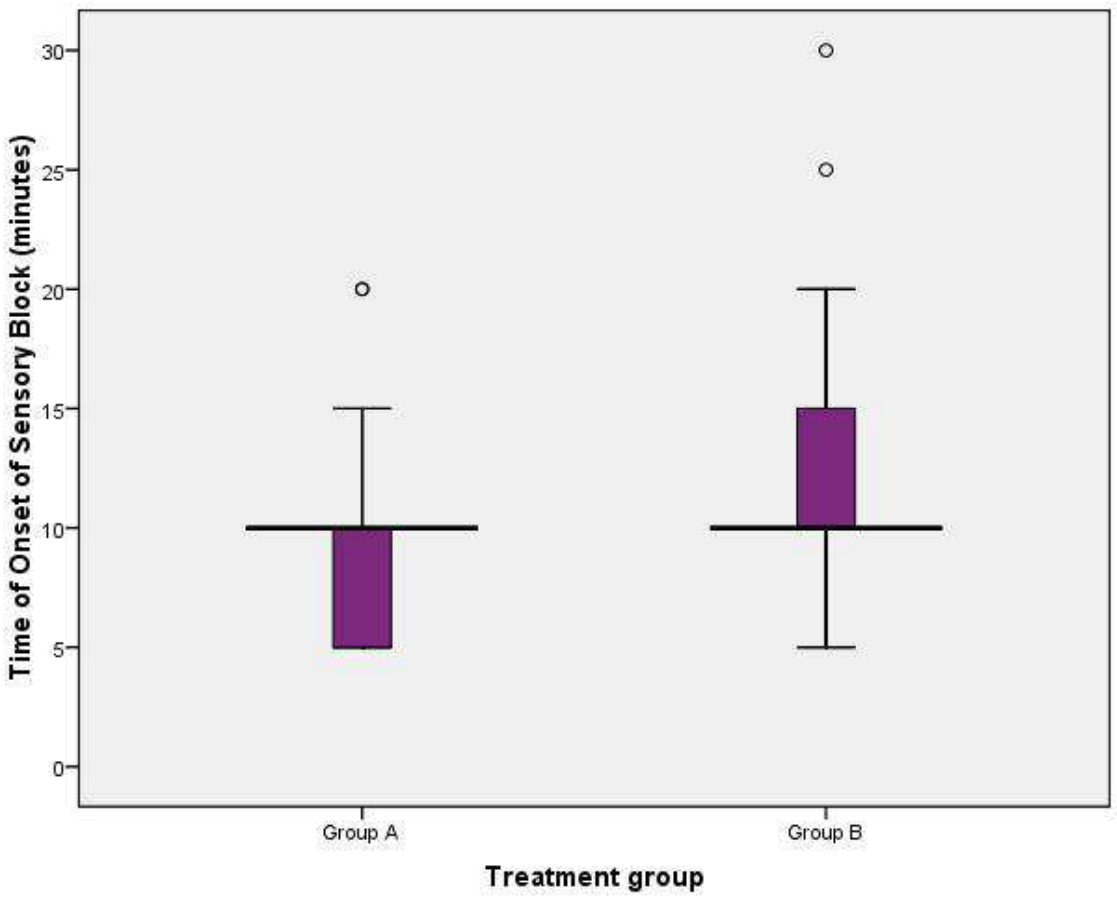


Figure 11: Comparison of Time of onset of sensory block (in minutes) between Group A (0.5% Levobupivacaine) and Group B (0.5% Ropivacaine).

The above boxplot compares the time of onset of sensory block (in minutes) between patients in Group A (0.5% Levobupivacaine) and Group B (0.5% Ropivacaine).The median time of onset of sensory blockade in Group A is 10 minutes and in Group B is 10 minutes. The coloured portion of the boxplot represents the interquartile range which is 10-15 minutes in Group A patients and 5 -10 minutes in Group B patients.

- **Onset of Motor Block**

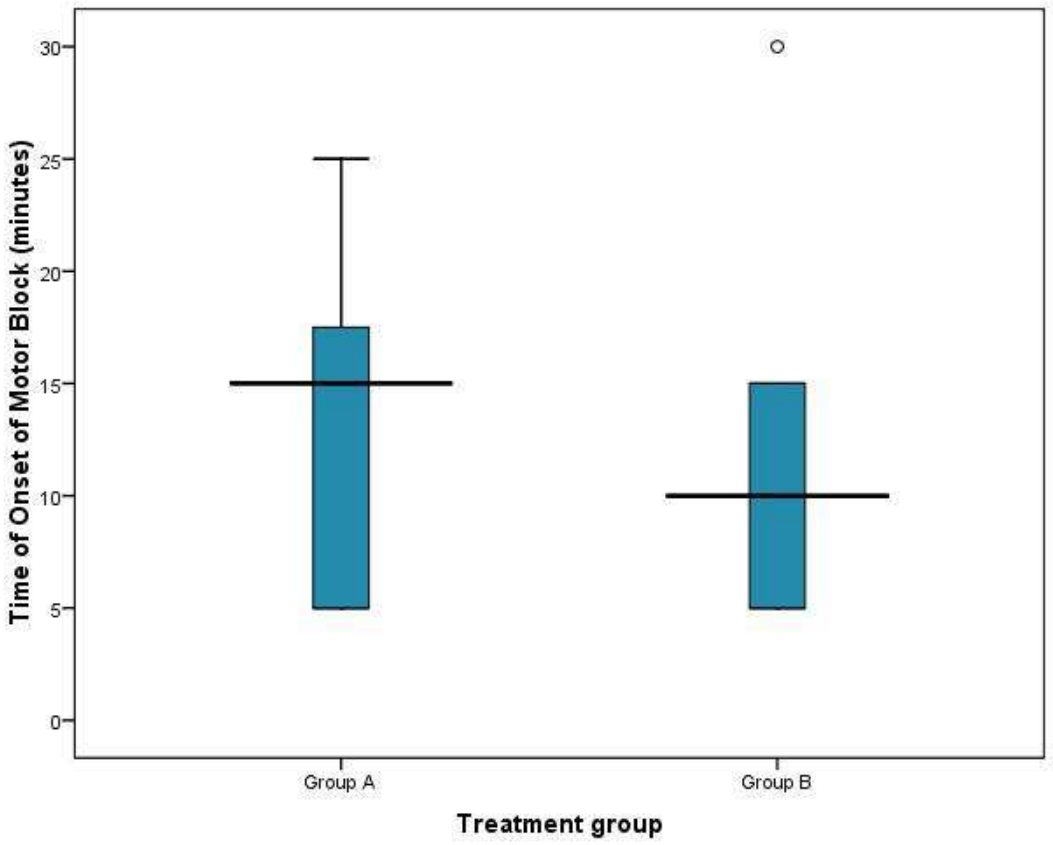


Figure 12: Comparison of time of onset of motor blockade (in minutes) between patients in Group A (0.5% Levobupivacaine) and Group B (0.5% Ropivacaine).

The above box plot represents the time of onset of motor blockade between Group A (0.5% Levobupivacaine) and Group B (0.5% Ropivacaine) patients. The median time of onset of motor blockade is 10 minutes in Group A patients and 15 minutes in Group B patients. The coloured portion of the boxplot represents the interquartile range which is 5-15 minutes for Group a patients and 5-18.75 minutes in Group B patients.

- **Post-operative Analgesia**

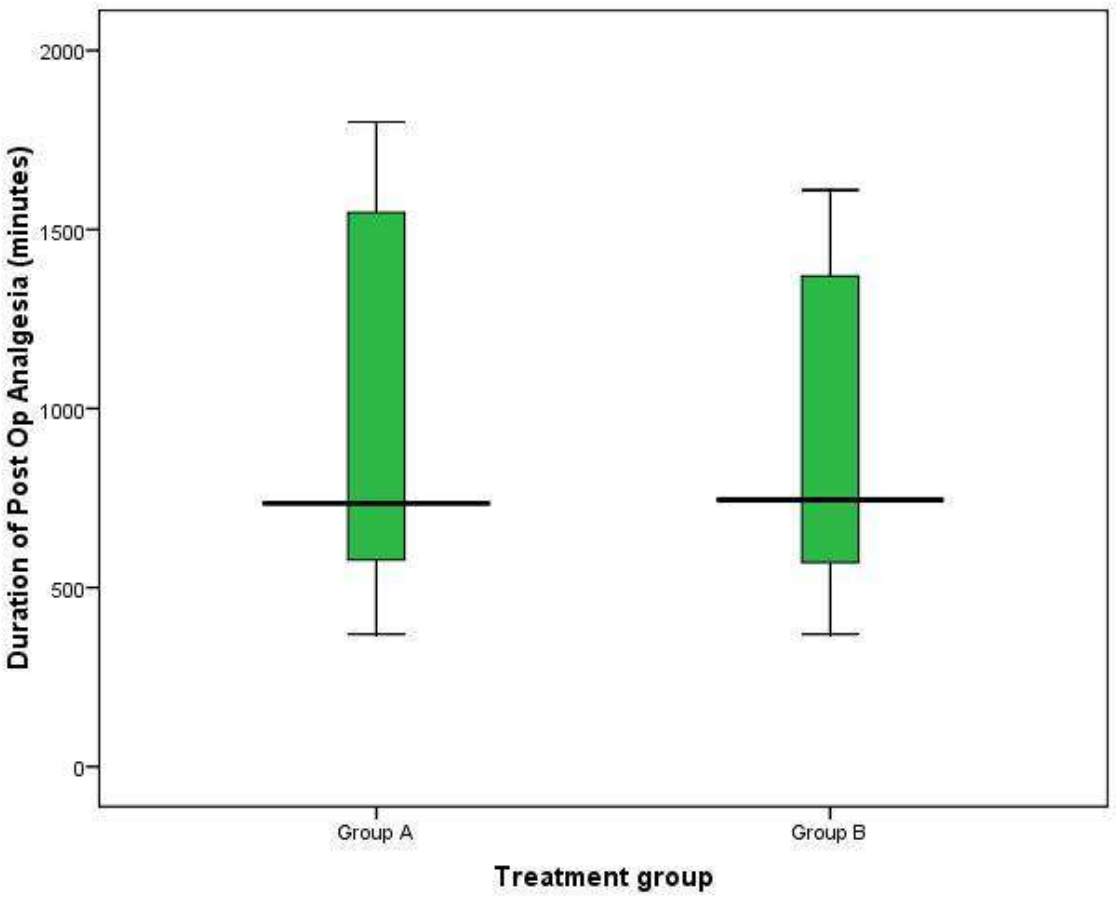


Figure 13: Comparison of Duration of Post-operative Analgesia between Group A (0.5% Levobupivacaine) and Group B (0.5% Ropivacaine) Patients.

The above box plot represents the duration of post-operative analgesia between Group A (0.5% Levobupivacaine) and Group B (0.5% Ropivacaine).The median value is 370 minutes in Group A patients and 735 minutes in Group B patients. The coloured portion of the box plot represents the interquartile range which is 510-1420 minutes in Group A patients and 551-1548 minutes in Group B patients.

Sub Analysis

a) Comparison of post-op VAS score between Group A (0.5% Levobupivacaine) and Group B (0.5% Ropivacaine) patients.

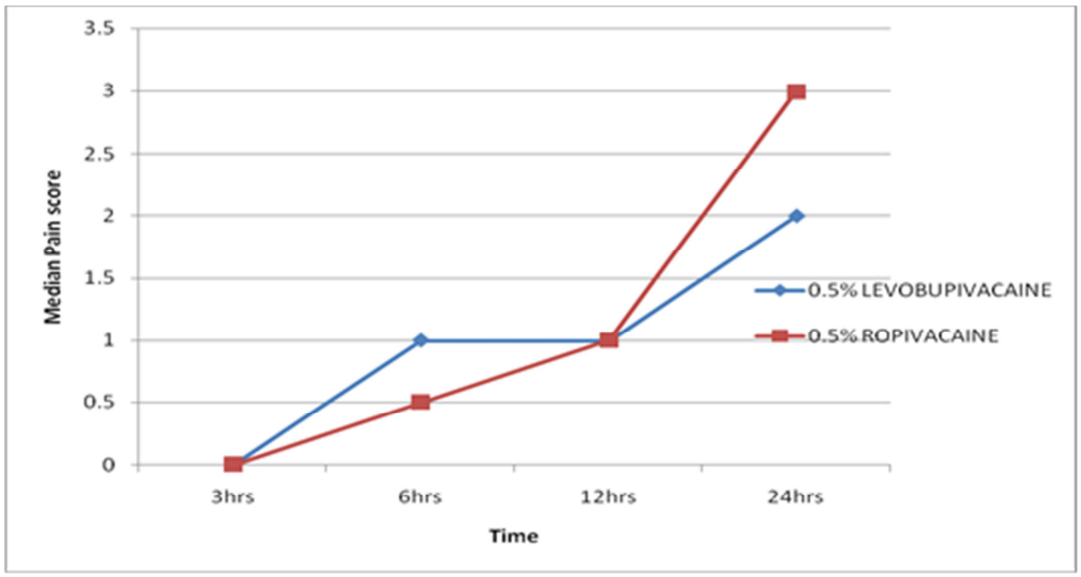


Figure 14: Trend of Post-Operative VAS score of Group A and Group B patients

The above line graph depicts the trend in post-operative VAS score between Group A (0.5% Levobupivacaine) and Group B (0.5% Ropivacaine) patients over a period of 24 hours. Patients in Group A have a rapid increase in pain scores at 12 hours postoperatively. At the end of 24 hours Group A patients have a median pain score of 2 while Group B patients have a median pain score of 3.

b) Comparison of onset of complete and partial sensory blockade (in minutes) between Group A 0.5% Levobupivacaine) and Group B (0.5% Ropivacaine) patients.

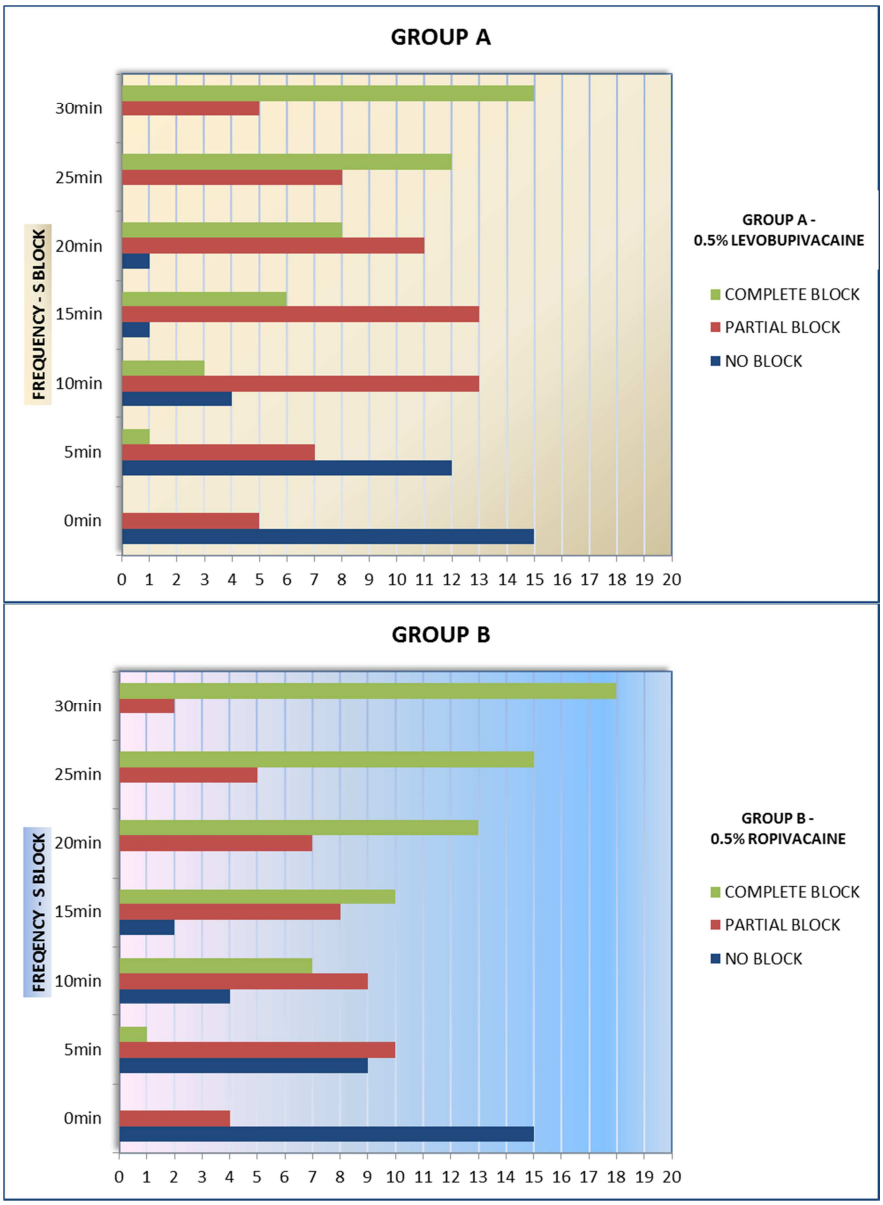


Figure 15: Onset of Partial and Complete Sensory Block (S Block)

The above graphs depict the time of onset of partial and complete sensory blockade in Group A and Group B patients. Complete Sensory blockade occurs as early as 5 min in Group A and Group B. The onset of sensory block was achieved in 20 min for all Group A patients and in 15 min for all Group B patients.

c) Comparison of onset of partial and complete motor blockade (in minutes) between Group A (0.5% Levobupivacaine) and Group B (0.5% Ropivacaine).

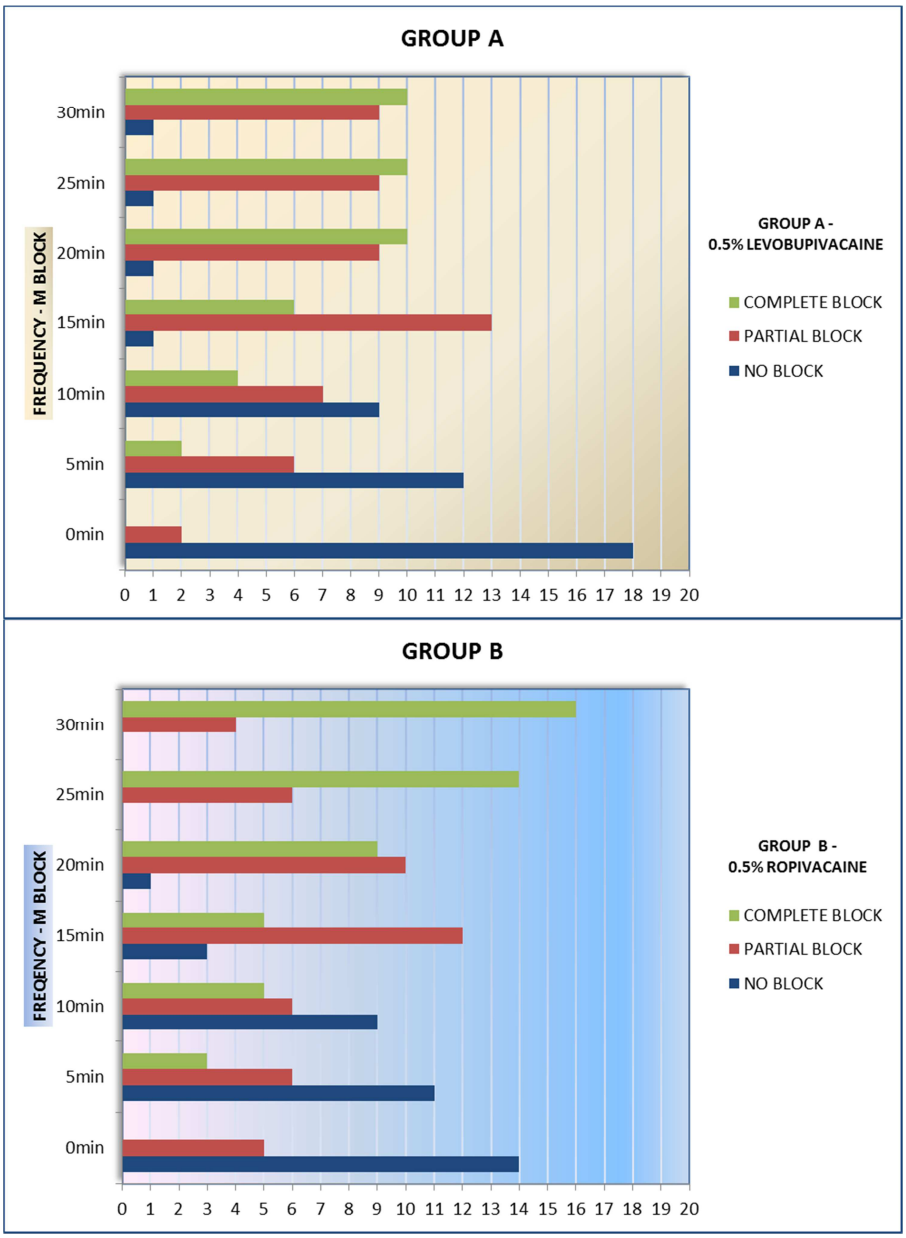


Figure 16: Onset of Partial and Complete Motor Block (M Block)

The above graphs depict the onset of complete and partial blockade (in min) between Group A (0.5% Levobupivacaine) and Group B (0.5% Ropivacaine) patients. Complete motor blockade was achieved as early as 5 minutes by 2 patients in Group A and 3 patients in Group B. Either partial or complete motor block was achieved by

all patients in Group B within 20 minutes. In the case of Group A, all except one patient achieved partial or complete motor block within 15 min and one patient achieved motor blockade after 30 minutes.

DISCUSSION

Discussion

It appears that demographic data such as age, sex, patient weight and ASA grade, diagnoses and surgery duration are equally distributed between the two groups of 20 patients each and are, hence, comparable.

In our study, the primary objective was to compare the onset of motor and sensory blockade between Group B (0.5% Ropivacaine) and Group A (0.5% Levobupivacaine) patients. In Group A and Group B patients the median time for onset of sensory blockade was found to be 10 minutes. The median time for onset of motor blockade in Group A was 10 minutes and Group B was 15 minutes. This difference was found to be not significant at the 5% significance level ('P value' of 0.123 for time of onset of sensory blockade and 'P value' of 0.310 for time of onset of motor blockade).

The secondary objective was to compare the duration of post-operative analgesia between Group A and Group B patients. In Group A patients, the median duration of post-operative analgesia was 745 minutes which is slightly longer than Group B patients whose median value was 735 minutes. However this difference was found to be not significant at the 5% significance level as 'P value' is 0.588.

In sub-analysis, comparing the VAS score between two groups, it was found that the median pain scores in Group A (0.5% Levobupivacaine) was two (2) while that in Group B (0.5% Ropivacaine) was three (3).

In a similar study conducted by LT Erike cline et al, it was found that the duration of sensory analgesia was longer in the Levobupivacaine group (831 minutes) than in the Ropivacaine group (642 minutes) with a 'P value' of 0.013. This difference

was probably due to the fact that they had used higher volume (40 ml of 0.5% Levobupivacaine and 40 ml of 0.5% Ropivacaine) of local anaesthetics and also had added additives to prolong the action (1 : 200000 of epinephrine).The technique used in their study was ‘axillary brachial plexus block’.

CONCLUSION

Conclusion

In our study, the onset of sensory and motor blockade and the duration of postoperative analgesia between 0.5% Ropivacaine and 0.5% Levobupivacaine were comparable.

LIMITATION

Limitation

- Sample size calculated to detect a significant difference in the block onset and duration between the two groups amounted to 31 patients in each arm. However, only 20 patients were recruited in each arm owing to time constraints.
- Duration of post-operative analgesia could have been better assessed if more volume of local anaesthetic was used. Complete onset of motor and sensory blockade could have been better assessed if the patients were monitored for at least 1 hour after the block in the pre-operative period.

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ANNEXURES

1. Data Collection in Excel

All collected data was tabulated in "Excel" and analysed for obtaining the onset of motor and sensory blocks and duration of post-op analgesia and the various graphs and pie charts.

Btle No.	Date	ASA Grade	Time Block	Time Incis	Time 0 min	S Block 0 min	M block 0 min	S Block 5 min	M block 5 min	S Block 20 min	M block 20 min	S Block 25 min	M block 25 min	S Block 30 min	M block 30 min	3hrs Pain	6hrs Pain	24hrs Pain	Time Rescue	Time Onset of S BLOCK (mts)	Time Onset of M BLOCK (mts)	Duration of Post Op Analgesia (mts)
1	18-09-15	1	13:38	14:17	13:38	0	0	0	1	1	2	1	2	2	2	2	4		22:50	10	5	370
2	22-09-15	1	07:55	8:30	7:55	0	0	0	1	1	2	1	2	1	2	0	0	2	11:20	10	5	1560
3	22-09-15	1	09:30	10:13	9:30	0	0	0	0	1	0	1	1	2	1	1	2		9:20	20	25	1100
4	25-09-15	1	07:45	8:15	7:45	0	0	0	0	0	0	1	0	1	1	0	2		0:21	25	30	801
5	02-10-15	1	13:10		13:10	0	0	0	0	1	1	2	1	2	1	0	1	2	17:00	15	15	1500
6	02-10-15	1	15:05		15:05	0	0	1	1	2	2	2	2	2	2	0	0	3	20:00	5	5	1560
7	09-10-15	1	10:30	11:15	10:30	0	0	0	0	1	1	1	1	1	2	0	2	2	16:00	15	15	1500
8	09-10-15	2	13:40	14:06	13:40	1	1	1	1	2	2	2	2	2	2	0	1		2:00	10	15	525
9	09-10-15	1	15:40	16:25	15:40	0	0	1	0	2	1	2	2	2	2	0	1	2	21:00	5	10	1545
10	16-10-15	1	07:50	8:20	7:50	0	0	0	0	1	1	1	1	2	2	0	0		9:40	10	15	1270
11	16-10-15	1	13:50	14:20	13:50	0	0	1	0	1	1	2	1	2	2	0	2		6:40	5	10	790
12	16-10-15	1	16:20	16:50	16:20	0	0	0	0	1	1	1	1	2	1	1	3		8:00	10	10	750
13	23-10-15	1	12:25	13:00	12:25	1	0	1	0	2	1	2	1	2	1	0	3		23:00	15	15	420
14	23-10-15	2	14:25	15:00	14:25	0	0	1	0	2	1	2	2	2	2	0	1	3	19:00	5	15	1550
15	29-10-15	1	18:15	19:30	18:15	1	1	1	1	2	1	2	2	2	2	2	5		5:30	10	25	390

Figure: Print of data-sheet from MS Excel.

Btle No.	Date	ASA Grade	Diagnosis	Time Block	Time Incis	Heart Rate	Sys BP	Dias BP	Time 0 min	S Block 0 min	M block 0 min	S Block 5 min	M block 5 min	S Block 10 min	M block 10 min	S Block 15 min	M block 15 min	S Block 20 min	M block 20 min	S Block 25 min	M block 25 min	S Block 30 min	M block 30 min	3hrs Pain	6hrs Pain	12hrs Pain	24hrs Pain	Time Rescue	Time Onset of S BLOCK (mts)	Time Onset of M BLOCK (mts)	Duration of Post Op Analgesia (mts)
1	18-09-15	1	SPILT NAIL I MALIET DEFORMITY	13:38	14:17	64	140	80	13:38	0	0	0	1	1	2	1	2	1	2	1	2	2	2	2	4			22:50	10	5	370
2	22-09-15	1	R. VALOR WRIST GANGLION	07:55	8:30	80	100	60	7:55	0	0	0	1	1	1	1	1	1	2	1	2	1	2	0	0	1	2	11:20	10	5	1560
3	22-09-15	1	R. ring finger fdp avulsion	09:30	10:13	90	120	80	9:30	0	0	0	0	0	0	0	0	1	0	1	1	2	1	1	2	2		9:20	20	25	1100
4	25-09-15	1	L. VOLAR ASPECT OF WRIST GANGLION	07:45	8:15	66	120	60	7:45	0	0	0	0	0	0	0	0	0	0	1	0	1	1	0	2	4		0:21	25	30	801
5	02-10-15	1	R. INDEX FINGER CONTRACTURE	13:10		68	130	90	13:10	0	0	0	0	0	0	1	1	1	1	2	1	2	1	0	1	1	2	17:00	15	15	1500
6	02-10-15	1		15:05		60	150	90	15:05	0	0	1	1	1	2	2	1	2	2	2	2	2	2	0	0	1	3	20:00	5	5	1560
7	09-10-15	1	R. FOREARM VIC	10:30	11:15	64	140	70	10:30	0	0	0	0	0	0	1	1	1	1	1	1	1	2	0	2	2	2	16:00	15	15	1500
8	09-10-15	2	L. median nerve schwanoma	13:40	14:06	66	140	70	13:40	1	1	1	1	2	1	2	2	2	2	2	2	2	2	0	1			2:00	10	15	525
9	09-10-15	1	R. wrist sl and lt ligament injury	15:40	16:25	81	130	70	15:40	0	0	1	0	1	1	1	1	2	1	2	2	2	2	0	1	1	2	21:00	5	10	1545
10	16-10-15	1	R. PIN PALSY	07:50	8:20	76	136	75	7:50	0	0	0	0	1	0	1	1	1	1	1	1	2	2	0	0	1		9:40	10	15	1270
11	16-10-15	1	R. INDEX MIDDLE AND RING FINGER INJURY	13:50	14:20	72	140	80	13:50	0	0	1	0	1	1	1	1	1	1	2	1	2	2	0	2	3		6:40	5	10	790
12	16-10-15	1	CUT INJURY RT. MULTIPLE FERDESS	16:20	16:50	92	148	75	16:20	0	0	0	0	1	1	1	1	1	1	1	1	2	1	1	3	4		8:00	10	10	750
13	23-10-15	1	L. MIDDLE FINGER TENOSYNOVITIS	12:25	13:00	88	130	70	12:25	1	0	1	0	1	0	2	1	2	1	2	1	2	1	0	3			23:00	15	15	420
14	23-10-15	2	L. PALM PYOGENIC GRANULOMA	14:25	15:00	76	168	76	14:25	0	0	1	0	2	0	2	1	2	1	2	2	2	2	0	1	1	3	19:00	5	15	1550

Figure: Print of section of the data-sheet (from MS Excel) for clarity.

2. PROFORMA FOR DATA COLLECTION

A Randomized Controlled Trial to Compare the Effect of Supraclavicular Brachial Plexus Blocks using 0.5% Levobupivacaine and 0.5% Ropivacaine in Patients Undergoing Upper Limb Surgery.

RANDOMIZATION NO ON THE BOTTLE:

DATE OF THE SURGERY:

NAME: AGE: SEX:

HOSPITAL NUMBER:

ASA GRADE:

DIAGNOSIS:

TIME AT WHICH BLOCK WAS GIVEN:

TIME OF INCISION:

PREOPERATIVE VITALS: HEART RATE: BLOOD PRESSURE:

PREOPERATIVELY

	TIME	SENSORY BLOCKADE	MOTOR BLOCKADE
End of procedure 0 minutes			
5 minutes			
10 minutes			
15 minutes			
20 minutes			
25 minutes			
30 minutes			

ANY INTERVENTIONS INTRAOP
(OPIODS / PROPOFOL / CONVERSION TO GENERAL ANAESTHESIA):

TIME OF COMPLETION OF SURGERY:

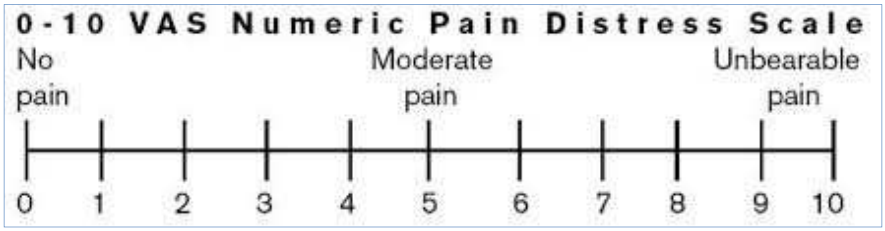
TIME OF ARRIVAL IN THE WARD:

POSTOPERATIVELY

	3 hrs post op	6 hrs post op	12 hrs post o p	24 hrs post o p	
PAIN SCORE					

TIME OF ADMINISTRATION OF RESCUE ANALGESIC (IF VAS SCORE>/=4)

PAIN SCORE (VISUAL ANALOGUE SCALE)



BLOCKADE ASSESSMENT

GRADE	MOTOR BLOCKADE	SENSORY BLOCKADE
0	No blockade - able to touch pulp of little finger with pulp of thumb	No blockade - No sensory loss over C5-T1 dermatomes when assessed with blunt end of 26 gauge needle
1	Partial blockade- able to touch pulp of index finger with pulp of thumb.	Partial blockade- patient feels touch but no pain on pinprick
2	Complete blockade/lateral pinch (able to approximate thumb to lateral aspect of index finger)	Complete blockade- patient do not feel touch or pin prick.

PRIMARY INVESTIGATOR:

Dr. Deepthy D. Pillai, Department of Anaesthesiology,

Christian Medical College, Vellore

Contact: +91 41 62282105 (Office)

3. INFORMED CONSENT FORM

Study Title: To compare the effect of supraclavicular brachial plexus block using 0.5% Levobupivacaine and 0.5% Ropivacaine in patients undergoing upper limb surgeries.

Study Number: _____

Subject's Initials: _____ **Subject's Name:** _____

Date of Birth / Age: _____

(Subject)
(i) I confirm that I have read and understood the information sheet dated _____ for the above study and have had the opportunity to ask questions. [ ]

(ii) I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. [ ]

(iii) I understand that the Sponsor of the clinical trial, others working on the Sponsor's behalf, the Ethics Committee and the regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the trial. I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published. [ ]

(iv) I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s). [ ]

(v) I agree to take part in the above study. [ ]

(vi) I am aware of the Audio-visual recording of the Informed Consent. [ ]
(Click here for Audio Visual guidelines)

Signature (or Thumb impression) of the Subject/Legally Acceptable

Date: _____/_____/_____

Signatory's Name: _____ Signature:

Or

Representative: _____

Date: _____/_____/_____

Signatory's Name: _____

Signature of the Investigator: _____

Date: _____/_____/_____

Study Investigator's Name: _____

Signature or thumb impression of the Witness: _____

Date: _____/_____/_____

Name & Address of the Witness: _____

4. INFORMATION SHEET

INTRODUCTION:

I am Dr. Deepthy D. Pillai, MD Postgraduate in Department of Anaesthesia. This is to provide you with all the information regarding my research topic that is concerned with pain relief in patients undergoing elective upper limb surgeries under regional anaesthesia. I invite you to participate in this research after reading the information sheet. If you have any doubts it can be clarified with me or the anaesthetist on the day of the surgery.

PURPOSE OF THE STUDY:

Regional anaesthesia for upper limb surgeries is found to be better as it causes better post-operative pain relief and less complication compared to general anaesthesia. In this study we are comparing two (2) pain killing medications in order to find out which one provides better pain relief and also the time taken for the onset of its action.

PARTICIPANT SELECTION:

You have been invited to participate because you are undergoing upper limb surgery and you meet the study selection criteria.

VOLUNTARY PARTICIPATION:

Your participation in this research is entirely voluntary. Your decision on whether to participate or not in this study will not have any influence on the management of your disease condition and in the quality of the treatment given to you.

INFORMATION ON THE RESEARCH DRUGS:

Ropivacaine 0.5% is an anaesthetic (numbing medicine) that blocks the nerve impulses that send pain signals to your brain. Levobupivacaine 0.5% is also a local anaesthetic drug which is safe when used within the allowable dose. In high doses it can cause seizures and heart dysfunction but in this study the dose used is much less than the maximum allowable dose.

PROCEDURES AND PROTOCOL:

A drug to relieve your anxiety will be given before taking you inside the theatre. After appropriate positioning and determination of the side of the surgery the drug will be given via a small injection in your neck under ultrasound guidance. You will receive either of the two drugs based on random selection. You will be monitored 20 minutes prior to the surgery and then postoperatively for 24 hours. Pain will be assessed postoperatively for 24 hours.

BENEFITS:

Reduction in postoperative pain.

CONFIDENTIALITY:

Your name will not be published in the data sheet or the final published results. Your data will bear a study number that will be used till analysis.

RESULTS:

The results of the study will remain as the property of Christian Medical College, Vellore.

This proposal has been reviewed and approved by Institutional Review Board (IRB) of Christian Medical College, Vellore. The task of this committee is to make sure the research participants are protected from any harm.

PRIMARY INVESTIGATOR:

Dr. Deepthy D. Pillai,

PG. Registrar

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