"COMPARISON OF EFFICACY OF LEVOBUPIVACAINE AND LEVOBUPIVACAINE WITH DEXMEDETOMIDINE FOR SUPRACLAVICULAR BRACHIAL PLEXUS BLOCK IN PATIENTS UNDERGOING UPPERLIMB SURGERIES – A ONE YEAR RANDOMISED CONTROLLED TRIAL"

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ENDORSEMENT

This is to certify that the dissertation entitled "COMPARISON OF EFFICACY OF LEVOBUPIVACAINE AND LEVOBUPIVACAINE WITH DEXMEDETOMIDINE FOR SUPRACLAVICULAR BRACHIAL PLEXUS BLOCK IN PATIENTS UNDERGOING UPPERLIMB SURGERIES – A ONE YEAR RANDOMISED CONTROLLED TRIAL" is a bonafide research work done by **REG NO. BA0113002.**

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ABBREVIATIONS

AP	-	Action potential
ASA	-	American society of Anaesthesiologists
AV node	-	Atrioventricular node
CNS	-	Central nervous system
CVS	-	Cardiovascular system
DBP	-	Diastolic Blood Pressure
ECG	-	Electrocardiography
GI	-	Gastrointestinal system
GABA	-	Gama Amino Butyric Acid
HR	-	Heart Rate
IV line	-	Intravenous line
IUPAC	-	International union of pure and applied chemistry
LA	-	Local anaesthetic
ml	-	millilitre
mcg	-	microgram
mg	-	milligram
mmhg	-	millimetres of mercury

mA	-	milli Ampere
Pka	-	pH of dissociation constant of acid
PNS	-	Peripheral nerve stimulator
PACU	-	Post Anaesthesia Care Unit
RBS	-	Random Blood Sugar
SBP	-	systolic blood pressure
SA node	-	Sino atrial node
SBPB	-	Supraclavicular brachial plexus block

ABSTRACT

INTRODUCTION:

Supraclavicular approach to brachial plexus block provides the most effective regional anaesthesic technique for surgeries of upper extremity. Levobupivacaine has strongly emerged as a safer alternative to the commonly used bupivacaine for regional anesthesia. Among the various adjuvants, alpha 2 agonists like dexmedetomidine combined with local anaesthetics improve the quality of regional anesthesia.

AIMS AND OBJECTIVES:

This study was conducted to compare the onset and duration of sensory and motor blockade and duration of analgesia along with changes in Heart rate, Systolic Blood Pressure and Diastolic Blood Pressure following administration of either levobupivacaine or levobupivacaine – dexmedetomidine for supraclavicular brachial plexus block in patients undergoing upper limb surgeries.

MATERIALS AND METHODS:

This prospective randomised controlled study was carried out in the Department of Anaesthesiology at KLE'S Dr. Prabhakar Kore Hospital and Medical Research Centre, Nehru nagar, Belagavi which included 50 ASA grade I and II patients between the ages of 18 and 60 years who underwent elective upper limb surgeries. After obtaining ethical committee clearance and informed consent, the patients were randomly allocated into two groups of 25 each by computer generated table to recieve 39 ml of 0.5% levobupivacaine and 1ml (100mcgs) of dexmedetomidine in Group LD and 39 ml of 0.5% levobupivacaine and 1 ml of

normal saline in Group LS. The onset, duration of sensory and motor blockade and duration of analgesia were observed between the groups.

RESULTS:

The onset of sensory and motor blockade was faster in Group LD when compared to Group LS ($p < 0.001$). The duration of sensory and motor blockade was longer in Group LD when compared to Group LS ($p < 0.001$). The mean duration of analgesia was significantly longer in Group LD compared to Group LS ($p < 0.001$). Group LD also had a better hemodynamic stability than Group LS in the intraoperative period.

CONCLUSION: Dexmedetomidine when added to levobupivacaine in supraclavicular brachial plexus block shortens the onset time, prolongs the duration of sensory and motor blockade as well as the duration of analgesia without any systemic side effects.

KEYWORDS: dexmedetomidine, supraclavicular, brachial plexus block, levobupivacaine, upper limb surgeries.

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INTRODUCTION

Regional blocks have assumed a prominent role in modern anaesthetic practice as they provide ideal operative conditions without any significant systemic effects. They offer an excellent alternative for patients who are haemodynamically compromised or too ill to tolerate general anaesthesia.[1] With the advent of various gadgets to locate the nerve plexus, regional blocks are nowadays preferred more often because they provide safe and effective perioperative analgesia with minimal side effects.

Upper extremity orthopaedic and plastic reconstructive surgeries are complex, major and of prolonged duration, hence along with adequate intra-operative sensory and motor blockade, requirement of postoperative analgesia is quite essential for such procedures. Brachial plexus block provides adequate intraoperative anaesthesia, prevents complications of laryngoscopy and intubation of general anaesthesia, preserves mental functions and provides a better postoperative profile with an uneventful recovery and effective postoperative analgesia. It is also advantageous over general anaesthesia in emergency situations, where the patients are either high risk or not adequately nil by mouth.

There are four common approaches to block the brachial plexus namely - Interscalene, Supraclavicular, Infraclavicular and Axillary. Blockade of the plexus can provide surgical anaesthesia for hands, upper/lower arms or shoulder depending on the approach. A thorough knowledge of the brachial plexus anatomy is warranted for success of the block. Among the approaches, supraclavicular approach is associated with a rapid onset of anaesthesia and a higher success rate.

Supraclavicular brachial plexus block is a very popular anaesthetic technique for various upper limb surgeries, due to its effectiveness in terms of cost, performance, success rate, margin of safety and efficient post operative analgesia[2]. The first supraclavicular brachial plexus block was performed by Kulenkampff in 1912.[3]

Supraclavicular approach to brachial plexus block is carried out at the level of its trunks at the middle of brachial plexus where it is most compact, resulting in homogenous spread of the anaesthetic throughout the plexus with a faster onset and complete block of the upper extremity. The performance of supraclavicular brachial plexus block by eliciting paraesthesia was a traditional but an unpleasant technique with more failure rates and occasional neural damage. Although peripheral nerve stimulators help in optimal needle placements minimising unpleasant paraesthesia and neural damage, ultrasound guided peripheral nerve blockade produces shorter procedure times, faster onset of action and higher block success rates without neural injuries. It also improves efficacy of peripheral nerve block when compared to peripheral nerve stimulators for nerve localisation.[4]

Bupivacaine due to its longer duration of action combined with its high quality sensory anaesthesia relative to motor has been the most commonly used local anaesthetic for peripheral nerve blocks in the past but has a considerable limiting cardiac toxicity which deffered much of its use recently. Ropivacaine and levobupivacaine are the two newer longer acting local anaesthetics, whose neuronal blocking potential used in peripheral nerve blockade seem to be similar to bupivacaine and they also have a significantly greater safety margin over bupivacaine because of lower CNS and cardiac toxicity . Levobupivacaine is also 50% more potent and 30% more efficient than Ropivacaine in peripheral nerve blocks.[5]

Levobupivacaine, has a higher toxic threshold produces less cardiac effects and a similar duration of analgesia compared to Bupivacaine.[6] This favourable clinical profile has prompted many clinicians to choose Levobupivacaine over Bupivacaine for all types of peripheral nerve blockade.

Various methods have been tried including use of adjuvants to provide better quality of intraoperative anaesthesia and prolonged postoperative analgesia. The adjuvant drugs used along with local anaesthetics include Adrenaline, Midazolam, Neostigmine, Opioids and recently Clonidine and Dexmedetomidine.

Dexmedetomidine, a pharmacologically active dextroisomer of medetomidine, is a selective α2-adrenoceptor agonist which is used as an adjuvant during regional and local anesthesia. Dexmedetomidine has an alpha-2:alpha 1 selectivity ratio which is eight times as clonidine.[7,8] It also has shorter half life of 2-3 hrs compared to 12 – 24 hrs of clonidine.[9] The other advantage of dexmedetomidine is that it can be titrated to desired level of sedation without significant respiratory depression.[10-13] It has a potent analgesic sparing effect, reducing the opioid requirements significantly both during intraoperative and postoperative periods.[14,15]

Several studies have shown that the addition of dexmedetomidine to local anesthetic improves the quality of subarachnoid, epidural and caudal blocks. However, there remains limited knowledge on the efficacy of dexmedetomidine when added to a local anaesthetic on the onset and duration in peripheral nerve plexus blockade. Hence an attempt is being made to study the clinical effects of addition of dexmedetomidine to levobupivacaine for supraclavicular brachial plexus block in patients undergoing elective upperlimb surgeries.

OBJECTIVES

The aims and objectives of the study are:

Primary objective: To compare the onset and duration of sensory and motor block and duration of post-operative analgesia

Secondary objective: To compare the changes in Heart rate, Systolic Blood Pressure and Diastolic Blood Pressure

following administration of either levobupivacaine or levobupivacaine-dexmedetomidine for supraclavicular brachial plexus block in patients undergoing upper limb surgeries.

REVIEW OF LITERATURE

HISTORY OF BRACHIAL PLEXUS BLOCK

The successful development of local anaesthetic began in 19th century, but the idea of preparing a regional area with reduced sensations before surgical incision was evident in earlier surgical writings.

In 1846, Benjamin ward Richardson introduced ether spray producing local cooling and insensibility of the underlying skin.[16]

In 1884 Hall first injected 4% cocaine (15 mg) into his forearm and concluded that it blocked transmission in the cutaneous nerves because it provided analgesia distal to the point of injection.[16] Additional blocks were then performed in the brachial plexus, infra orbital, inferior dental nerves and sciatic nerves for all operative procedures.

Carl Schliech introduced infiltration anaesthesia in 1892 as an alternative to direct injection at the nerve trunks. August Bier in 1909, first described intravenous regional anaesthesia with an Esmarch warp of the concerned upper limb. After application of two tourniquets, he injected a dilute solution of procaine intravenously. Analgesia was found to develop within minutes and persisted until the release of the tourniquet.[16]

The first brachial plexus block was performed by William Stewart Halsted in 1885, a year after Koller demonstrated the anaesthetic properties of cocaine on the eye of patient. Halsted exposed the roots surgically under local infiltration and injected about 0.5 ml of cocaine (0.1%) to produce complete anaesthesia.

In 1897, 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, as a therapeutic measure in a 12 year old boy with tetanic spasms following a compound fracture of the forearm, and later the technique was used to provide anaesthesia for upper limb surgeries.

G Hirschel performed the first percutaneous brachial plexus block in 1911 through an axillary approach and D Kulenkampff introduced the supra clavicular brachial plexus block in 1912. Several modifications of supra clavicular approach emerged in an effort to avoid pneumothorax. In an attempt to approach brachial plexus in the neck and thereby avoid pulmonary complications , M Kappis (1912) attempted to perform the block through a posterior para vertebral approach.[16]

Because of high incidence of failures with the posterior approach, various investigators , including J Etienne, V Pauchet, and G Pitkin used various anterior approaches for the brachial plexus in the neck . Infraclavicular approaches to brachial plexus were first described by L Bazy and V Pauchet in 1917 and later popularised by P Raj in 1973.

In 1922, Ohen Labat used the axillary approach. In 1927 he also described the interscalene or cervical approach. Murphy modified Labat's technique of brachial plexus block in 1944 by using clavicle, subclavian artery, scalene muscles and 1st rib as the landmarks.

In 1983, Thompson G, Rorie DK, in a study examined the brachial plexus sheath in cadavers by using a combination of anatomic dissection, histologic preparations and x-rays made after injection of x-ray contrast media, and in surgical

patients by using computed tomography (CT) dye studies. They found that the sheath is a multi-compartmental structure, formed by the thin connective tissue sheath surrounding the plexus and by the septa which extend inward from the sheath. This study also indicate that injected anaesthetic solutions spread easily in longitudinal manner up and down the nerves.[17]

With the advent of peripheral nerve stimulators (PNS) in 19 th century, blocks were performed with the use of nerve locators. Saranoff in 1950 and Pearson in 1955 located peripheral motor nerves using electrical stimulation with an insulated needles.[18] In 1984, Pither, Raj and Ford demonstrated use of PNS for regional anaesthesia. The continued success of regional anaesthetic techniques was credited with newer local anaesthetics with less toxicity and longer durations of action.

Lignocaine introduced in 1948 by Torsten Gordh, had several advantages including lower toxicity and intermediate duration of action and it is still widely used. Other agents introduced later include chlorprocaine(1952), mepivacaine(1957) and bupivacaine (1963). Concerns about therapy resistant cardiotoxicity lead to the development of ropivacaine (1996) and levobupivacaine. [16]

Pedro et al in 2009 in a comparative clinical study between bupivacaine and levobupivacaine for supraclavicular brachial plexus block evaluated the time of onset of sensory blockade between the two groups. They concluded that the onset time of sensory blockade were significantly faster with P values < 0.05 in Group levobupivacaine compared to Group bupivacaine with mean onset times of 5 min in levobupivacaine Group compared to 8 min in the bupivacaine Group along the course of C_5 to C_8 ditribution.[19]

In a similar study, Pandya CJ et al in 2012 evaluated analgesic and anaesthetic property of levobupivacaine compared to bupivacaine in supraclavicular

brachial plexus block. 60 ASA I and II patients posted for elective upper limb surgeries received either 0.8 ml/kg of 0.5% levobupivacaine or 0.8 ml/kg of 0.5% bupivacaine. There was significant difference in duration of sensory block ($p < 0.05$), and analgesia (<0.05) between the groups. The average duration of sensory block was 630±95.22 minutes in levobupivacaine group and 525±.8 minutes in bupivacaine group which was statistically significant. The average duration of motor blockade was 520±20 minutes in levobupivacaine group and 612±89.41 minutes in bupivacaine group. The average duration of analgesia was 781 minutes in levobupivacaine group as compared to 622 minutes in bupivacaine group which was statistically significant($P<0.05$).[20]

In an attempt to prolong the duration of sensory and motor blockade a variety of adjuvants like verapamil, opioids, tramadol, midazolam,neostigmine and clonidine have been administered concomitantly with local anaesthetics.

Several experimental studies have proved that alpha 2 adrenoceptor agonists can prolong the duration of action of local anaesthetic after epidural or intrathecal administration by activation of post synaptic alpha 2 receptors in the substantia gelatinosa of the spinal cord.

Clonidine, an alpha2 agonist was first introduced into adult clinical practice as an anti hypertensive agent in 1960 and into paediatric practice in 1973 as a treatment for migraine. Subsequently its clinical role has expanded to include its use as a sedative, premedicative and analgesic.

Dexmedetomidine, another selective α2-adrenoceptor agonist, has been used as an adjuvant during regional and local anesthesia. Several studies have shown the

efficacy of adding dexmedetomidine to local anesthetic for subarachnoid, epidural, and caudal blocks to improve the quality of the block.

Chakraborty S et al in 2010 conducted a study to evaluate the effect of clonidine as an adjuvant in bupivacaine-induced supraclavicular brachial plexus block. Seventy ASA I and II patients scheduled for elective orthopedic surgeries of the upper limb were randomised into two groups of 35 each to receive 25 ml of 0.5% bupivacaine and 0.2 ml (30 mcg) clonidine or 25 ml of 0.5% bupivacaine and 0.2 ml of 0.9% normal. It was observed that onsets of both sensory and motor block were significantly shorter whereas durations were significantly greater in the group receiving clonidine. The mean duration of analgesia was also significantly longer in clonidine group with 415.4 ± 38.18 min against 194.2 ± 28.74 min in the control Group.[21]

Gandhi R et al in 2012 conducted a prospective double blind comparative analysis of the postoperative analgesic efficacy and safety of dexmedetomidine (30mcg) for brachial plexus blockade along with bupivacaine (0.25%).Control group-C received bupivacaine (0.25%) 38 ml with 2 ml normal saline and dexmedetomidine group-D received bupivacaine (0.25%) 38 ml with 30 mcg dexmedetomidine. It was observed that in control group onset of sensory and motor blockade was faster but the duration of sensory (560 mins) and motor (585 mins) blockade in dexmedetomidine group was prolonged with better hemodynamic stability and greater postoperative analgesia. [22]

In a similar prospective randomised controlled trial by Amany S et al (2012), ultrasound-guided infraclavicular brachial plexus block using 0.33%(30cc) bupivacaine or combined with 0.75µg/kg of dexmedetomidine was performed and

the success rate, onset time and duration of sensory blockade, onset time and duration of motor blockade and duration of analgesia were evaluated. They concluded that adding dexmedetomidine to bupivacaine provides enhancement of onset of sensory and motor blockade, prolonged duration of analgesia, increases duration of sensory and motor blockade, yields lower VRS pain scores and reduces supplemental opioid requirements.[23]

In another study, Swamy SS et al in 2012 compared clonidine and dexmedetomidine as an adjuvant to bupivacaine (0.25%) in supraclavicular brachial plexus block in sixty ASA I and II patients scheduled for elective upper limb surgeries. Group C received clonidine 1 μg/kg and Group D received dexmedetomidine 1 μg/kg added to bupivacaine 0.25% (35 cc). Onset and recovery time of sensory and motor block, duration of analgesia and quality of block were studied in both the groups. It was concluded that dexmedetomidine when added to bupivacaine enhanced the duration of sensory block by 186 mins and motor block by 180 mins and also the duration of analgesia was increased by 167 mins compared to addition of clonidine. The time for rescue analgesia was prolonged in patients receiving dexmedetomidine. It also enhanced the quality of block as compared with clonidine by 80%.[24]

Patki Y S et al (2013) conducted a study to know the efficacy of dexmedetomidine as an adjuvant to 0.5% ropivacaine in supraclavicular Block. 60 patients were randomised into two groups of 30 each. Group R received 30 ml of 0.5% ropivacaine + 0.5 ml of normal saline and Group RD received 30 ml of 0.5% ropovacaine + 1 mcg/kg of dexmedetomidine. The mean onset of sensory block in group R was 19 minutes while, it was 13 minutes in group RD which was significant.

The mean time of onset of motor block was 24 minutes in group R while, it was 19 minutes in group RD with the difference being significant between the groups (p value < 0.001). Mean time of recovery of motor block in group R was 462 minutes but was 608 minutes in group RD with a statistically significant difference (p value<0.001). Mean time of recovery from sensory block in group R was 566 minutes while, it was 728 minutes in group RD (p value < 0.001). Mean time of post operative analgesia in group R was 576 minutes and was 738 minutes in group RD, the difference being significant with prolonged analgesia in dexmedetomidine group.[25]

In a similar study conducted by Harshavardhana H S (2014) to evaluate the efficacy of dexmedetomidine compared to clonidine added to ropivacaine in Supraclavicular Nerve Block, one hundred ASA I & II patients undergoing elective upper limb surgeries were assigned to receive 29 ml of ropivacaine and 1mcg/kg of clonidine or 29 ml of ropivacaine and 1 mcg/kg of dexmedetomidine . The sensory onset times were 3.26 min in RC group compared to 2.59 mins in RD group. Motor onset times were 5.36 min in RC group compared to 4.12 min in RD group. Duration of sensory and motor blockade were 212 and 189 min in group RC compared to 363 and 412 min in the group RD respectively. They concluded that dexmedetomidine shortens the onset time, prolongs the duration of sensory and motor block and enhances the quality of block as compared with clonidine when used as an adjuvant to ropivacaine in peripheral nerve block.[26]

Esmaoglu et al (2010) conducted a double blind randomised controlled trial on 60 patients and reported that dexmedetomidine added to levobupivacaine for axillary brachial plexus block shortens the onset time and prolongs the duration of block and duration of postoperative analgesia. The mean onset times for motor blockade was

9.5 mins in dexmedetomidine group compared to 11.1 mins in the levobupivacaine group and duration of motor blockade was 773 mins compared to 575 mins in the control group.[2]

In a similar randomised controlled trial, K Kaygusuz et al (2012) studied the effects of adding dexmedetomidine to levobupivacaine in axillary brachial plexus block in a total of 64 patients undergoing forearm and hand surgeries. The patients were randomly divided into 2 groups, group L patients (n =32) received 39 mL levobupivacaine 0.5% and 1 mL of isotonic sodium chloride. In group D (n = 32) patients received 39 mL of levobupivacaine 0.5% and 1 mL (1mcg/kg) of dexmedetomidine. They concluded that the sensory block onset time was shorter in dexmedetomidine group (P <0.05). The sensory and motor block duration and time to first analgesic use were significantly longer in dexmedetomidine group (P <0.01), and the total need for analgesics was also lower in dexmedetomidine group (P <0.05) compared to control group.[27]

In a similar randomised controlled trial by Saumya et al (2014) dexmedetomidine was used as an adjuvant with levobupivacaine in supraclavicular brachial plexus block and the duration of sensory and motor blockade along with duration of analgesia was compared. 60 ASA I & II patients were enrolled into two groups of 30 each. Group L received 35 ml of 0.5% levobupuivacaine with 1 ml of isotonic normal saline. Group LD received 35 ml of 0.5% levobupiuvacaine with 1 ml of 100 mcg of dexmedetomidine. They concluded that the duration of sensory and motor blockade and duration of analgesia were significantly longer in dexmedetomidine group compared to saline group with p values < 0.001 proving dexmedetomidine to be an effective adjuvant in supraclavicular brachial plexus blocks.[28]

BASIC SCIENCES

ANATOMY OF BRACHIAL PLEXUS[29]

Knowledge of formation of brachial plexus and its ultimate cutaneous and muscular distribution is absolutely essential to the intelligent and effective use of brachial plexus anaesthesia for upper limb surgeries. Close familiarity with the vascular, muscular and fascial relationships of the plexus is equally essential to the mastery of various techniques, for it is these perineural structures which serve as the landmark by which needle may accurately locate the plexus percutaneously.

In its course from intervertebral foramina to the upper arm, the fibres are composed consecutively of roots, trunks, divisions, cords and terminal nerves.

FORMATION OF BRACHIAL PLEXUS:

Brachial plexus is formed by the union of ventral rami of lower four cervical nerves (C5, 6, 7, 8) and first thoracic nerve (Tl) with frequent contributions from C4 or T2.

When contribution from C4 is large and from T2 is lacking, the plexus appears to have a more cephaloid position and is termed "Prefixed". When contribution from T2 is large and from C4 is lacking, the plexus appears to have a caudal position and is termed "postfixed". Usually prefixed or postfixed positions are associated with the presence either of a cervical rib or of an anomalous first rib.

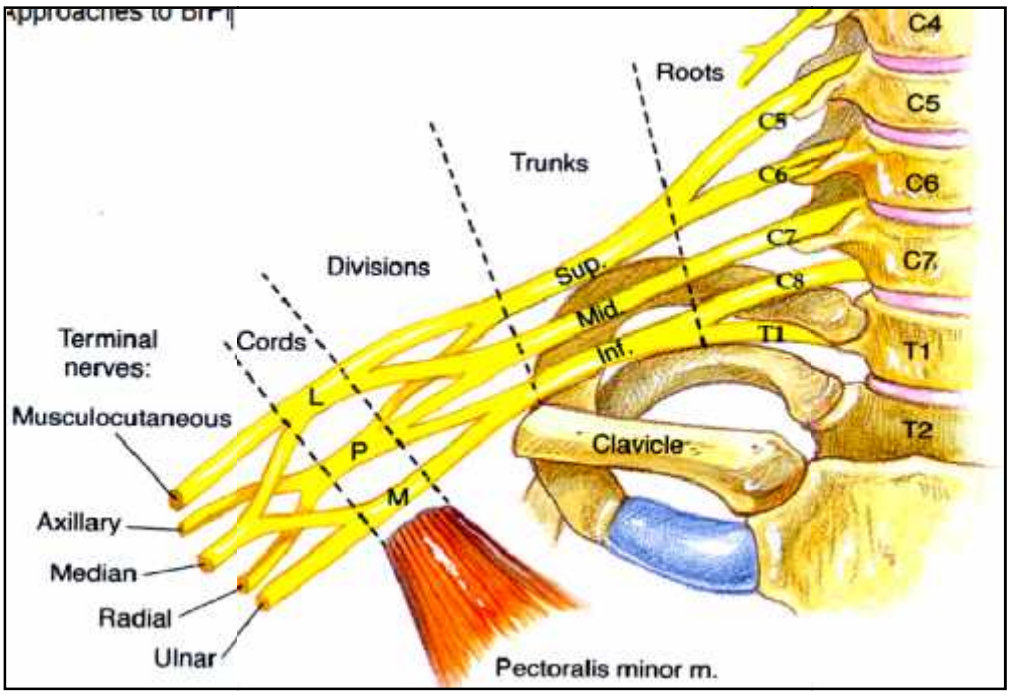


Fig 1: Anatomy of brachial plexus

ROOTS:

Represent the anterior primary divisions of lower four cervical and first thoracic nerves. They emerge from the intervertebral foramina and fuse above the first rib to form the trunks.

TRUNKS:

The roots combine above the first rib to form the three trunks of the plexus. C5 and C6 unite at the lateral border of the scalenus medius and form the "Upper trunk", C8 and Tl unite behind the scalenus anterior to form "lower trunk" and C7 continues as a sole contributor to the "middle trunk".

DIVISIONS:

As the trunks pass over the first rib and under the clavicle, each one of them divides into anterior and posterior divisions.

CORDS:

The fibres, as they emerge from under the clavicle, recombine to form three cords. The "lateral cord" is formed by anterior divisions of upper and middle trunks, lateral to the axillary artery. The anterior division of lower trunk descend medial to the axillary artery forming the "medial cord". The posterior divisions of all three trunks unite to form the "posterior cord", at first above and then behind the axillary artery

MAJOR TERMINAL NERVES:

Each of these cords gives off a branch that contributes to or becomes one of the major nerves to the upper extremity and then terminates as a major nerve. The lateral and medial cords give off lateral and medial heads of the median nerve and continue as major terminal nerves, the lateral cord terminating as musculocutaneous nerve and medial cord as ulnar nerve.

Posterior cord gives off, axillary nerve as its major branch and then continues as the radial nerve. In summary, conveniently it can be considered that brachial plexus begins with five nerves (C5-T1) and terminates in five nerves (Musculocutaneous, radial, axillary, median and ulnar nerves) with its intermediate portions displaying in sets of three, that is, three main trunks which divide into 2 sets of three, which reunite and give rise to three cords.

These three cords give off three lateral branches before becoming the major terminal branches of the plexus.

DISTRIBUTION OF BRACHIAL PLEXUS

These are divided into those that arise above the clavicle the supraclavicular branches and those that arise below it, the infraclavicular branches.

Supraclavicular branches:

From roots:

1. Nerves to scaleni and longus colli - C5,6,7,8
2. Branch to phrenic nerve - C5
3. Dorsal scapular nerve - C5
4. Long thoracic nerve – C5,6,(7)

From trunks:

1. Nerve to subclavius – C5,6
2. suprascapular nerve - C5,6,

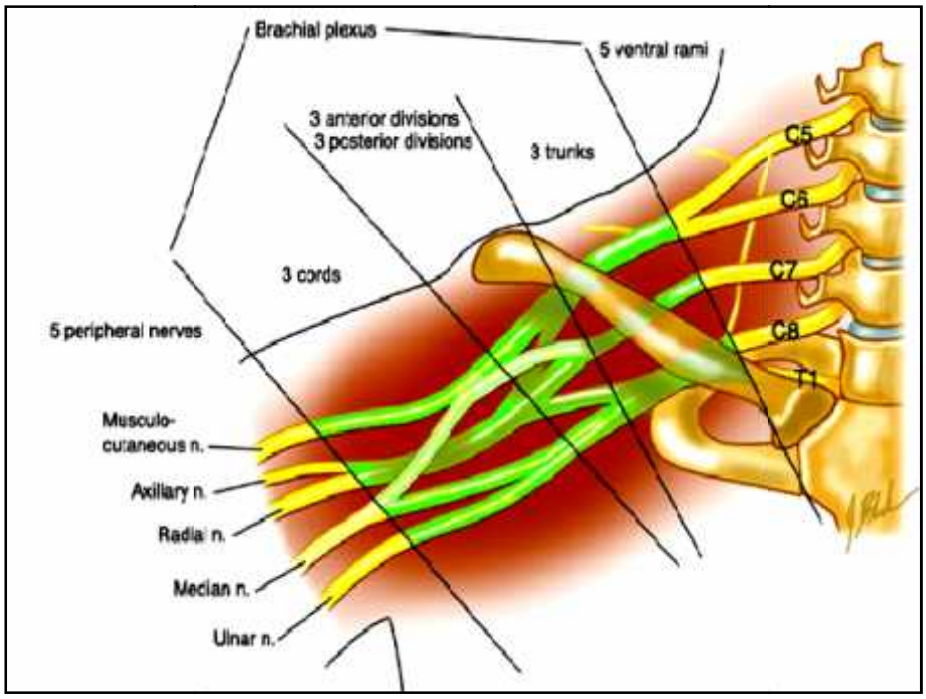


Fig 2: Branches of brachial plexus

Infraclavicular branches: They branch from cords but their fibres may be tracked back to spinal nerves.

Lateral cord:

1. Lateral pectoral nerve - C5,6,7
2. Musculocutaneous nerve – C5,6,7
3. Lateral root of median nerve - C5.6,7

Medial cord:

4. Medial pectoral nerve – C8, T1
5. Medial cutaneous nerve of forearm – C8, T1
6. Ulnar nerve-C7, T1
7. Medial root of median nerve-C8, T1
8. Medial cutaneous nerve of arm – C8,

Posterior cord:

1. Upper subscapular nerve - C5,6
2. Thoracodorsal nerve – C6,7,8
3. Lower subscapular nerve - C5,6
4. Axillary nerve - C5,6
5. Radial nerve — C5,6,7,8,T1

Supraclavicular branches:

The nerves to scalene and longus colli (C5, 6, 7, 8)

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 colli muscle (C2 - C7), Anterior scalene muscle (C4-C6), Middle scalene muscle (C6-C8), Posterior scalene muscle (C6-C8), Scalene minimus muscle (C7-C8).

Branch to phrenic nerve: C5

A branch from the fifth cervical nerve joins the phrenic nerve, anterior to the scalenus anterior.

Dorsal scapular nerve: C5

Arises from fifth cervical ventral ramus, pierces scalenus medius, passes behind the levator scapulae and runs to rhomboids.

It supplies

- Levator scapulae muscle C3
- Rhomboid minor muscle C5
- Rhomboid major muscle C5

Long thoracic nerve (C5, 6, (7)):

It arises from C5, C6 and C7 in 42% of cases, C5 and C6 pierce the scalenus medius, uniting lateral to it and descends dorsal to the brachial plexus and first part of axillary artery. It crosses superior border of serratus anterior and continue downwards to the lower border of serratus anterior, supplying; branches to each of its digitations.

It supplies - serratus anterior muscle. Injury to this nerve causes scapular angle to be drawn medially by unopposed action of rhomboids and levator scapulae and tends to project (winging of the scapula) when horizontal arm is used for forward pushing movements. The arm cannot be raised above the horizontal level.

Branches from Trunks:

1. The nerve to subclavius (C5-6):

The nerve arises from C5 and C6 descends anterior to the plexus and third part of subclavian artery and vein to reach subclavius muscle. Accessory phrenic nerve may occasionally be a branch of this. It supplies to subclavius muscle.

2. The suprascapular nerve:

The nerve arises from superior aspect of the superior trunk and runs laterally deep to trapezius and omohyoid, enter supraspinous fossa through the suprascapular notch and supplies: Supraspinatus muscle C5 and Infraspinatus muscles C5-6. Occasionally, it also supplies sensory branches to the shoulder joint, the only sensory fibres that arise above the clavicle. When present, it pierces the deltoid muscle and supply the skin of the proximal third of the arm within the territory of the axillary nerve.

Because of its position superior to the plexus, this nerve may be stimulated during the subclavian perivascular technique, giving rise to paresthesia to the shoulder, which cannot be relied upon. Because the nerve leaves the plexus and its investment fascia shortly after arising from the superior trunk and paresthesia in this distribution could indicate stimulation of fibres before or after the nerve has left the sheath.

Infraclavicular branches:

They comprise all of the motor and sensory nerves to the upper extremity proper. Apart from some exceptions, there are no branches arising from the divisions of plexus, Rest of the branches are from the three cords.

Branches from the Cords:

A. LATERAL CORD:

1) Lateral Pectoral nerve (C5, 6,7)

It is larger than the medial, which passes superficial to the first part of the axillary artery and vein, pierces the clavipectoral fascia and supplies the pectoralis major. It sends ramus to the medial pectoral nerve, to supply some fibres to the pectoralis minor. It supplies Pectoralis major muscle (C5-T1).

2) Musculocutaneous nerve:

It pierces the deep fascia lateral to the tendon of biceps, just below the elbow and continues as the lateral cutaneous nerve of the forearm.

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 lateral cutaneous nerve of the forearm supplies the skin of forearm's anterolateral surface.

3) Lateral head of median nerve The median nerve: C6,7,8 T1

The nerve arises from two roots, the lateral root of median (from lateral cord) and medial root of median (From the medial cord). The two roots straddle the third part of axillary artery before they unite on its ventral surface. It descends along the course of the brachial artery. In the arm it is first lateral to the brachial artery; medial to the cubital fossa where it is posterior to the bicipital aponeurosis and anterior to the brachialis. It enters the forearm between the heads of the pronator teres, crossing lateral to the ulnar artery.

It proceeds behind a tendinous bridge between the two heads of flexor digitorum superficialis (FDS) descending posterior to this muscle and anterior to flexor digitorum profundus. About 5 cm proximal to the flexor retinaculum (FR), it becomes superficial between the tendons of the flexor digitorum superficialis and carpiradialis. Then it passes deep to flexor retinaculum into the palm to terminate 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

Flexor pollicis brevis

Lumbricals Palmar cutaneous branches (Sensory) to Skin of palmar aspect of thumb, the lateral two and middle half finger and distal end of the dorsal aspect of the same fingers. It may encroach upon the area usually innervated by radial nerve, also providing sensory innervations of the dorsal surface of the entire thumb and first three

fingers as far as metacarpophalangeal joint and an area supplied by ulnar nerve and may provide sensory innervation of entire ring finger.

Articular branches are to the elbow joint and proximal radioulnar joint. Some of intercarpal, carpometacarpal and intermetacarpal joints are said to be supplied by the branches of median nerve, precise details being uncertain.

Median nerve injury can occur in forearm, proximal to its muscular and interosseous branches, flexion of second phalanges of all digits is lost, and of the terminal phalanges of index and medius. Terminal phalanges of other two fingers may be flexed by the part of flexor digitorum profundus, supplied by ulnar nerve. Proximal phalanges may be flexed by the interossei. The thumb cannot be opposed or abducted, nor flexed at its interphalangeal joint. Sensation in the area of distribution is lost. Owing to paralysis of intrinsic pollicis muscles and unopposed action of the extensor pollicis longus an "apelike" hand exists.[30]

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 cause 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. This is called "carpal tunnel syndrome".[31]

MEDIAN CORD:

1) Medial head of median nerve C8, T1

It joins the lateral head from lateral cord to form the median nerve.

2) The medial pectoral nerve C8,T1

It passes between the axillary artery and vein, joins the lateral pectoral nerve, forming 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) The medial cutaneous nerve of the arm C8, T1

It leaves the axillary sheath high in the axilla, where part of it forms a loop with the intercostobrachial nerve, with which it has a reciprocal relationship with respect to size and distribution.

It supplies the medial portion of the upper arm as far distally as the medial epicondyle. Frequently this nerve innervates the lower portion and the intercostobrachial nerve the upper portion.

4) The medial cutaneous nerve of the forearm C8, T1

Initially the nerve is between the axillary artery and vein and supplies a ramus piercing the deep fascia to supply the skin over the biceps almost to the elbow. It travels down the arm medial to the brachial artery, dividing into a larger anterior branch and a posterior branch to supply the skin over the entire medial aspect of the forearm as far as the wrist.

5) The ulnar nerve: (C7) C8 T1

It runs distally through the axilla, medial to the axillary artery, till the middle of the forearm, parallel to and between the median and medial cutaneous nerve of the forearm. Then it angles dorsally and laterally to descend in groove on the medial head of the triceps.

Then it passes behind the medial epicondyle of the humerus, 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

Articular branches to elbow, wrist joint, intercarpal, carpometacarpal and intermetacarpal joints, though precise details are uncertain.

Cutaneous branches to 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 in the area served by radial nerve in the dorsal aspect.

The ulnar nerve may be injured in the forearm leading to impaired abduction; when attempt is made to flex the wrist. The hand is abducted by the flexor carpi radialis, owing to paralysis of the dorsal interossei, the fingers cannot be spread or flexed at metacarpophalangeal joints or extended at the interphalangeal joints, and the arm assumes a "clawed" shape from the active opposing muscles. Flexion of the fourth and fifth digits is weakened and the thumb cannot adduct, hypothenar muscles waste. Sensation is lost or impaired on the skin supplied by the nerve.

C. POSTERIOR CORD:

1) The upper sub scapular nerve

2) The thoracodorsal nerve (C6-6)

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

It supplies latissimus dorsi muscle (C6-8), inferiorly, enters the subscapularis. It supplies the subscapularis muscle

3) The 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

4) The axillary (circumflex humeral) nerve (C5-6)

It is at first lateral to radial nerve, posterior to axillary artery and anterior to the subscapularis, at whose lower border it curves back and traverses a quadrangular space, bounded above by the subscapularis and teres minor, below by the teres major, medially long head of triceps and laterally by the humoral surgical neck, finally branching into anterior and posterior branches, the lateral continuing as the upper lateral cutaneous nerve of the arm.

Anterior branch supplies the deltoid (C5 C6) and cutaneous branches to the skin over its lower part, posterior branch supplies - the teres minor (C5) and posterior part of the deltoid. On the branch to teres minor, a pseudoganglion usually exists.

Upper lateral cutaneous nerve of the arm supplies the skin over the lower part of the deltoid and the upper part of the long head of triceps. An articular branch supplies the shoulder joint

The axillary nerve is liable to injury in its course around the surgical neck of humerus causing paralysis of deltoid and anaesthesia of the skin over the lower part of the muscle. Effective abduction of the arm is not possible

5) The 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 musculo spiral groove and then reaches the lower anterior side of the forearm where its terminal branches arise.

Muscular branches supply the -

a. Triceps brachi - C7,8
b. Supinator – C6
c. Extensor carpi radialis brevis – C6,7
d. Abductor pollicis longus – C6,7
e. Extensor pollicis longus – C6-8
f. Extensor indicis – C6-8
g. Extensor pollicis brevis – C6,7
h. Brachioradialis – C5,6
i. Extensor carpi radialis longus - C6,7
j. Extensor carpi ulnaris – C6-8
k. Extensor digitorum – C6-8
l. Extensor digiti minimi – C6-8

Sensory supply via, the dorsal cutaneous nerve of the arm (C5, 6) which supply through four to five small nerves (digiti nerves), the 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.

DERMATOMAL DISTRIBUTION OF UPPER LIMB

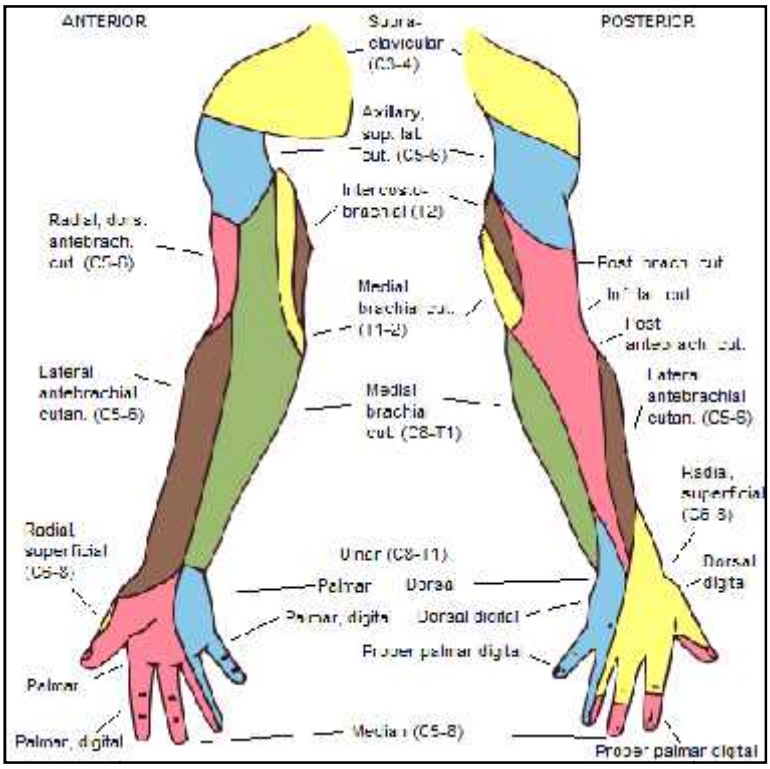


Fig 3: Dermatomal distribution of the upper limb

SYMPATHETIC CONTRIBUTION TO BRACHIAL PLEXUS:

The segmental preganglionic sympathetic contributions are variable, but generally extend more caudal. The highest contribution is usually T2 with T1 contributing only rarely, while lowest may be as far as T8, T9 or even T10.[32] The post ganglionic contributions are from grey rami communicants from the sympathetic chain.

RELATIONS OF BRACHIAL PLEXUS:

In its passage from the cervical transverse processes to the first rib, the plexus is "sandwiched" between the anterior and middle scalene muscles and invested in the fascia of those two muscles.

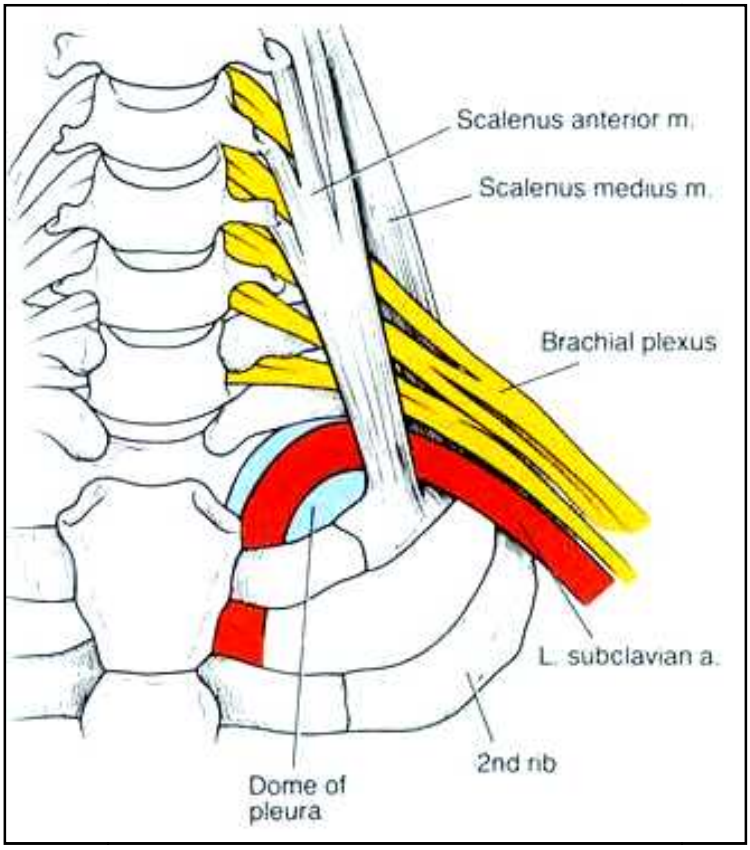


Figure 4: Major relations of the brachial plexus

The interfascial comapartment, along with subclavian artery which crosses the first rib immediately in front of the trunks. Artery is close to the scalenus anterior and the plexus close to the scalenus medius. Subclavian vein is separated from the artery by the scalenus anterior. The fascia covering the muscles is derived from the prevertebral fascia, which splits to invest these muscles and re-joins again at their lateral margins to form an enclosed space, the interscalene space. As the plexus cross the first rib, the three trunks are 'stacked' one on top of the other vertically. Not infrequently, the inferior trunk gets trapped behind and even beneath the subclavian artery above the rib, during embryologic development.

This may be reason why local anaesthetics injected via the interscalene technique sometimes fail to provide anaesthesia in the distribution of the ulnar nerve,

which may be buried deep within inferior trunk behind or beneath the subclavian artery.

After crossing the first rib, they the split to form two divisions and the cords and subclavian artery becomes the axillary artery. Above the clavicle, the axillary artery lies central to the three cords, in the axilla the lateral and posterior cords are lateral to the first part of the axillary artery, the medial cord being behind it. Around the second part of the artery, they are related according to their names. In the lower axilla, cords divide into nerves for the upper limb.

In passing over the first rib under the clavicle, the subclavian vein also becomes the axillary vein and its relationship with the neurovascular bundle Changes. Above the first rib the subclavian vein does not lie within the neurovascular bundle, it is separated by the insertion of scalenus anterior.

As it passes over the first rib, becoming the axillary vein it joins the neurovascular bundle so that parts of the plexus are sandwiched between artery and vein. As all the three enter the axilla, they invaginate the perivertebral fascia at the lateral margins of the anterior and medial scalene muscles, carrying this fascial investment of the neurovascular bundle into the axilla as the axillary fascia, an extension of the perivertebral or scalene fascia forming the axillary perivascular space, a tubular extension of the interscalene space. In its course through the axilla and upper arm the fascia of the surrounding muscles contribute to the axillary sheath, making it thick and tough, providing the 'fascial click' to the anaesthetic while entering the sheath.

It is important to note that major terminal nerves leave the sheath high in the axilla under cover of pectoralis minor muscle. The musculocutaneous nerve enters the substance of coracobrachialis and continues down within this muscle. The axillary nerve also leaves the sheath immediately after arising from the posterior cord. The interocostobrachial nerve travels parallel to but outside the axillary sheath and medial cutaneous nerve of the arm runs similarly but occasionally it may remain within the sheath.

THE BRACHIAL PLEXUS SHEATH

Volume of the sheath: 42ml.

Shape of the sheath : Cylindrical to conical - Wide proximally and narrow distally

Length: 8-10cms long.

The connective tissue of the prevertebral fascia and the anterior and middle scalene envelops the brachial plexus as well as the subclavian and axillary artery in a neurovascular "sheath".

The tissue is densely organized as it leaves the deep cervical fascia proximally, but becomes more loosely arranged distally. The sheath blends with the fascia of the biceps and brachialis muscle distally.

Anatomic dissection, histologic examination and CT scanning after injection of radio contrast into the sheath demonstrate the existence of connective tissue septae which extend inward from the fascia surrounding the sheath. The thin connective

tissue septae frequently adhere to nerves and vessels leaving no free space between layers and compartmentalizing the components of the sheath.

APPROACHES TO BRACHIAL PLEXUS	INDICATIONS	COMPLICATIONS	ADVANTAGES
Supraclavicular(3052)	-Any surgical procedure of the upper extremity (not involving the shoulder) -Surgeries on the elbow,forearm,wrist & hand	-Pneumothorax (2-6 %) – may develop over 24 hours; cupula of the lung can be pierced if the needle overshoots the rib. -Accidental subclavian arterial puncture causing haematoma formation, but compression in an attempt to stop bleeding is not beneficial as the artery lies beneath the clavicle -Stellate ganglion and vagus nerve blockade from spread of local anaesthetic	-Complete sensory and motor bloackade hence called “spinal anaesthesia of upperlimb”.
Interscalene	-Shoulder and proximal humerus sugeries -Elbow surgeries -Neck surgeries – carotid endarterectomise -Brachial plexus explorations	-Phrenic nerve injuries leading to ipsilateral diaphragmatic paresis – caution in patients with pulmonary diseases. -Accidental injections in subarachnoid & epidural space and in vertebral artery -Horner’s syndrome -Neuropraxia	Interscalene approach can provide anaesthesia to shoulder sugeries

		-Pneumothorax -Hoarseness of voice – recurrent laryngeal nerve palsy	
Infraclavicular	-Provides complete anaesthesia to upper extremities similar to supraclavicular block	-Pneumothorax- especially with medially directed needle -Haematoma formation due to vascular puncture -Intravascular injection	-Stable location for catheter based techniques -less infections -Avoidance of injury to neurovascular structures of the neck -Blockade of musculocutaneous nerve
Axillary	-Pulmonary diseases when the risk of pneumothorax or phrenic nerve paralysis must be avoided -For children with fractures of the arm -when disease exists in the supraclavicular area like infection,injury or tumours -When bilateral brachial plexus block is desired	-Injury to nerves and vessels. -Haematoma formation -Intravascular drug injections	-Simple technique -Low incidence of complications like pneumothorax -Phrenic nerve is spared -Excellent anaesthesia and analgesia distal to elbow -Suitable for continuous catheter technique required for prolonged analgesia, immobilisation & sympathetic blockade.

PHARMACOLOGY

PHARMACOLOGY OF LEVOBUPIVACAINE[33,34,35]

Local Anaesthetic Drugs[33]:

Local anaesthetics are drugs that produce reversible conduction blockade of impulse along central and peripheral nerve pathways after regional anaesthesia. With progressive increases in concentrations of local anaesthetics the transmission of autonomic, somatic sensory and somatic motor impulses are interrupted, producing autonomic nervous system blockade, sensory anaesthesia, and skeletal muscle paralysis in the area innervated by the affected nerve. Removal of the local anaesthetic is followed by spontaneous and complete return of nerve conductions, with no evidence of structural damage to nerve fibres.

Local anaesthetics have similar configuration. They have one aromatic lipophilic part (Benzene ring) and one hydrophilic part (quaternary ring) connected by an intermediate ring either ester (-COO-) or an amide(-NHCO-).

LEVOBUPIVACAINE[34]

It is the S- enantiomer of Bupivacaine. Compared to Bupivacaine, it is associated with less vasodilatation and has a longer duration of action. It is approximately 13 % less potent (by molarity) than racemic bupivacaine. Levobupivacaine, a single enantiomer of bupivacaine, has recently been introduced as a new long-acting local anaesthetic with a potentially reduced toxicity compared with bupivacaine.(Figure 5)

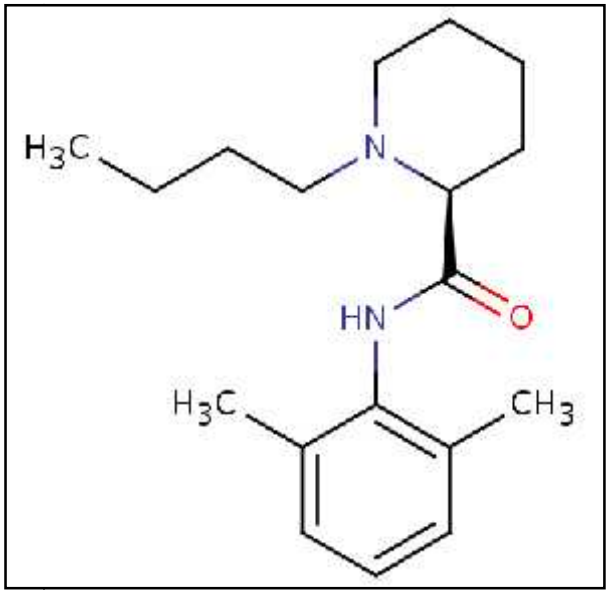


Fig 5 : Structure of Levobupivacaine

Numerous preclinical and clinical studies have compared levobupivacaine with bupivacaine and in most studies there is evidence that levobupivacaine is less toxic. Advantages for levobupivacaine are seen on cardiac sodium and potassium channels, on isolated animal hearts and in whole animals, anaesthetised or awake. In particular the intravascular dose of levobupivacaine required to cause lethality in animals is consistently higher compared with bupivacaine. In awake sheep, for example, almost 78% more levobupivacaine was required to cause death. In contrast, in anaesthetised dogs no differences were seen in the incidence of spontaneous or electrical stimulation- induced ventricular tachycardia and fibrillations among animals exposed to levobupivacaine or bupivacaine.

The reversibility of levobupivacaine-induced cardiotoxicity has also been assessed. Levobupivacaine was found to cause smaller changes in indices of cardiac contractility and the QTc interval of the electrocardiogram and also to have less depressant effect on the electroencephalogram.

Assuming that levobupivacaine has the same local anaesthetic potency as bupivacaine, then, all things being equal, it is difficult to argue that levobupivacaine should not displace bupivacaine as the long-acting local anaesthetic of choice. It would appear, however, that levobupivacaine has not yet significantly displaced bupivacaine from the markets in which it is sold.

This may be due to a lack of perceived safety benefit and/or consideration of the additional costs that are associated with switching to levobupivacaine, which is approximately 57% more expensive than bupivacaine

Physiochemical properties:

1) Solubility: The base is sparingly soluble, but the hydrochloride is readily soluble in water.
2) Stability and sterilization:highly stable and can withstand repeated autoclaving.
3) pKa – 8.1
4) Specific gravity : 1.021 at 37°C
5) Melting point: 247-258°C
6) Protein binding: > 97%
7) Half life: 3.3 hours
8) Volume of distribution – 66.91 + 18.23 L
9) Clearance - 39.06 ±13.29 L/h

Potency:

Levoupivacaine has similar potency compared to bupivacaine and is approximately three to four times more potent than Lidocaine.

The duration of action for local anaesthesia is two to three times longer than

Lidocaine.

Mechanism of action[35:]

It is similar to that of any other local anaesthetics. The primary action of local anaesthetics is on the cell membrane of the axon, on which it produces electrical stabilization. The large transient increase in permeability to sodium ions necessary for propagation of the impulse is prevented. Thus the resting membrane potential is maintained and depolarization in response to stimulation is inhibited.

The mechanism by which local anaesthetics block sodium conductance is as follows

a) Local anaesthetics in the cationic form act on the receptors within the sodium channels, on the cell membrane and block it. The local anaesthetic can reach the sodium channel either via the lipophilic pathway directly across the lipid membrane, or via the axoplasmic opening. This mechanism accounts for 90% of the nerve blocking effects of amide local anaesthetics.
b) The second mechanism of action is by membrane expansion. This is a non-specific action in contrast to the more specific drug receptor interaction.

Available concentration: 0.25%, 0.5%., 0.75%

Dosage for peripheral nerve blocks – 0.25 – 0.5% of solution upto 40 ml (maximum of 150 mg).

These doses may be repeated in 3-4 hours but 400mg is the maximum dose in 24 hours. The addition of vasoconstrictor produces a very slight increase in the duration of action. However the peak blood level is significantly reduced, thereby minimizing the systemic toxicity.

ACTIONS:

Central nervous system:

Overdose of levobupivacaine produces light headedness and dizziness followed by visual and auditory disturbances such as difficult to focus and tinnitus. Disorientation and drowsiness can also occur. Shivering, muscular tremors and tremors of muscles of face and distal part of extremities can occur.

Ultimately generalized convulsions of tonic clinic nature occurs. Further increase in doses causes respiratory arrest.

Since levobupivacaine is a potent drug, smaller doses can cause rapid onset of toxic symptoms when compared to other drugs.

Autonomic nervous system:

Levobupivacaine does not inhibit the Noradrenaline uptake and hence has no sympathetic potentiating effect. Myelinated preganglionic beta fibres have a faster conduction time and are more sensitive to the action of local anesthetics including levobupivacaine. Involvement of preganglionic sympathetic fibres is the cause of widespread vasodilatation and consequent hypotension that occurs is epidural and paravertebral block. When used for conduction blockade, all local anaesthetics particularly Bupivacaine produce higher incidence of sensory than motor fibres blockade.

Neuro-muscular junctions:

Levobupivacaine like other local anaesthetics can block motor nerves if present in sufficient concentration but has no effect on the neuromuscular junction as such.

Cardiovascular system:

The primary cardiac electrophysiologic effect of local anaesthetic is a decrease in the maximum rate of depolarization in the purkinje fibres and ventricular muscle. This is due to a decrease in the availability of sodium channels.

Action potential duration and the effective refractory period is also decreased. The depression of rapid phase of depolarization (V-max) in purkinje fibres and ventricular muscle by levoupivacaine is less compared to bupivacaine. Also the rate of recovery of block is slower with Bupivacaine. Therefore there is incomplete restoration of V-max between action potential particularly at higher heart rates. Therefore, Bupivacaine is highly arrythmogenic. The cardiac contractility is reduced, this is by blocking the calcium transport. Hence Levobupivacaine is more cardiostable than bupivacaine.

Respiratory system:

Respiratory depression may be caused if excessive plasma level is reached which in turn results in depression of medullary respiratory center. Respiratory depression may also be caused by paralysis of respiratory muscles as may occur in high spinal or total spinal anesthesia.

Pharmacodynamics

The onset of action of levobupivacaine is between 4 and 6 minutes and maximum anaesthesia is obtained between 15 and 20 minutes. The duration of anaesthesia varies according to the type of block, the average duration for peridural block is about 3.5-5 hours, for nerve blocks, it is about 5 to 6 hours.

Toxicity:

The toxic plasma concentration is set at 4-5 µg/ml. Maximum plasma concentration rarely approach toxic levels. Nonspecific local irritant effects on nerve tissue have been noted in human subjects. No evidence of permanent damage has been found in clinical dosage. There is no alteration is blood picture or methaemoglobin formation due to this drug.

Pharmacokinetics:

Levobupivacaine can be detected in the blood within 5 minutes of infiltration or following either epidural or intercostal nerve blocks. Plasma levels are related to the total dose administered. Peak levels of 0.14 to1.18 µg/ml were found within 5 minutes to 2 hours after the administration of anaesthesia and they gradually declined to 0.1 to 0.34µg/ml by 4 hours.

Metabolism - elimination:

Levobupivacaine is extensively metabolized with no unchanged levobupivacaine detected in urine or feces. In vitro studies using [14 C] levobupivacaine showed that CYP3A4 isoform and CYP1A2 isoform mediate the metabolism of levobupivacaine to desbutyl levobupivacaine and 3-hydroxy levobupivacaine, respectively. In vivo, the 3-hydroxy levobupivacaine appears to undergo further transformation to glucuronide and sulfate conjugates. Metabolic inversion of levobupivacaine to R(+)-bupivacaine was not evident both in vitro and in vivo. Following intravenous administration, recovery of the radiolabelled dose of levobupivacaine was essentially quantitative with a mean total of about 95% being recovered in urine and feces in 48 hours. Of this 95%, about 71% was in urine while

24% was in feces.

Adverse reactions:

Adverse reactions occur with excessive plasma levels which may be due to overdose, inadvertent IV injections or slow metabolic degradation. These manifest by effects on CNS and CVS.

The CNS effects are characterized by excitation or depression. The first manifestation may be nervousness, dizziness, blurring of vision or tremors following drowsiness, convulsions unconsciousness and probably respiratory arrest.

Other effects may be nausea, vomiting, chills, constriction of pupils and tinnitus. The CVS manifestation include myocardial depression, hypotension and cardiac arrest, in obstetrics fetal bradycardia may occur. Allergic reactions include urticaria, bronchospasm and hypotension.

DEXMEDETOMIDINE [36]

Dexmedetomidine is a short acting alpha agonist with a plasma half life 1600 times greater selectivity to alpha2 receptors when compared with alpha1 receptors. It was introduced in clinical practice in USA in 1999 and was approved by the Food and Drug Administration (FDA) as a short term sedative (<24 hrs) for mechanically ventilated ICU adult patients. Dexmedetomidine is now being used off label for various settings including sedation, adjunct analgesia in the operating room, and in sedation in diagnostic and procedure units.

CHEMICAL STRUCTURE:

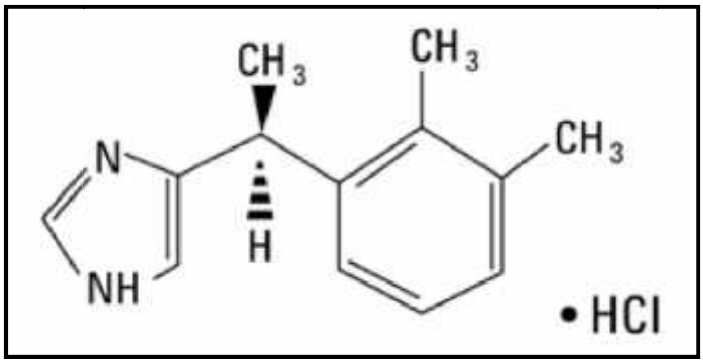


Fig 6 : Structure Of Dexmedetomidine

Molecular formulae – C13H16N2

IUPAC name – 5-[1-(2,3-dimethylphenyl)ethyl]- 1H1-imidazole

PHYSIOLOGY OF ALPHA RECEPTORS :

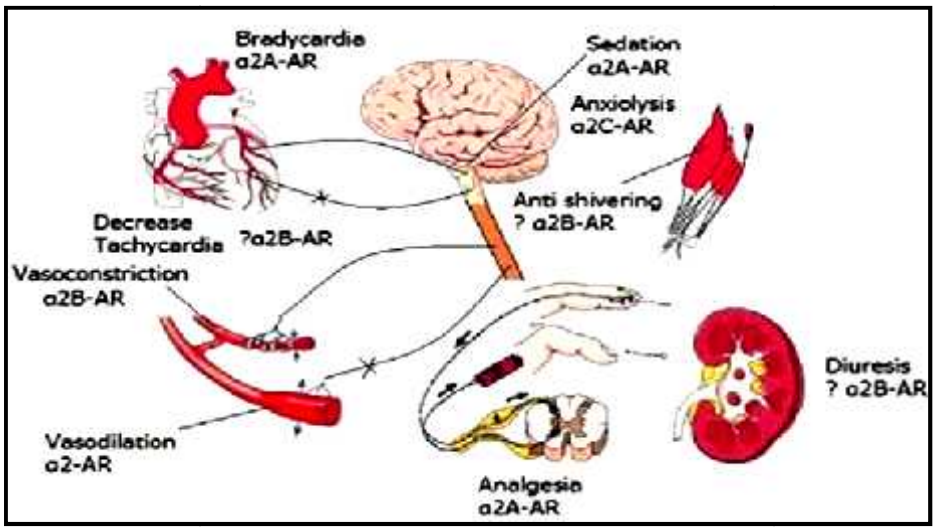


Fig 7 : Physiology of alpha 2 receptors

Alpha adrenoceptor agonist act both at presynaptic and postsynaptic receptors with a complex pharmacology. Alpha receptors can be classified into α2A, α2B, α2C types. Each of these receptors may be responsible for a specific action of alpha 2 agonists.[37,38]

Alpha 2A adrenoceptors mediates sedative and antinociceptive actions whereas stimulation of alpha 2B mediates vasoconstrictive cardiovascular effect, that causes initial hypertension observed after the administration of alpha 2 adrenoceptor agonists.[39,40] Alpha 2C subtype modulates dopaminergic neurotransmission, hypothermia, and a variety of behavioural responses.

MECHANISM OF ACTION : The hypnotic effect of Dexmedetomidine is mediated by the hyperpolarisation of noradnergic neurons located in the locus ceruleus and spinal cord which is the principal site for analgesic action, both acting through α2A.[41] Dexmedetomidine acts through inhibition of adenyl cyclise in the G – protein coupled

receptors that results in decreased formation of cyclic AMP which is an important regulator of various cellular functions acting in many intracellular subsystems like control of phosphorylation state of regulatory proteins. Other effects of α2 agonists include potassium channel activation leading to efflux of potassium and inhibition of calcium entry into calcium channels in neuronal cells.[42] These effects collectively lead to change in membrane ion conductance and produce α2 agonist hyperpolarisation of the membrane which suppresses neuronal activity. The main effect is inhibition of noradrenaline release causing reduction in excitation in locus ceruleus. The locus ceruleus is a neuronal nucleus that is located bilaterally in the upper brainstem and is the α2 receptor agonist major site of noradrenergic innervations in the brain.[43] Locus ceruleus is also important for brain functions like arousal, sleep, anxiety, and drug withdrawal associated with CNS depressant, like opioids.[44,45]

MECHANISM OF ACTION IN PERIPHERAL NERVE BLOCKADE:[46]

There have been four proposed mechanisms of action of α2-AR agonists in peripheral nerve blocks. These mechanisms include:

1. Direct action on the peripheral nerve
2. Centrally mediated analgesia
3. α-2B-AR2 mediated vasoconstrictive effects
4. Attenuation of the inflammatory response.

Despite the fact that there is no α2-AR representation on peripheral nerves, there is prolongation of action by perineural administration of α2-AR agonist as an adjuvant to local anesthetics. They prolong the duration of analgesia by blocking the so-called hyperpolarization-activated cation current (Ih current). This is the most

well-defined mechanism of α2-AR agonists. After an action potential (AP) has occurred, the nerve will have to repolarize to be able to produce new APs. The early repolarization phase will result in a hyperpolarized state that will make the generation of new APs virtually impossible, and the nerve is, during this period, judged to be refractory to stimulation. Thus, blocking the Ih current will result in prolonged hyperpolarization of the nerve, which in turn will result in an analgesic action. Blocking the Ih current may also have the potential to produce a selective sensory effect as this effect appears to be more pronounced in C fibers (pain) than in A alpha fibers (motor). Dexmedetomidine has more pronounced effect on inhibition of nerve fiber action potentials as compared to clonidine.

INTRAVENOUS DOSAGE: loading dose- 1 mcg/kg to be given over a period of 10 minutes followed by maintenance dose of 0.2-0.7 mcg/kg/hr.

DOSAGE FOR PERIPHERAL NERVE BLOCKS: 0.5 to 1 mcg/kg mixed with the local anaesthetic.

PHYSICAL PROPERTIES [47]

Molecular weight : 236.74 gm/mol

Half – life : 2 hours

Protein binding : 94 %

Dexmedetomidine hydrochloridhe is freely water soluble.

PHARMACOKINETICS:

Dexmedetomidine exhibits linear pharmacokinetics in the dose range of 0.2 to 0.7 mcg/kg/hr when administered by IV infusion upto 24 hrs. The pharmacokinetic profile is not altered by age. Dexmed is rapidly distributed and extensively metabolised in liver and excreted in urine and faeces.

Distribution : The volume of distribution is approximately 118 litres. It has 94% protein binding, which is similar in both sexes and is decreased in patients with liver pathologies.

Metabolism : It is extensively metabolised in liver by glucuronide conjugation and undergoes biotranformation in cytochrome P450 enzyme system. There are no known active or toxic metabolite. However, drug clearance is reduced by as much as 50% in severe liver diseases. Pharmacokinetics is not altered much in renal impairment.

Elimination : the terminal half-life is 2 hours and clearance is 39 L/hr.

EFFECTS ON ORGAN SYSTEMS:

A) NERVOUS SYSYTEM:

1. Sedation: Dexmeds sedative – hypnotic effect is by its action on α2 receptors in the locus ceruleus i the brain. The sedation produced by dexmedetomidine is different when compared to other sedatives which act through GABA systems. Patients receiving dexmedetomidine infusions are easily aroused yet appear calm and comfortable. Patients return to hypnotic state when they remain unstimulated. Sedation produced by dexmedetomidine has limited respiratory depression and wide safety margins. The α2 agonists act through sleep promoting pathways to exert their sedative effects. Dexmedetomidine

produces a decrease in activity of projection of locus ceruleus to the ventrolateral preoptic nucleus. The similarity between natural sleep and dexmedetomidine induced hypnosis has been speculated to maintain cognitive and immunologic function in the sleep deprived state.

2. Anxiolysis: it is mediated by action on pontine locus ceruleus. It decreases the activity of projections of the locus ceruleus to the ventrolateral preoptic nucleus.
3. Analgesia: it is mediated through central and peripheral nervous system. In the CNS, locus ceruleus is also the site of origin for tthe descending medullospinal noradrenergic pathway, known to be an important modulator of nociceptive transmission. The analgesic effects have been attributed to α2 agonism of this site. Analgesic potency is synergistically enhanced by concomitant opioids.
4. Anaesthetic effects: dexmedetomidine modifies the action of potassium channels in the CNS (cell membranes become hyperpolarised) and inhibit the firing of cells in the locus ceruleus, thereby decreasing the anaesthetic requirements.
5. Neuroprotection: Action on imidazole receptor may be involved in neuroprotective effect in cerebral ischemia.
6. Cerebral blood flow: It decreases CBF, and may be favourable in protecting the brain from an abruot increase in cerebral blood flow.

B) CARDIOVASCULAR SYSTEM:

1. Bradycardia: The primary effect on the heart rate is negative chronotropic effect by blocking cardio-accelerator nerves, augmenting vagal nerves and inhibition of noradrenaline release from peripheral junctional nerve endings.

2. Hypotension: The alpha 2 action on autonomic ganglia includes decrease in sympathetic outflow which leads to hypotension and bradycardia. In the spinal cord dexmedetomidine inhibits the firing of preganglionic sympathetic neurons and decreases the sympathetic outflow. Thus, blood pressure dcreases more after intra-thecal than epidural administration. It produces peripheral vasoconstriction by direct post-synaptic actions. Hence intravenous infusion causes acute rise in blood pressure which is followed by more prolonged hypotension resulting from decreased central sympathetic outflow. No rebound hypertensionhave been found even after discontinuing dexmedetomidine infusions even after 24 hrs.
3. Rhythm: By enhancing the vagal rhythm it decreases the firing rate of SA node and depresses AV nodal conduction at higher doses. There is slight prolongation in the PR ansd QT interval in the healthy subjects.
4. Coronary circulation: It causes peripheral vasoconstriction by direct effect. It also mediates the release of endothelial derived relaxation factor.

C) RESPIRATORY SYSTEM:

Dexmedetomidine does not cause respiratory depression. Nevertheless, co-administration of dexmed with other anaesthetic agents, sedatives, hypnotics, or opioids is likely to cause additive effects. Dexemedetomidine at concentrations producing significant sedations reduces minute ventilation. But retains the slope of ventilator response to increasing carbon dioxide. It also exhibits a hypercarbic arousal phenomenon, which has been described during normal sleep and is a safety feature.

D) THERMOREGULATION:

It attenuates potoperative shivering by inhibiting transmission of affferant thermal signals at the level of spinal cord decreasing the central thermoregulatory threshold for shivering and by depressing the efferent pathways responsible for shivering.

INDICATION:

1) Intensive care unit sedation: dexmedetomidine is indicated for sedation of initially intubated mechanically ventilated patients during treatment in an high dependency unit.
2) Procedural sedation: dexmedetomidine is indicated for sedation of nonintubated patients prior to or during a surgical procedure. The usual dose of dexmed for procedural sedation is 1mcg/kg followed by an infusion of 0.2 mcg/kg/hr.
3) Premedication: It is a good sedative, anxiolytic, attenuates the heamodynamic response to laryngoscopy and intubation. Premedication dose is 0.33 to 0.67 mg/kg IV given 15 min before surgery.
4) Maintenance of anaesthesia: Continuos intravenous infusion of dexmedetomidine is used for maintenece of anaesthesia. It reduces the need for other anaesthetic agents used for maintenance.
5) Postoperative analgesia: Dexmedetomidine produces postoperative analgesia without respiratory depression and motor and sensory as seen with narcotic analgesics and local anaesthetics respectively.

6) Shivering: It decreases postoperative shivering, decreasing oxygen consumption which is important in patients with compromised oxygen supply and demand imbalance.

ADVERSE EFFECTS:

1) Cardiovascular system: Adverse events like bradycardia, hypotension, transient hypertension, agtrial fibrillation can occur. Dexmedetomidine is not recommended in patients with advanced heart block and ventricular dysfunctions.
2) Respiratory system: Adverse events like hypoxia, hypoventilation, and hypercarbia can occur.
3) GI system: Nausea, vomiting or dryness of mouth can occur.
4) Central nervous system: Dizziness, headache can occur.
5) General: Fever and confusion may occur

ANTAGONIST: All effects of dexmedetomidine can be antagonized easily by administering the α2-adrenoceptor antagonist Atipamezole. It reverses sedation and sympatholysis and has a half-life of 1.5 - 2 hr.

Supportive care may include atropine sulfate for bradycardia, intravenous fluids and/or vasopressors for hypotension and vasodilators for hypertension.

METHODOLOGY

The present study titled **"COMPARISON OF EFFICACY OF LEVOBUPIVACAINE AND LEVOBUPIVACAINE WITH DEXMEDETOMIDINE FOR SUPRACLAVICULAR BRACHIAL PLEXUS BLOCK IN PATIENTS UNDERGOING UPPERLIMB SURGERIES – A ONE YEAR RANDOMISED CONTROLLED TRIAL"** was conducted in the Department of Anaesthesiology, Jawaharlal Nehru Medical College KLE university during the period January 2014 to December 2014. A total of 50 pateints belonging to ASA grade I and II between the age group of 18 – 60 years of either gender, scheduled for elective upper limb surgeries under supraclavicular brachial plexus block were included in the study.

a) Selection Criteria:

Inclusion

1. Elective upper limb surgeries (i.e elbow,forearm and hand).
2. Age: 18 to 60 years.
3. ASA Grade I and Grade II patients.

Exclusion

1. Patient refusal to consent.
2. Patients with history of bleeding disorders.
3. Patients with local infection at the site of block.
4. Patients with documented neuromuscular disorders.
5. Patients with acute/chronic respiratory diseases.
6. Patients with known allergy to local anaesthetic drugs & alpha agonists.
7. ASA grade III and IV patients.

b) Sample size (n):

From data available from previous studies

X_1 = Onset time of motor block in control group[2]

X_2 = Onset time of motor block in study group[2]

X_1=11.1 X_2=9.5

X_1-X_2=1.6

S_1=1.24 S_2=1.04

α =0 .05m Zα = 1.96

β = 0.1 Z_β = 1.28

$n = 2(Z_\alpha + Z_\beta)^2 (S^2_1 + S^2_2)^2 \div (X_1 - X_2)^2$

substituting the values in the above formula

$n = 2(1.96 + 1.28)^2(1.24^2 + 1.04^2)^2 \div (1.6)^2$

n = 21.48

= approximating to 25.

25 patients were taken as study group and 25 patients were taken as control group. (total 50 patients)

c) Sample procedure: After obtaining Institutional review board and ethical committee clearance 50 patients were allocated in a randomised manner by computer generated randomization chart into two groups of 25 each.

- Group LS: received 39ml of 0.5% levobupivacaine + 1ml normal saline
- Group LD: received 39ml of 0.5% levobupivacaine + 1ml (100mcg) of dexmedetomidine.

d) Methodology:

After having met inclusion and exclusion criteria and having obtained informed consent, a meticulous history and clinical examination was carried out and all the patients were subjected to routine blood investigations namely,

- **Complete Blood count**
- **RBS**
- **Serum Creatinine**
- **Urine routine**
- **Chest X-ray, ECG**

Anaesthesiologist involved in the data collection as well as the patients were blinded to the content of the study solution.

In the preoperative room, an intravenous (IV) line was secured with either 18 G or 20 G branula and Ringer lactate was started at 5 ml/kg/hr. The patients were then shifted to the operation theatre and standard monitors namely electrocardiograph (ECG), pulse oximeter and non-invasive blood pressure were attached and baseline readings were taken. The patients were placed in supine position, with head extended and turned towards opposite side and the arm adducted and fully extended towards the ipsilateral knee as far as possible. The midpoint of clavicle was identified and marked. The patients were told to raise the head slightly and posterior border of sternocleidomastoid was palpated. The palpating fingers was then rolled over the belly of the anterior scalene muscle into the interscalene groove, where a mark was made approximately 1.5 to 2.0 cm posterior to the midpoint of the clavicle with palpation of the subclavian artery at the site confirming the landmark.

Under strict aseptic precautions and preparation of parts, the subclavian artery was palpated and a skin wheal was injected using a 2ml of 2% lignocaine. Neural localization was achieved using a nerve stimulator connected to a 22 gauge, 4 cm long stimulating needle. The position of the needle was felt adequate when an output current of <0.5 mA elicited a slight distal motor response. On localization of the brachial plexus and conformation of negative aspiration for blood/air, incremental injections of a total volume of 40 ml of solution was administered. Patients in Group LS received 39 ml of 0.5% isobaric levobupivacaine with 1 ml of isotonic normal saline and patients in Group LD received 39 ml of 0.5% isobaric levobupivacaine with 1 ml of 100 mcg dexmedetomidine in a double blind fashion.

The drug solutions were prepared by an anaesthesiologist not involved in the study.

The parameters studied were onset and duration of sensory and motor blockade, duration of post-operative analgesia and haemodyamic parameters namely Heart Rate, Systolic Blood Pressure and Diastolic Blood Pressure.

Sensory block was assessed by pinprick test using a 3-point scale in all nerve territories:

0=sharp pin felt

1=dull sensation felt (analgesia)

2=no sensation felt (anaesthesia).

Motor block was assessed by thumb abduction(radial nerve),thumb adduction(ulnar nerve), thumb opposition(median nerve),and flexion at the elbow(musculocutaneous nerve) on a 3-point scale for motor function

0=normal motor function with full flexion and extension of elbow, wrist and fingers

1=reduced motor strength but able to move fingers

2=complete motor blocks with inability to move fingers.

Sensory and motor blockade were assessed every 3 minutes for the first 30 minutes after the drug injection, every 30 minutes during the intraoperative period and then every hour until they had resolved.

Onset of sensory block was defined as the time interval between the end of total local anaesthetic administration and complete sensory block.(score 2)

Complete sensory block – defined by anaesthetic block (score 2) on all nerve territories.

Duration of sensory block – defined as the time interval between the end of local anaesthetic administration and the complete resolution of anaesthesia in all nerve distributions.

Onset of motor block - the time interval between administration of local anesthetic solution to loss of movements.(score 2)

Complete motor block – absence of voluntary movements in hand and forearm (score 2).

Duration of motor block – defined as the time interval between the end of local anaesthetic administration and the recovery of complete motor function of the hand and forearm.

Duration of post-op analgesia – defined as the time interval between the end of local anaesthetic administration to the first request for rescue analgesia.

After completion of 30 mins if the desired sensory and motor levels of block was not achieved, then the block was considered as a failure and the patients were excluded from the study and general anaesthesia was administered.

Heart rate, systolic blood pressure(SBP) and diastolic blood pressure(DBP) and sedation scores were recorded at 0,5,10,15,30,45,60 and every thirty minutes till the end of surgery. Adverse events such as hypotension was defined as decrease in systolic B.P by 20% from baseline values and treated with Inj mephentermine 6 mg IV. Bradycardia was defined as decrease in heart rate less than 50 beats per minute and treated with Inj Atropine 0.6 mg IV. Hypoxia was defined as SPO_2<90% and treated with oxygen by mask.

Sedation was measured by **Ramsay sedation scale**.

Ramsay Sedation Scale

If Awake

Ramsay 1:

Anxious, agitated, restless

Ramsay 2:

Cooperative, oriented, tranquil

Ramsay 3:

Responsive to commands only

If Asleep

Ramsay 4:

Brisk response to light glabellar tap or loud auditory stimulus

Ramsay 5:

Sluggish response to light glabellar tap or loud auditory stimulus

Ramsay 6:

No response to light glabellar tap or loud auditory stimulus

In the post anaesthesia care unit(PACU), pain was assessed using a visual analog scale(0-10) by a trained Nursing staff and was instructed to administer 75 mg of IV diclofenac in 100 ml normal saline as an infusion when the visual analog scale>4. The time of first dose of rescue analgesic administered was noted.

Statistical Analysis :

All the data are expressed as mean +/-SD. Quantitative data was compared using student's unpaired t test while Qualitative data was compared using chi- square test.The p value of <0.05 was considered significant.

OBSERVATIONS AND RESULTS

The objectives of the present study were to compare the onset and duration of sensory and motor block, duration of post-operative analgesia and hemodynamic changes following administration of either levobupivacaine or levobupivacaine-dexmedetomidine in patients undergoing upper limb surgeries under supraclavicular brachial plexus block.

50 patients were randomly enrolled into two groups of 25 each.

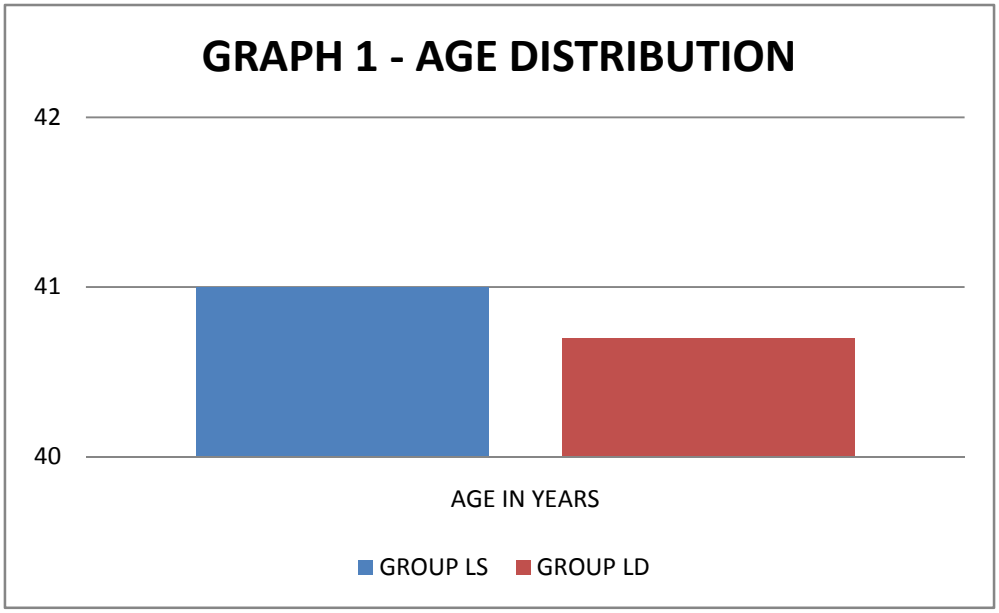
Group LS	Received 39 ml of 0.5% levobupivacaine + 1 ml of normal saline
Group LD	Received 39 ml of 0.5% levobupivacaine + 1 ml (100mcg) of Dexmedetomidine

The data obtained were analysed and the observations and results are tabulated as below:

DEMOGRAPHIC DATA

AGE Table 1: Mean age of patients

GROUP	Mean age (in years) + Standard deviation	p- value	Statistical significance
LS	41.7 ± 14.71	0.811	NS
LD	40.7 ± 15.83		

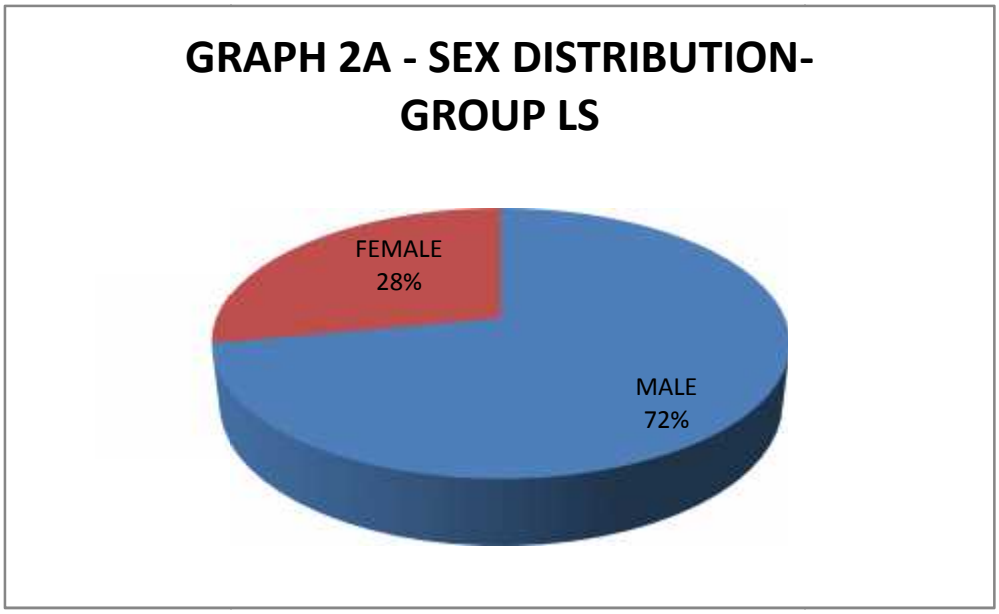


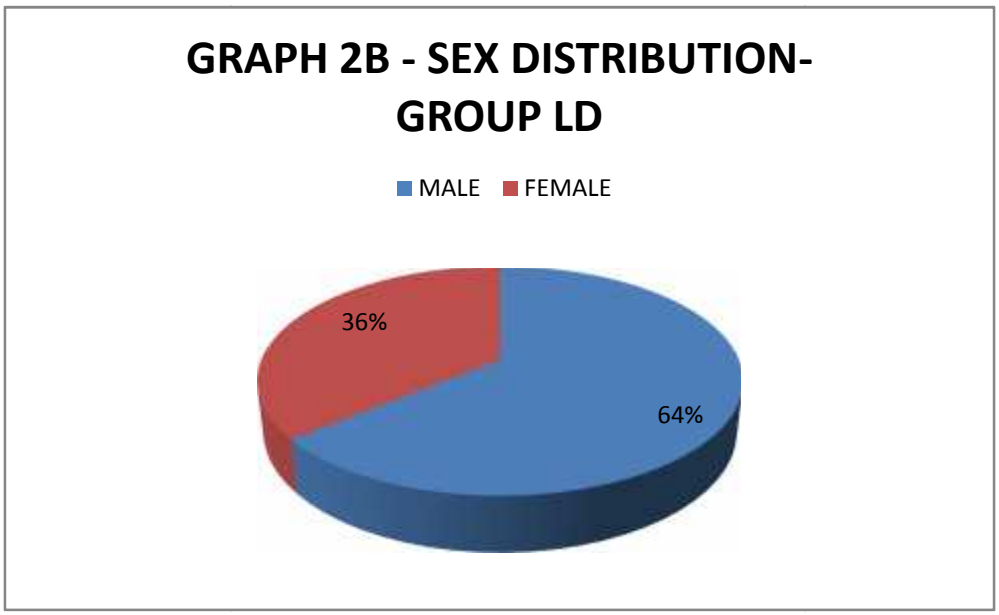
The mean age in years was 41.7 ± 14.71 in Group LS and 40.7 ± 15.83 in Group LD. The two groups did not differ significantly with respect to their age.

SEX DISTRIBUTION

Table 2: Sex distribution

Gender	Group LS (n)	Group LD (n)	p- Value	Statistical signifiance
Male	18	16	0.544	NS
Female	7	9		
Total	25	25		



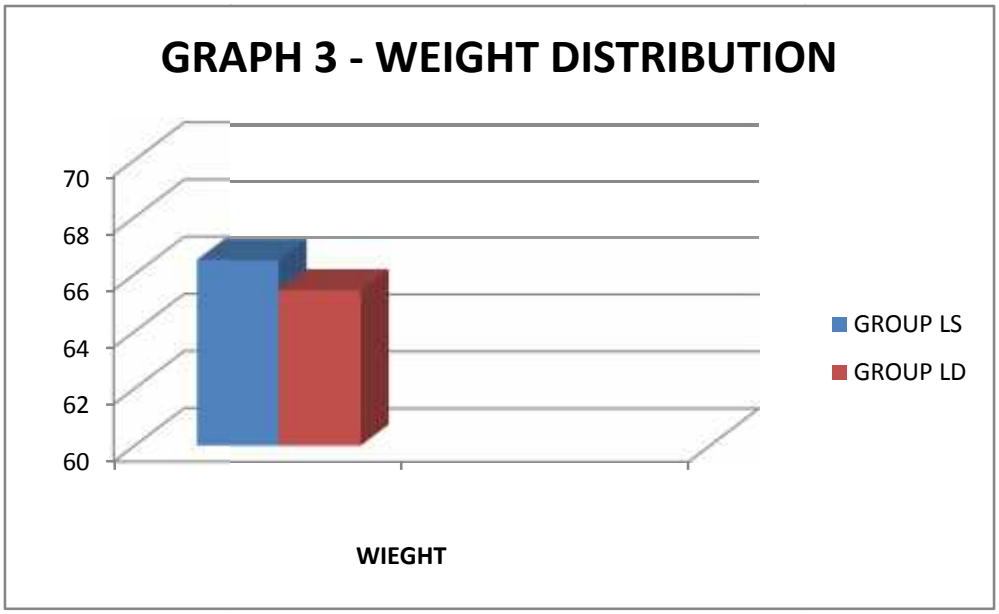


There were 18 males and 7 females in Group LS and 16 males and 9 females in Group LD. The groups were comparable with respect to sex distribution with no significant difference between the groups.

Comprison of Mean Weight between the Groups

Table 3: Mean weight of patients

Group	Mean Weight(kg) + Standard deviation	p- value	Statistical significance
LS	66.5 ± 10.16	0.724	NS
LD	65.4 ± 12.03		

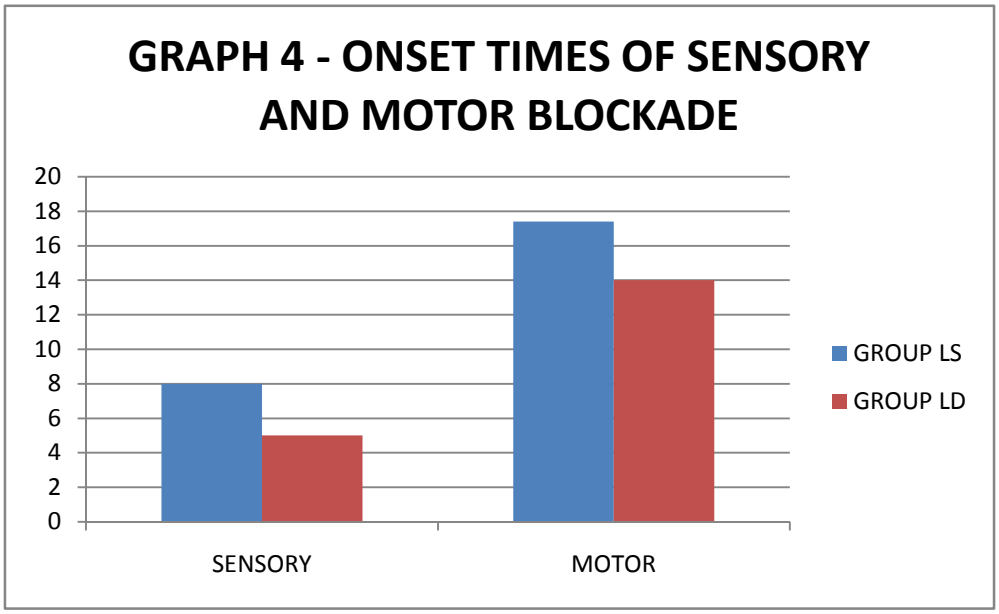


The mean weight was 66.5 ± 10.16 kgs in Group LS and 65.4 ± 12.03 kgs in Group LD. The two groups did not differ significantly with respect to weight.

BLOCK CHARACTERESTICS:

Table 4 : Onset time of sensory and motor blockade:

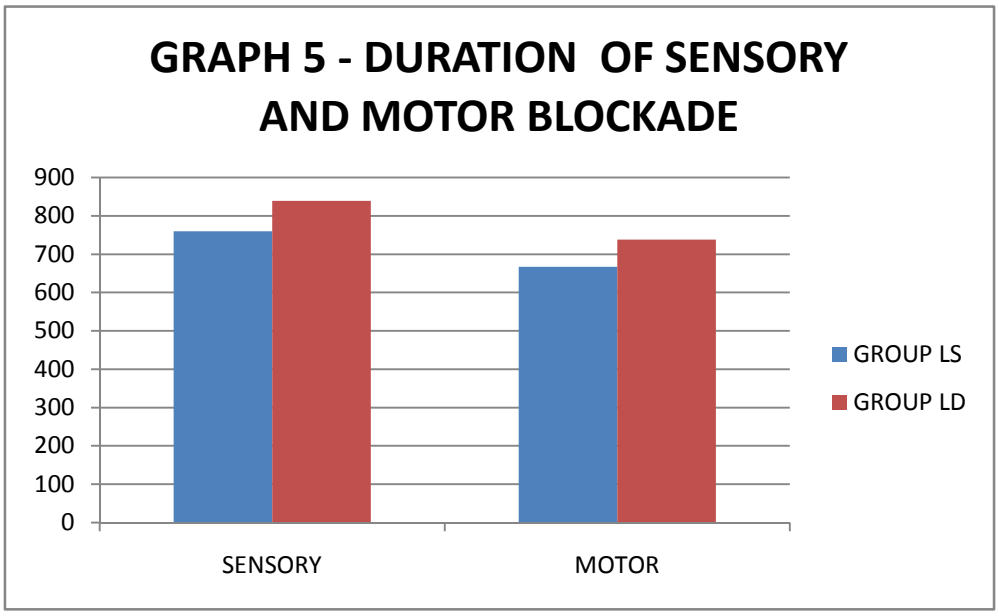
	Group LS	Group LD	't'value	P	sig
Onset of sensory blockade (min)	8 ± 0.76	5 ± 0.73	13.964	<0.001	Sig*
Onset of motor blockade (min)	17.4 ± 1.26	14 ± 1.33	9.24	<0.001	Sig*



The mean time for onset of sensory block was 8 ± 0.76 min in Group LS and 5 ± 0.73 min in Group LD. The mean time for onset of motor block was 17.4 + 1.26 min in Group LS and 14 + 1.33 min in Group LD. The statistical analysis by students unpaired t test showed that there is a significant difference in the mean onset times of sensory and motor block between the two groups with p value < 0.001 which was statistically significant.

Table 5 : Duration of sensory and motor blockade:

	Group LS	Group LD	t - value	P value	SIG
Duration of sensory blockade (mins)	759.6± 37.24	838.8± 42.35	7.020	<0.001	Sig*
Duration of motor blockade (mins)	667.2±42.67	738±45.64	5.665	<0.001	Sig*

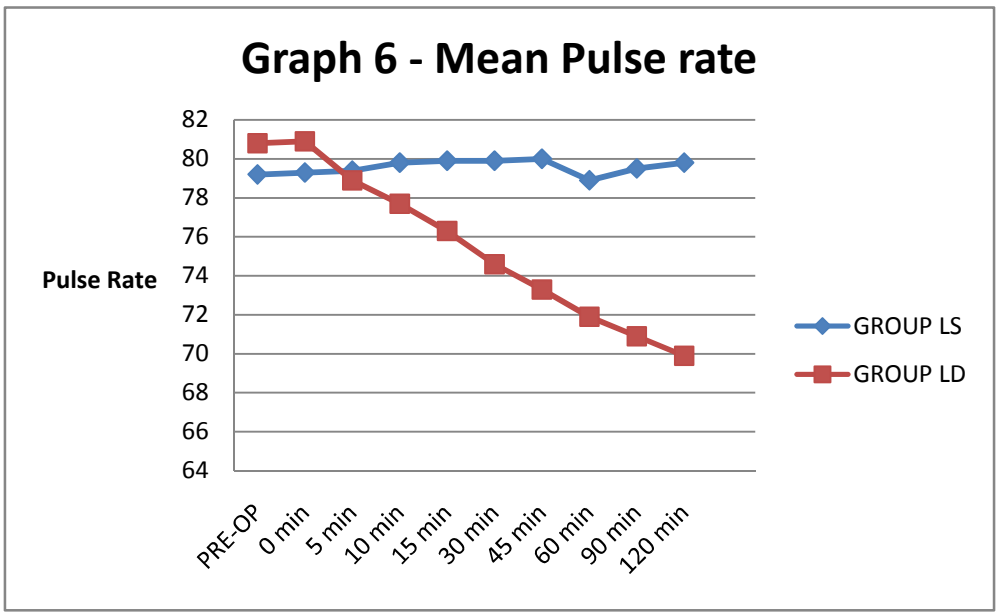


The mean time for duration of sensory block was 759.6 ± 37.24 min in Group LS and 838.8 ± 42.35 min in Group LD . The mean time for duration of motor block was 667.2 ± 42.67 min in Group LS and 738 ± 45.64 min in Group LD. The statistical analysis by student's unpaired t test showed that there is a significant difference in the duration of sensory and motor block between the two groups with p value < 0.001 which was statistically significant.

Table 6 : Mean Pulse Rate:

Time of Assessment	Mean+/-SD(rpm)		t*Value	P Value	Sig
	Group LS	GroupLD			
Pre – op	79.2 ± 5.93	80.8 ± 7.22	.877	.325	NS
0min	79.3±5.63	80.9 ±6.85	.879	.384	NS
5min	79.4±6.01	78.9±6.70	.267	.291	NS
10min	79.8±5.53	77.7 ±6.40	1.240	.221	NS
15min	79.9±6.19	76.3±6.23	2.135	.038	NS
30min	79.9± 6.19	74.6±6.9	3.033	.004	Sig
45 min	80±6.32	73.3±6.53	3.674	.001	Sig
60 min	78.9±5.94	71.9± 5.98	4.197	<.001	Sig
90 min	79.5±5.21	70.9±5.58	5.601	<.001	Sig
120 min	79.8±5.31	69.9± 4.89	6.809	<.001	Sig

Sig – significant NS – Not Significant



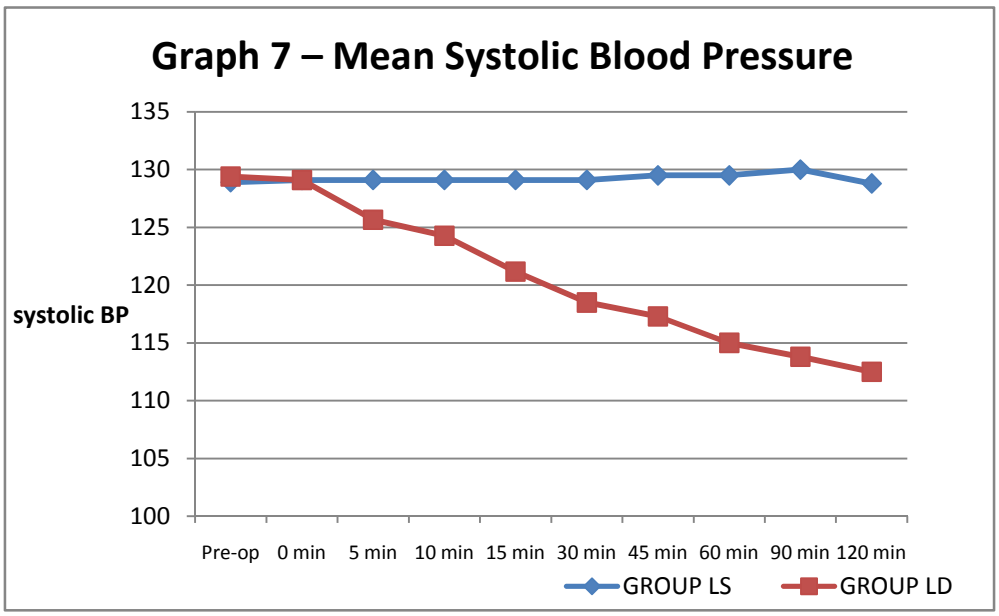
The above table shows that the intraoperative mean pulse rate was comparable between the groups till the first 15 min. A steady decline in the mean pulse rate was seen in Group LD compared to Group LS at 30 mins and in all the readings thereafter during the inta-operative period.

At 30 min the mean pulse rate was 79.9± 6.19 per min in Group LS and 74.6±6.9 per min in Group LD. The lowest decline in the mean pulse rate was at 120 min with mean pulse rate of 69.9± 4.89 per min in Group LD and 79.8±5.31 per min in Group LS. This difference was statistically significant between the groups with P value < 0.001.

TABLE 7 : Mean Systolic Blood Pressure:

Time of Assessment	Mean+/-SD mmHg		t*Value	P Value	Sig
	Group LS	Group LD			
Pre – op	128.9 ± 6.48	129.4 ± 8.83	.219	.828	NS
0min	129.1±6.16	129.1 ±8.69	.019	.985	NS
5min	129.1±6.57	125.67±11.29	1.331	.190	NS
10min	129.1±6.72	124.27±10.60	1.976	.054	NS
15min	129.1±6.57	121.17±10.28	3.260	.002	Sig
30min	129.1± 6.72	118.5±10.93	4.097	<.001	Sig
45 min	129.5±4.59	117.3±9.97	5.574	<.001	Sig
60 min	129.5±4.61	115± 10.65	6.255	<.001	Sig
90 min	130 ±6.44	113.8±9.55	7.046	<.001	Sig
120 min	128.8±5.59	112.5± 8.15	8.213	<.001	Sig

Sig – Significant Ns – Not Significant



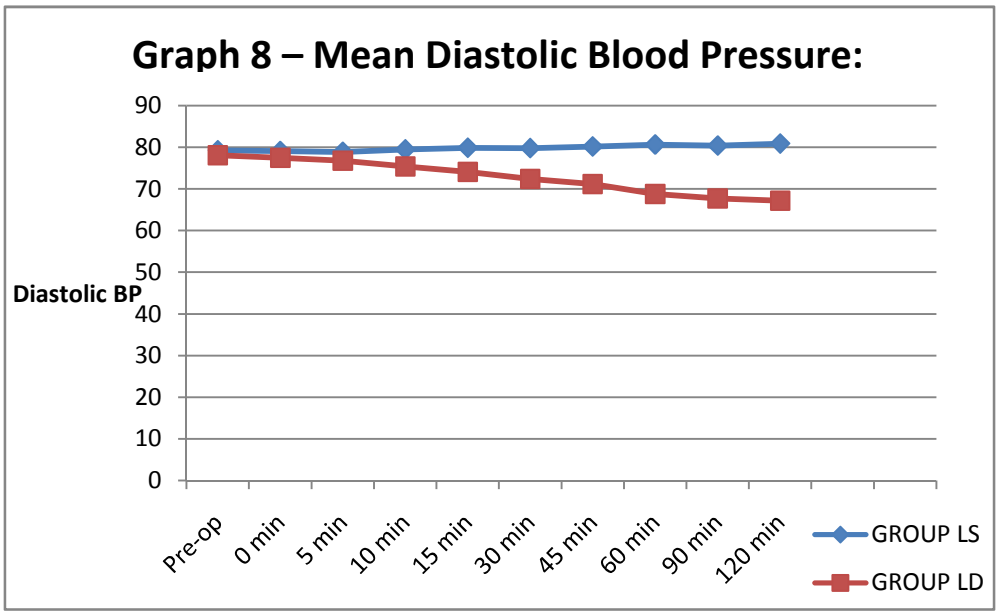
The above table shows that the intraoperative Systolic Blood Pressure (SBP) was comparable between the groups till the first 10 min. A steady decline in the mean systolic blood pressure was seen in Group LD compared to Group LS at 15 min and thereafter during the inta-operative period.

At 15 min the mean SBP was 121.17±10.28 mmHg in Group LD and 129.1±6.57 mmHg in Group LS. The maximum difference in the mean SBP between the two groups was seen at 120 mins with the mean SBP of 112.5± 8.15 mmHg in Group LD and 128.8±5.59 mmHg in Group LS. The difference in the mean SBP between 15 min to 120 min was statistically significant with P value < 0.001.

TABLE 8 : Mean Diastolic Blood Pressure:

Time of Assessment	Mean+/-SD mmHg		t*Value	P Value	Sig
	Group LS	Group LD			
Pre – op	79.3 ± 6.63	78.1 ± 7.25	.631	.531	NS
0min	79.1±6.40	77.5 ±6.96	.845	.402	NS
5min	78.9±6.07	76.8 ± 6.32	1.163	.251	NS
10min	79.5±6.40	75.4 ±6.35	2.283	.027	NS
15min	79.9±6.64	74.1 ± 7.03	2.999	.004	Sig
30min	79.8± 6.24	72.4 ±6.49	4.107	<.001	Sig
45 min	80.2 ±6.27	71.2±6.01	5.182	<.001	Sig
60 min	80.7± 6.18	68.8± 5.98	6.880	<.001	Sig
90 min	80.4 ±5.12	67.7±5.31	7.715	<.001	Sig
120 min	80.9 ±5.88	67.2± 5.12	8.791	<.001	Sig

Sig – significant NS – Not Significant



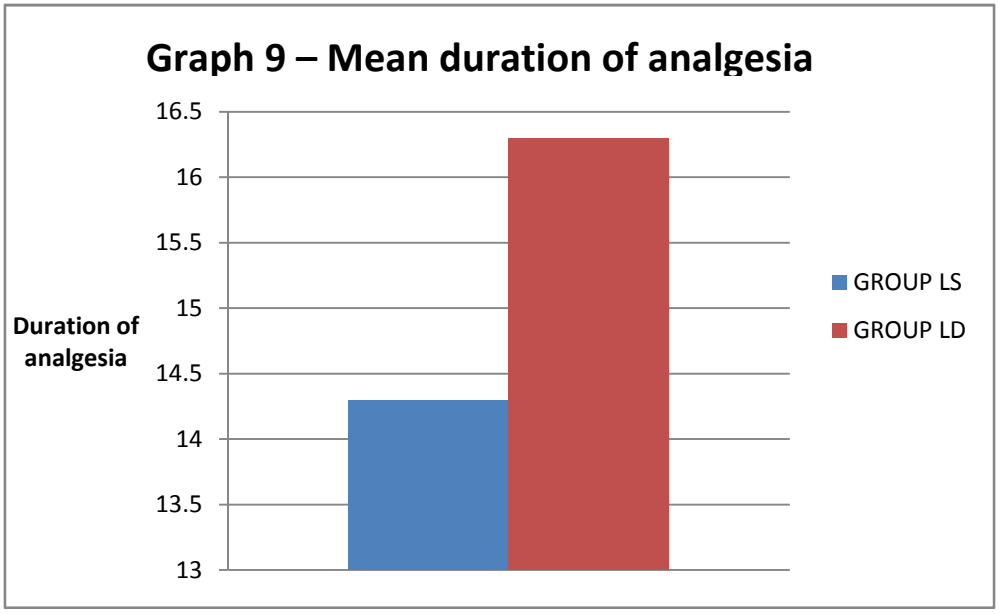
The above table shows that the intraoperative Diastolic Blood Pressure (DBP) was comparable between the groups till the first 10 min. A steady decline in the mean Diastolic Blood Pressure was seen in Group LD compared to Group LS at 15 min and thereafter during the inta-operative period.

At 15 min the mean DBP was 74.1 ± 7.03 mmHg in Group LD and 79.9±6.64 mmHg in Group LS. The maximum difference between the mean DBP between the two groups was seen at 120 mins with the mean DBP of 67.2± 5.12 mmHg in Group LD and 80.9 ±5.88 mmHg in Group LS. The difference in the mean DBP between 15 min to 120 min was statistically significant with P value < 0.001.

DURATION OF ANALGESIA

Table 9: Mean duration of analgesia

Group	Mean duration of analgesia(hrs) + Standard deviation	p- value	Statistical significance
LS	14.3 ± 0.61	< 0.001	Significant
LD	16.3 ± 0.64		



The mean duration of analgesia was 16.3 ± 0.64 hours in Group LD and 14.3 ± 0.61 hours in Group LS. This difference between the two groups is highly significant with P value < 0.001 which proves that addition of dexmedetomidine to levobupivacaine significantly increases the duration of analgesia.

There were no side effects like nausea, vomiting, respiratory depression or sedation in both groups.

DISCUSSION

Brachial plexus block is commonly performed anaesthetic technique for surgeries on the upper limb. Supraclavicular block the commonest approach to brachial plexus is performed at the level of the trunks of brachial plexus. Here, almost the entire sensory, motor and sympathetic innervations of the upper extremity are carried in just three nerve trunks, confined to a very small surface area. Consequently, typical features of this block include rapid onset, predictable and dense anaesthesia along with a high success rate.[48]

Several studies have compared levobupivacaine, ropivacaine and bupivacaine in peripheral nerve plexus blocks. Levobupivacaine is a good substitute for bupivacaine as it provides a longer duration of sensory block along with good analgesia with less systemic toxicity.

Local anaesthetics alone for supraclavicular brachial plexus block provide good operative conditions but variable quality and duration of postoperative analgesia. Various methods like higher concentrations of local anaesthetics, continuous catheters and adjuvants have been employed to improve the quality and duration of peripheral nerve blocks.

Alpha 2 adrenergic agonists like dexmedetomidine have recently been popular because of their sedative, analgesic, antihypertensive, antiemetic actions in addition to reducing the anaesthetic drugs requirement. Several studies have concluded that dexmedetomidine is a safer and effective adjuvant to local anaesthetics for epidural, intrathecal and various regional anaesthetic techniques, providing prolonged duration of anaesthesia.

In the present study 50 patients were randomised into two groups of 25 each

- Group LS: received 39ml of 0.5% levobupivacaine + 1ml saline
- Group LD: received 39ml of 0.5% levobupivacaine + 1ml (100mcg) of dexmedetomidine.

The mean age, sex and weight between the two groups was comparable with no significant difference between the demographic parameters.

The mean time for onset of sensory block was 8 $\pm$ 0.76 min in Group LS and 5 $\pm$ .073 min in Group LD. The mean time for onset of motor block was 17.4 + 1.26 min in Group LS and 14 $\pm$ 1.33 min in Group LD. The onset times were faster in dexmedetomidine group compared to the control group. The results of our study are similar to a study conducted by **Kaur et al (2015)** who observed that the onset times of sensory and motor block were 6.9 and 7.6 mins in dexmedetomidine group compared to 7.6 and 8.3 mins respectively in the control group.[49]

Levobupivacaine prevent transmission of nerve impulses by inhibiting passage of sodium ions through ion-selective sodium channels in the nerve membrane providing a conduction blockade. The addition of dexmedetomidine to levobupivacaine induces a vasoconstriction around the site of injection resulting in delay of absorption of the local anaesthetic thereby providing increased volume of levobupivacaine at the site of action. Peripherally dexmedetomidine reduces the release of norepinephrine and causes alpha 2 receptor independent inhibitory effect on nerve fibre action potentials. The different mechanism of action of both the drugs can have a additive effect and hence when mixed together can shorten the onset of sensory and motor blockade.

The mean time for duration of sensory block in our study was 759.6 ± 37.24 min in Group LS and 838.8 ± 42.35 min in Group LD and the mean time for duration of motor block was 667.2 ± 42.67 min in Group LS and 738 ± 45.64 min in Group LD. The prolonged duration of both sensory and motor blockade in the dexmedetomidine group observed in our study are similar to the results in a study by **Sauwmya et al (2014)** where duration of sensory block in the dexmedetomidine group was 898 mins compared to 645 mins in the saline group and the duration of motor block was 840 mins in dexmedetomidine group compared to 512 mins in the saline group which was statistically significant.[28]

The mean duration of analgesia in our study was 14.3 ± 0.61 hours in Group LS and 16.3 ± 0.64 hours in Group LD. These findings are similar to a study by **Esmaoglu et al (2010)** who compared the efficacy of dexmedetomidine added to levobupivacaine in supraclavicular brachial block and observed a significantly prolonged duration of analgesia of 16.6 hours in dexmedetomidine group compared to 14.7 hours in the control group.[2]

The prolonged duration of sensory and motor blockade and analgesia observed in dexmedetomidine group can be attributed to suppression of activity in the descending noradrenergic pathway by dexmedetomidine which modulates nociceptive neurotransmission and terminates propagation of pain signals. It also inhibits the release of substance P in the nociceptive pathway at the level of the dorsal root neurons and activates α2-Adrenergic receptors in the locus coeruleus. In the central nervous system, dexmedetomidine causes presynaptic activation of α2 adrenoceptor inhibiting release of norepinephrine, terminating the propagation of pain signals resulting in prolonged analgesia.

There was a specific change in trend of vital parameters that was observed in our study. The mean pulse rate was comparable between the groups until the first 15 min of intraoperative period but there was a significant fall in the mean pulse rate in dexmedetomidine group from 30 mins of intraoperative period until the completion of the study. There was a similar trend in fall of both systolic and diastolic blood pressure in the dexmedetomidine group from 15 mins onwards in the intraoperative period.

These changes in the vital parameters are due to postsynaptic activation of alpha 2 receptors by dexmedetomidine that inhibits sympathetic activity, thereby decreasing Heart Rate (HR) and BP. Bradycardia persists subsequently due to central sympathetic inhibition. Baroreceptor reflex and HR response to a pressor agent is well preserved with the use of dexmedetomidine, thus hypotension and bradycardia are readily treatable conferring hemodynamic stability.

Similar findings were also observed by **Sandhya et al** on evaluating the efficacy of dexmedetomidine to bupivacaine in supraclavicular brachial plexus block. The mean HR, SBP, and DBP in dexmedetomidine group at 15, 30, 45, 60, 90, and 120 min were significantly lower than in control group with a *P value* < 0.001.[50]

Hence the addition of dexmedetomidine to levobupivacaine shorten the onset times and prolong the duration of sensory and motor blockade and provides effective postoperative analgesia with minimal hemodynamic changes in supraclavicular brachial plexus block.

CONCLUSION

In conclusion, dexmedetomidine shortens the onset and prolongs the duration of sensory and motor blockade effectively enhancing the quality of blockade when used as an adjuvant to levobupivacaine in supraclavicular brachial plexus block. The duration of analgesia was significantly prolonged with minimal heamodynamic changes thus making dexmedetomidine a potential adjuvant for peripheral nerve blocks.

SUMMARY

In this prospective randomised controlled trial, 50 ASA grade I and II patients were randomly enrolled to receive 39 ml of 0.5% levobupivacaine with 1 ml (100 mcg) dexmedetomidine (Group LD) or 39 ml of 0.5% levobupivacaine with 1 ml of normal saline (Group LS). The onset and duration of sensory and motor block and the duration of analgesia was compared between the two groups.

There was a significant decrease in onset of sensory block in group LD (5 $\pm$ 0.73 min) compared to group LS (8 $\pm$ 0.76 min). There was also a significant decrease in the onset of motor block in group LD (14 + 1.33 min) compared to group LS (17.4 + 1.26min). The mean duration of sensory and motor block was prolonged in group LD (838.8 ± 42.35 min and 738 $\pm$ 45.64 min) compared to Group LS (759.6 ± 37.24 min and 667.2 $\pm$ 42.67 min) respectively. The duration of analgesia was 16.3 ± 0.64 hours in group LD compared to 14.3 ± 0.61 hours in Group LS. The haemodynamic changes between the groups were statistically significant but clinically were not significant. Hence we conclude that dexmedetomidine shortens the onset and prolongs the duration of sensory and motor blockade enhancing the quality of block when used as an adjuvant to levobupivacaine in supraclavicular brachial plexus block for upper limb surgeries. Dexmedetomidine significantly prolongs the duration of analgesia with minimal hemodynamic effects thus making it a potential adjuvant for peripheral nerve blockade.

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ANNEXURE-I

CONSENT FOR PARTICIPATION IN RESEARCH STUDY

Mr/Mrs/Miss. _____ we are requesting you to enroll yourself in study titled "**COMPARISON OF EFFICACY OF LEVOBUPIVACAINE AND LEVOBUPIVACAINE WITH DEXMEDETOMIDINE FOR SUPRACLAVICULAR BRACHIAL PLEXUS BLOCK IN PATIENTS UNDERGOING UPPERLIMB SURGERIES – A ONE YEAR RANDOMISED CONTROLLED TRIAL**",

Respected Sir/Madam we request you to enroll yourself to participate in our study as you are eligible for participating in the study. During the study you will be asked some questions regarding your present complaint and you are supposed to answer to the best of your knowledge.

Your participation in research is voluntary. Your decision whether or not to participate in the study will not affect your relationship with J.N. Medical College. If you decide to participate you are free to withdraw at any time.

The purpose of research is to compare efficacy between Levobupivacaine and Levobupivacaine - dexmedetomidine on onset and duration of motor block, onset and duration of sensory block, hemodynamic changes in upper limb surgeries under brachial plexus block.

Procedure Involved:

If you agree to enroll yourself in my study, you will be interviewed regarding your present, past and family history, then you will be clinically examined in detail and investigated accordingly. You will be randomly allocated either into control Group LS or study Group LD and will be given the study drug as per the randomization protocol. You will receive 39 ml of 0.5% levobupivacaine with 1 ml of normal saline or 39 ml of 0.5% levobupivacaine with 1ml (100mcg) of dexmedetomidine for brachial plexus block.

Risks and Benefits:

The benefits of taking part in this research are that we can avoid General Anaesthesia with good quality of Analgesia during and after the surgery. The risks of the procedure as such are minimal but with the use of the new drug dexmedetomidine you may have mild side effects which include, hypotension, bradycardia, headache,nausea,vomiting, syncope, paraesthesia and sedation.

Voluntary Participation/Withdrawal:

Taking part in the study is voluntary. You may choose not to enroll yourself in this study. Your decision will not change present or future health care services offered to you at K.L.E.S hospital.

Alternatives:

Even if you decline the participation in the study, you will get the routine line of management.

Privacy and Confidentiality:

The only people to know that you are a research subject are members of the research team. No information about you or information provided by you during the research will be disclosed to other without your written permission except:

1. In emergency to protect your rights and welfare.

2. If required by law.

Authorization to Publish Results:

When the results of the research are published or discussed, in a conference, no information will be displayed that would disclose your identity. Any information that is obtained in connection with this study and that can be identified with you will remain confidential.

Financial Incentives for participation:

No financial incentives are being offered to enrolled patients. It is purely being done with the idea of research and all the cost of the study will be borne by the investigator.

Compensation:

Questions:

If you have any queries about your rights as a study subject, you may call Dr.Ganga Pilli., Prof. & Head of Pathology as Chairman of J. N. Medical College Institutional Ethical Committee of Human Subjects Research, Phone No.0831 2473777 ext-1527 at J. N. Medical College, Belagavi.

CONSENT FOR PARTICIPATION IN RESEARCH TRIAL

I, _____ voluntarily agree for the participation as a subject of study. By signing this consent form I am not giving up any of my legal rights, I may withdraw from the study anytime. I am signing the consent form after having read or been read from in my vernacular language, including the risks and the benefits and having all my questions answered.

Subject Name : _____

Signature or the Left Thumb Print of Subject : _____ Date :

Witness Name : _____ Signature: _____ Date :

Investigators Name: _____Signature: _____ Date :

Place : _____

ANNEXURE-II

PROFORMA

"COMPARISON OF EFFICACY OF LEVOBUPIVACAINE AND LEVOBUPIVACAINE WITH DEXMEDETOMIDINE FOR SUPRACLAVICULAR BRACHIAL PLEXUS BLOCK IN PATIENTS UNDERGOING UPPERLIMB SURGERIES – A ONE YEAR RANDOMISED CONTROLLED TRIAL".

Name& Address of the patient: _____

_____

Age of the Patient:_____ IP. No. _____

Weight of Patient:_____ ***Random No._____***

Anaesthesiologist : _____ ***Surgeon : _____***

PREANAESTHETIC EVALUATION :

Chief Complaints:

Past History:

1. HTN/ DM/Asthma/Drug allergy:
2. Drug therapy:
3. Previous exposure to anaesthesia:

Family History

I. General Physical Examination :

Weight: Temperature:

Pallor/ Icterus/ Cyanosis/Clubbing/ Lymphadenopathy/ Oedema

Pulse : B.P: RR:

M.P Grading

Teeth: Mouth opening:

Jaw examination:

SYSTEMIC EXAMINATION:

Respiratory System:

Cardiovascular System:

Central Nervous system:

Per Abdomen:

Spine assessment:

INVESTIGATIONS:

Complete Blood count: **RBS:** **Serum**

Creatinine: **Urine routine:** **Chest X-ray:**

ECG:

Any others:

Pre-operative physical status: ASA grade **I** **II**

Diagnosis:

Proposed Surgery:

Selection Criteria:

Inclusion

1. Patients undergoing upper limb surgeries.
2. Age: 18 to 60 years.
3. ASA Grade I and Grade II patients

Exclusion

1. Patients who refuse.
2. Patients with history of bleeding disorders.
3. Patients with local infection at the site of block.
4. Patients with documented neuromuscular disorders.
5. Patients with respiratory compromise.
6. Patients with known allergy to local anaesthetic drugs.
7. ASA grade III and IV patients.

Procedure:

After obtaining Institutional review board, ethical committee clearance, informed consent was obtained from the patients who met inclusion and exclusion criteriae, patients will then be randomised based on computer generated randomization table into one of the two groups.

- Group LS: Will receive 39ml of 0.5% Levobupivacaine + 1ml of normal saline
- Group LD: Will receive 39ml of 0.5% Levobupivacaine +1 ml (100mcg) of dexmedetomidine.

Anaesthesiologist involved in the data collection as well as the patient will be blinded to the content of the study solution.

Preoperatively the patient's intravenous (IV) line will be secured with either 18 G or 20 G branula and IV ringer lactate solution is started at 5 ml/kg/hr. The patient then will be shifted to the operation theatre and monitors like electrocardiograph (ECG), pulse oximeter and non-invasive blood pressure will be attached and baseline

reading is taken. The patient will be placed in supine position with upper arm placed by the side of the patient.

Under strict aseptic precautions and preparation of parts, the subclavian artery was palpated and a skin wheal was injected using a 2ml of 2% lignocaine. Neural localization was achieved using a nerve stimulator connected to a 22 gauge, 4 cm long stimulating needle. The position of the needle was found adequate when an output current <0.5 mA elicited a slight distal motor response.

Patients were randomly allocated using a sealed envelope technique to receive either 39ml of levobupivacaine with 1ml of isotonic saline(group LS,n=25) or 39ml of levobupivacaine with 1ml of dexmedetomidine (group LD,n=25) in a double blinded fashion. The drug solutions were prepared by an anaesthesiologist not involved in the study.

Sensory block will be assessed by pinprick test using a 3-point scale in all nerve territories:

0=sharp pin felt

1=dull sensation felt (analgesia)

2=no sensation felt (anaesthesia).

Motor block was assessed by thumb abduction(radial nerve),thumb adduction(ulnar nerve),thumb opposition(median nerve),and flexion at the elbow(musculocutaneous nerve) on a 3-point scale for motor function

0=normal motor function with full flexion and extension of elbow, wrist and fingers

1=reduced motor strength but able to move fingers

2=complete motor blocks with inability to move fingers.

Sensory and motor block was assessed every 3 minutes until 30 minutes after injection,and then every 30 minutes after the surgery,until they had resolved.

Onset time was defined as the time interval between the end of total local anaesthetic administration and complete sensory block.

Complete sensory block=defined by anaesthetic block (score 2) on all nerve territories.

Duration of sensory block=defined as the time interval between the end of local anaesthetic administration and the complete resolution of anaesthesia on all nerves.

Onset of motor block - the time interval between administration of local anesthetic solution to loss of movements.

Complete motor block=absence of voluntary movements in hand and forearm (score 0).

Duration of motor block= defined as the time interval between the end of local anaesthetic administration and the recovery of complete motor function of the hand and forearm.

Heart Rate, Systolic Blood Pressure(SBP),and Diastolic Blood Pressure(DBP) were recorded at 0,5,10,15,30,45,60,90,and 120minutes. Adverse events such as Hypotension will be defined as decrease in systolic B.P by 20% from baseline values. Bradycardia will be defined as decrease in heart rate less than 50 beats per minute and hypoxia defined as SPO_2<90%,or nausea and vomiting.

In the PACU, Pain was assessed using a visual analog scale(0-10). Nursing staff was instructed to administer Inj. diclofenac 75mg in 100 ml NS slow iv when the visual analog scale>4.The time between the end of local anaesthetic administration and the first dose of analgesic request was recorded as the duration of analgesia.

Preoperative baseline values

HR: SBP: DBP:

Monitors attached

Pulse oximetry : NIBP :

ECG:

II. Vital parameters:

Time	**HR**	**SBP**	**DBP**
0 min			
5 min			
10 min			
15 min			
20 min			
25 min			
30 min			
60 min			
90 min			
120 min			

Sensory and motor block onset time,block and analgesia duration in groups

Time(mins)	Group LS	Group LD
Onset time of sensory block(mins)		
Onset time of motor block(mins)		
Duration of sensory block (mins)		
Duration of motor block (mins)		
Duration of analgesia (hours)		

ANNEXURE III – PHOTOGRAPHS

Photograph : 1. Dexmedetomidine ampule

Photograph : 2. Levobupivacaine ampule

Photograph : 3. Brachial plexus block with nerve stimulator

Photograph : 4. Anaesthesia work station