COMPARISON OF TWO DIFFERENT DOSES OF DEXMEDETOMIDINE COMBINED WITH 0.5 % LEVOBUPIVACINE FOR POST OPERATIVE ANALGESIA IN ULTRASOUND GUIDED SUPRACLAVICULAR BRACHIAL PLEXUS BLOCK - A DOUBLE BLINDED RANDOMIZED CONTROLLED STUDY

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ABSTRACT

Dexmedetomidine, a α2 agonist, has been studied widely as an adjuvant to local anaesthetics in regional anaesthesia techniques to enhance the quality and duration of analgesia. This study was carried out to evaluate 50 µg or 100 µg of dexmedetomidine added to 0.5% levobupivacaine, with regard to the duration of analgesia. Our study also sought to assess the onset and duration of sensorimotor blockade, haemodynamic effects, sedation and adverse effects.

Study design: Prospective randomized double blinded randomized controlled study.

Patients and Methods: Study included 56 patients (28 patients in each group, assigned by compute generated randomized code. Group LD 50 will receive 29 ml of 0.5 percent levobupivacaine with 50 µg of dexmedetomidine diluted with normal saline. Group LD 75 will receive 29 ml of 0.5 percent of levobupivacaine with 75 µg of dexmedetomidine diluted with normal saline.

Results: Sensory onset and Motor onset are faster in patients who received dexmedetomidine 75 microgram (LD 75) added to 0.5 % Levobupivacaine. Duration of analgesia was prolonged in patients who received 75 microgram of dexmedetomidine (LD 75).

Conclusion: Prospective randomized trial conducted on 56 patients undergoing upper limb surgeries demonstrated that addition of 75µg dexmedetomidine added to 0.5% levobupivacaine in supraclavicular brachial plexus block produces a longer duration of analgesia than 50 µg of dexmedetomidine.
INTRODUCTION

The international association for the study of pain has defined pain as an unpleasant sensory and emotional experience associated with actual or potential tissue damage.\(^{(1)}\)

The world of regional anaesthesia took a tremendous leap over the past decade, with the introduction of ultrasound in the peripheral nerve block. In recent times there is increased demand for regional anaesthesia from patients and surgeon are mainly due to its superior pain management not only intra operatively but also post operatively. It is increasingly used in upper limb surgeries because of its higher success rate. Brachial plexus is a popular regional nerve block technique for anaesthesia and post-operative analgesia, this technique avoids the unwanted effect of stress of laryngoscopy and intubation\(^{(1)}\).

There are various approaches to the brachial plexus blockade; it depends on various factors like the site of surgery and ability of patient to tolerate the spill over to other nerves. They are supraclavicular approach, interscalene approach, infraclavicular approach, axillary approach. In 1911, Diedrich Kullenkampff performed the first percutaneous supraclavicular approach. Although supraclavicular block first became popular for surgery distal to shoulder, it has recently been used to provide analgesia for shoulder surgery. Block is performed at the level of the trunk where the entire sensory, motor and sympathetic innervations of the upper extremity is carried away in just three nerves where the structures confined to very small surface area.

Levobupivacaine is a relatively new long acting local anesthetic that has been produced to address the issue of cardiovascular and neurological toxicity following inadvertent intravascular injection. It is an amino-amide local anesthetic drug. Levobupivacaine has been found to be equally efficacious as bupivacaine, but with superior pharmacokinetic profile. It is the pure S (-) enantiomer of bupivacaine. It exerts its action by reversible blockade of the neuronal sodium channels.

The low cardiovascular and neurological toxicity has led to its application as local anaesthetic in applications including sub-arachnoid block, epidural anaesthesia, brachial plexus and peripheral nerve blocks, ocular as well as...
local infiltration. In nerve blocks it acts as a good substitute. It provides a longer duration of analgesia compared to ropivacaine\(^{(2)}\).

Since 1978, ultrasound has been widely used in several kinds of regional anesthetic practice. Recently, the improvements in ultrasound technology allow you to place the tip of the needle near the targeted nerve and monitor the spread of the local anesthetics precisely. It provides direct visualization of the best site for the injection and helps avoid accidental puncture of blood vessels and damage to nerves. It also helps in reducing the procedure performance time, monitoring of the spread of the local anesthetics which in turn helps in reducing the volume of the local anesthetics used.

Locus ceruleus is a nucleus located in pons and widely throughout the cortex. It secretes nor epinephrine. It mediates vigilance, memory, analgesia, arousal and sympathetic nervous system function. It has one of the highest densities of \(\alpha_2\) receptors are located in the pontine locus ceruleus. Sedative effect produced is mainly due to the inhibition of these nuclei. By acts by binding to the \(\alpha_2\) receptors in the presynaptic membrane in turn increasing sedation, analgesia, amnesia and decreasing heart rate, cardiac output and circulating catecholamines\(^{(3)}\). It reduces the MAC for volatile anesthetics, attenuates the hemodynamic response produced during intubation. It is also used to provide sedation for mechanical ventilation patients during weaning from the ventilator. An important characteristic of Dexmedetomidine that makes it attractive is “rousable” sedation that produces. In cardiovascular system it produces decreases heart rate and cardiac output; in respiratory system it produces minimal respiratory depression. In recent study it showed evidence of decrease in cerebral blood flow and cerebral metabolic rate. Dexmedetomidine is more potent and specific \(\alpha_2\) adrenergic agonist. It is more selective for \(\alpha_2\) adrenergic receptors compared to clonidine (1600:1) but shorter acting comparatively. It is the dextro-isomer and pharmacologically active component of medetomidine \(^{(4)}\).

**METHODOLOGY**

The study was conducted prospectively in 56 patients of 18 to 50 years of age scheduled to undergo upper limb surgeries at Chettinad Hospital and Research Institute. After obtaining approval from the human ethics committee, this study was conducted in the Department of Anesthesiology at Chettinad Hospital and Research Institute.

A Randomized prospective double blinded study will be conducted in Chettinad hospital and Research institute after approval of Human Institutional Ethics committee. Patients with American Society of Anesthesiologist Grade I and II status, between 16-65 years of either gender, posted for upper limb surgery will be included in the study. Pre-
anesthetic evaluation will be performed before the day of the surgery. The procedure of the block with possible complications will be explained to the patients and written informed consent will be obtained. All patients will be given oral diazepam 5mg and 150 mg of ranitidine on the night before the surgery and will be fasting overnight for 8 hours.

**MONITORING** Heart rate [HR], systolic blood pressure [SBP], diastolic blood pressure [DBP], mean arterial blood pressure [MAP], Peripheral oxygen saturation [Spo2] and 3 lead electrocardiogram will be monitored. Supplemental oxygen will be provided through face mask. Midazolam 1mg and fentanyl 50µg will be administered 15 minutes before the Supraclavicular block.

**RANDOMIZATION** Fifty six patients will be divided randomly into two groups [Group LD 50 and Group LD 75] using a computer generated programme. Assigned random group will be enclosed in a sealed envelope to ensure concealment of allocation sequence. The anesthesiologist who is not involved in the study will open the envelope in the operation theatre and prepare the drug accordingly.

Group LD 50 will receive 29 ml of 0.5 percent levobupivacaine with 50 µg of dexmedetomidine diluted with 1ml of normal saline.

Group LD 75 will receive 29 ml of 0.5 percent of levobupivacaine with 75 µg of dexmedetomidine diluted with 1 ml of normal saline will be given around brachial plexus.

The Supraclavicular block will be performed using a portable ultrasound machine with a linear ultrasound transducer (8-13 MHz). Under all the aseptic precautions with the patient lying in the supine position, the affected arm will be adducted and head will be turned to the contra lateral side, the brachial plexus will be visualized by placing the transducer in the supraclavicular fossa behind the middle third of the clavicle. The plexus either appears as a cluster of grapes (5-6 hypoechoic circles) or as 3 hypoechoic circles with the hyperechoic outer ring, located lateral and superior to subclavian artery between anterior and middle scelene muscles. The drug solution based on the group allocation will be injected after negative aspiration. Distention of the brachial plexus sheath will be considered as an indication of correct needle placement.

Sensory blockade will be assessed by cold cotton swab each minute after completion of block. Block of the median and ulnar nerves will be assessed by testing the palmar surfaces of the index and the little finger and the dorsal surface of the thumb will be used to test the radial nerve. Grading of sensory nerve will be done as following

Grade 0: Normal Sensation to cold cotton swab
Grade 1: Dull sensation to cold cotton swab

Grade 2: No Sensation felt

Motor block will be monitored by thumb adduction (ulnar nerve), thumb abduction (radial nerve), thumb opposition (median nerve) and flexion of elbow and pronation of forearm (musculocutaneous nerve) using a bromage three point score

Data will be collected every 3 min for first 15 min, Next every 5 min interval for next 15 min and after the completion of surgery sensory and motor blockade will be assessed every 30 min till the recovery of the blockade.

Post operative analgesia will be monitored as per a visual analogue scale of 0-10 at every hour till the onset of pain. If the visual analogue score was 3 or more, it will be considered that the analgesic action of block was terminated and Inj. Tramadol 100mg will be given as the rescue analgesia. As dexmedetomidine was used for study Ramsay sedation scale was used.

**STATISTICS**

The clinical data was entered the Excel file and then it was imported into SPSS 20.0 version to do statistical analysis. Normality of the statistical data was verified either by Shapiro-wilk test or by box plot. If the statistical data follows normal distribution, then we can apply parametric statistical test. Unpaired sample t test is the one of the parametric statistical tests which is used to compare two group numerical data if the data follows normal distribution. Mann-whitney U test is used to compare two group data if the data violates to normality assumption.

**DISCUSSION**

Supraclavicular Brachial Plexus block using ultrasound guidance is a ubiquitous, anaesthetic technique of choice for upper limb surgeries, with the added advantage of providing analgesia both intra-operatively, and post-operatively. With a catheter inserted into the trunks of the brachial plexus or by prolonging the duration of analgesia when additives such as dexamethasone, clonidine, dexmedetomidine and magnesium sulphate are used.

Chad M. Brummet performed review on more commonly used additives along with LA to prolong the duration local anaesthetics. He reviewed on epinephrine, dexamethasone, midazolam, magnesium sulphate, clonidine dexmedetomidine. He concluded that dexmedetomidine revealed promising results as compared to clonidine (6).

Significant distinctions were noticed when routinely used local anaesthetics (Bupivacaine) were made use of, for brachial plexus block, as compared to the novel local anaesthetics such as Levobupivacaine and Ropivacaine. The
utilization of Levobupivacaine for administration of a peripheral nerve block prolongs the duration of block as well as mean time to request of first dose of rescue analgesia in the postoperative period.

The current study was a prospective, double blinded randomized control study, conducted at Chettinad Hospital and Research Institute, from May 2018 till September 2019. Patients who underwent elective or emergency upper limb surgeries, classified under ASA-PS 1 & 2 were considered for the study. Parameters that were observed during the study were onset of sensory block, onset of the motor block, hemodynamic changes pre-operatively, intra-operatively & post-operatively, Ramsay sedation score, mean time to request of first rescue analgesia and the occurrence of any associated complications intra-operatively or postoperatively.

56 patients were randomly assigned into two groups, namely Group LD50 and Group LD75. Using a computer generated code. Group LD50 received 29 ml of 0.5 percent Levobupivacaine with 50mcgs of Dexmedetomidine and Group LD75 received 0.5% of Levobupivacaine with 75 mcgs of Dexmedetomidine. Patient characteristics we assessed across both the groups. Patients who were assigned into either group depicted nearly similar demographic parameters such as sex, height and weight. There appeared to be no statistical significance in between the groups on those terms.

Duration of the surgery performed was comparable in both the groups, no statistical significance was observed. The preoperative cardiovascular parameters were noted. Dexmedetomidine used as adjuvant to Levobupivacaine in Supraclavicular Brachial Plexus block is known to cause bradycardia & hypotension, and as such, hemodynamic changes were observed both intra-operatively and post-operatively in terms of decreased heart rate in both the groups.

Patients who received 50 microgram of dexmedetomidine had 5 percent decrease in heart rate after receiving the block, in contrast to patients who received 75 micrograms, whom were observed to have had a 10 percent fall in heart rate, within 15 minutes of receiving the block. Although a decrease in heart rate was noted, the blood pressure in both the groups was stable and hence no intervention was undertaken to increase the heart rate.

In the present study, it was observed that the onset of sensory block was faster in patients who received 0.5% Levobupivacaine with 75 micrograms of Dexmedetomidine(LD75) with a mean value of 10.72±1.05minutes, in comparison to patients who received 0.5% Levobupivacaine with Dexmedetomidine 50 micrograms(LD50) having a mean value of 14.25±1.14 minutes, and this was found to be statistically significant(P-Value 0.001) In the current study, it was observed that the onset of motor block was earlier in patients who had received 0.5% Levobupivacaine
with Dexmedetomidine 50 micrograms (LD50) having a mean value of 15.26±1.517 minutes in comparison with patients who received 0.5% Levobupivacaine with Dexmedetomidine 50 micrograms (LD50) having a mean value of 17.107±1.165, and this was found to be statistically significant (P-value 0.001).

Hamrit Paul Kaur, in his study observed that the addition of 1 microgram per kg Dexmedetomidine to 0.25 percent Levobupivacine in Supraclavicular Brachial Plexus block, decreased the onset time of both sensory and motor block(7).

Aravinder Pal Singh, in his study observed that Dexmedetomidine as an adjuvant to Levobupivacaine shortens the onset time for sensory and motor block and prolongs its duration of action. In a study conducted by Esmagolu et al, it was inferred that Dexmedetomidine added to Levobupivacaine for Axillary Brachial Plexus block shortens the time to onset of sensory and motor block and prolongs the duration of block in the post-operative analgesia(8).

In the present study, the mean duration of the sensory block with patients who received Levobupivacaine with additive dexametomidine (75 micrograms) was calculated as 1181 min±74.35 minutes. Mean duration of sensory block in patients who received Levobupivacaine with 50 micrograms Dexmedetomidine was 887.2±30.989 minutes. It was thereby deduced that the duration of sensory block was longer in patients whom received Dexametomidine 75 micrograms (LD 75) over patients whom received Dexametomidine 50 micrograms (LD50), and the results are statistically significant.

The duration of motor block in patients who received Dexametomidine 75 micrograms along with Levobupivacaine was 1139±70.202 minutes. The duration of motor block in patients whom received Dexametomidine 50 micrograms was 857±35.276 minutes. The results are statistically significant and it was thereby extrapolated that the duration of motor block is longer when a higher dose of Dexametomidine (75 micrograms) is used as an adjuvant over 50 micrograms Dexmedetomidine.

Brummet et al found that dexametomididine enhanced the duration of bupivacaine anaesthesia and analgesia of sciatic nerve block in rats without any evidence of histopathological damage to nerve. The action of the dexametomididine in peripheral nerve acts by increasing the hyperpolarisation there by activate cation currents that prevents nerve from returning to its resting membrane potential(9).

BikashBisui in his study ‘Effect of locally administered Dexametomididine as adjuvant to Levobupivacaine in Supraclavicular Brachial Plexus Block’ observed that addition of 0.75 μg/kg Dexametomididine to 0.5%
Levobupivacaine for Supraclavicular Brachial Plexus Block helps in shortening the time to of sensory and motor block, on the other hand increased the duration of motor block, sensory block and duration of analgesia\(^{(10)}\).

Srinivas Rao Nallam in his study “Comparison of varying doses of Dexmedetomidine combined with Levobupivacaine in Supraclavicular Brachial Plexus Block” observed that 100 micrograms Dexmedetomidine added to Levobupivacaine in Brachial Plexus Block produces a longer duration of analgesia than 50 micrograms of Dexmedetomidine added to Levobupivacaine\(^{(11)}\).

Bikash Bisui, in his study concluded that addition of Dexmedetomidine to 0.5 percent Levobupivacaine for Supraclavicular Brachial Plexus Block helps in increasing the duration of analgesia.

The results of the current study were found to be congruent with the aforementioned observations, and hence it was concluded that 75 micrograms of Dexmedetomidine added to 0.5% Levobupivacaine prolongs the duration of analgesia when compared to 50 micrograms of Dexmedetomidine, for Supraclavicular Brachial Plexus Block. No significant side effects was observed in the study We conclude that the side effects were negligible in the study as ultrasound was used for injection of the drug, and hence there was no incidence of intravascular injection or pneumothorax.

**CONCLUSION**

From this prospective, double blinded randomized control study; which evaluated the effectiveness of Dexmedetomidine 75 micrograms and Dexmedetomidine 50 micrograms as an adjuvant to the local anaesthetic 0.5% Levobupivacaine in providing post-operative analgesia to patients whom underwent upper limb surgeries under Supraclavicular Brachial Plexus Block; the following were observed:

- There was a 10 percent decrease in heart rate in patients whom received Dexmedetomidine 75 micrograms with 0.5% Levobupivacaine in Supraclavicular Brachial Plexus Block, whereas, a 5 percent decrease in heart rate of patients whom received 50 micrograms of Dexmedetomidine with 0.5% Levobupivacaine was observed. None of the patients received any treatment for the decreased heart rate observed as the blood pressure was stable in all the patients.

- Demographic profile such as age, sex, BMI, ASA status are comparable in both groups Sensory block occurs earlier on, in patients whom received Dexmedetomidine 75 micrograms as adjuvant to 0.5% Levobupivacaine (LD75 group) than patients whom received Dexmedetomidine 50 micrograms with 0.5% Levobupivacaine (LD50 group) in Supraclavicular Brachial Plexus Block.
Motor block occurs earlier on, in patients whom received Dexmedetomidine 75 micrograms as adjuvant to 0.5% Levobupivacaine (LD75 group) than patients whom received Dexmedetomidine 50 micrograms with 0.5 % Levobupivacaine (LD50 group) in Supraclavicular Brachial Plexus Block.

The quality of anaesthesia, duration of surgery and complications were comparable in both the groups.

The duration of sensory block was found to be longer in patients who received Dexmedetomidine 75 micrograms with 0.5% Levobupivacaine than in patients whom received Dexmedetomidine 50 micrograms with 0.5 % Levobupivacaine in Supraclavicular Brachial Plexus Block.

The duration of motor block was prolonged in patients whom received Dexmedetomidine 75 micrograms with 0.5% Levobupivacaine than in patients whom received Dexmedetomidine 50 micrograms with 0.5 % Levobupivacaine in Supraclavicular Brachial Plexus Block.

The duration of analgesia was prolonged in patients whom received Dexmedetomidine 75 micrograms with 0.5% Levobupivacaine than in patients whom received Dexmedetomidine 50 micrograms with 0.5 % Levobupivacaine in Supraclavicular Brachial Plexus Block.

From the current study, it was deduced that the addition of Dexmedetomidine 75 micrograms to 0.5% Levobupivacaine hastens the onset of sensory blockade, as well as motor blockade, and prolongs the duration of sensory blockade and motor blockade, thereby decreasing the demand for further analgesia in the post-operative period significantly.

REFERENCES


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