ORIGINAL ARTICLE

DEXMEDETOMIDINE AN ADJUVANT TO LEVOBUPIVACAINE IN SUPRACLAVICULAR BRACHIAL PLEXUS BLOCK: A RANDOMIZED DOUBLE BLIND PROSPECTIVE STUDY

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ABSTRACT

BACKGROUND: Apha-2 agonists are combined with local anesthetics to extend the duration of regional anesthesia. We evaluated the effect of combining dexmedetomidine with levobupivacine with respect to duration of motor and sensory block and duration of analgesia.
METHODS: Sixty patients scheduled for elective forearm and hand surgery were divided into two equal groups in a randomized double blind fashion. The patients received brachial plexus block via supraclavicular route with the help of nerve stimulator. In group L (n=30) 35cc of levobupivacaine with 1ml of isotonic saline and in group LD (n=30) 35cc of levobupivacine with 1 ml of (100 microgram) of dexmedetomidine was given. Duration of motor and sensory block and time to first rescue analgesia were recorded. Data analysis was done by SPSS version 16.0 [SPSS Inc ILLINOIS, USA, 2008]. Categorical variables were analyzed using Pearson"s Chi-square test. Normally distributed numerical variables were analyzed using unpaired "t" test. Skewed numerical variables within the group were analyzed using Man-Whitney "U" test. All tests were two tailed. Statistical significance was defined as P<0.05.
RESULTS: Sensory and motor block durations were longer in group LD as compared to L (P<0.01). Duration of analgesia was significantly longer in group LD as compared to group L (p<0.05).
CONCLUSION: Dexmedetomidine added to levobupivacaine in supraclavicular brachial plexus block prolongs the duration of block and the duration of postoperative analgesia.
KEYWORDS: Dexmedetomidine, levobupivacaine, supraclavicular block

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INTRODUCTION

Upper limb surgeries are preferably done under regional anesthesia. Peripheral nerve blocks not only provide for intra operative anesthesia but also ensure analgesia in the post operative period without any systemic side effects (1). Levobupivacaine, a new local anesthetic having, similar pharmacological profile, but was shown to posses less cardiotoxicity when compared to Bupivacaine (2).

There has always been a search for ideal adjuvants in peripheral nerve blocks which prolong the duration of analgesia with lesser adverse effects. Although the search continues we decided to use the new α2 adrenergic agonist, dexmedetomidine which is 8(eight) times more selective towards α2 adrenoreceptors compared to clonidine (3).Clinical studies have shown opoid sparing effects of dexmedetomidine when used intravenously along with decrease in inhalational anesthetic requirement (4). It has also been reported to improve quality of intrathecal and epidural anesthesia (5, 6). However, very few clinical trials have studied the effect of dexmedetomidine in supraclavicular brachial plexus block.

We decided to investigate the effects of adding dexmedetomidine to levobupivacine in supraclavicular brachial plexus block. Our primary

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aim was to study the duration of motor and sensory blocks as well as time required to first rescue analgesia following surgery.

METHODS

Institutional ethics committee approval was obtained. Seventy (70) American Society of Anesthesiologist (ASA) physical status patients scheduled for elective orthopaedic surgery of forearm and hand were enrolled in a prospective double blind controlled trial after obtaining written informed consent from the patients. After those who failed to satisfy the selection criteria were excluded the remaining patients were allocated into two groups of thirty patients (*n*=30) each using computer generated random number table in a double blinded manner into two groups L and LD to receive 35 cc of levobupivacaine (Levoanawin, Neon Laboratories, Mumbai)0.5% with 1 ml of isotonic normal saline and 35 cc of levobupivacaine(Levoanawin, Neon Laboratories, Mumbai)0.5% with 1 ml (100microgram[µg]) of demedetomidine (Dextomid Neon Laboratories, Mumbai) respectively.

Blinding was ensured in the following manner:

- The patients were unaware of the study drug administered.
- A different anesthesiologist not involved in the post operative monitoring performed the brachial plexus block and was unaware of group allocation and drug being administered.
- The statistician who analyzed the results was unaware of group allocation and aim of the study
- The local anesthetic solution was prepared by the hospital central pharmacy in coded transparent syringes labeled with the patients study number. In the case of emergency related or possibly related to the study or study drugs, the pharmacist was authorized to disclose the contents of the syringe to staff anesthetist. The study blinding was broken after the statistical analysis.

Patients on adrenoreceptor agonist or antagonist therapy; history of bleeding disorders; history of cardiac, respiratory, renal failure; and pregnant women were excluded from the study.

On arrival of the patients in the operation room baseline heart rate, blood pressure, and oxygen saturation were recorded. An intravenous line with a 18-gauge (G) intravenous (iv) cannula was secured in the unaffected limb and Ringer's Lactate infusion was stared. All patients received brachial plexus block through the supraclavicular route by an experienced anesthesiologist. Neural localization was achieved by a nerve locator (Fisher and Paykel, New Zeland) connected to a 22 G, 50-mm-long stimulating needle (Stimuplex, Braun, Germany). The location end point was a distal motor response with an output lower than 0.5 mA (miliampers) in the median nerve region. Following negative aspiration the local anesthetic solution in the labeled coded syringe was injected.

Sensory block was assessed by pin prick method. Sensory onset was considered when there was dull sensation to pin prick along the distribution of any two of the three nerves (median nerve, radial nerve, ulnar nerve, musculocutenous nerve). Complete sensory block was considered when there was complete loss of sensation to pin prick. Sensory block was graded as:

- Grade 0: Sharp pin felt
- Grade 1: Analgesia, dull sensation felt
- Grade 2: Anesthesia, no sensation felt

Motor block assessment was done according to modified Bromage scale for upper extremities on a three point scale:

- Grade 0: normal motor function with full flexion and extension of elbow, wrist and fingers.
- Grade 1: decreased motor strength with ability to move fingers only.
- Grade 2: complete motor block with inability to move fingers.

Sensory and motor blocks were evaluated every 3 minutes until 30 minutes after injection, and then every 30 minute until they have resolved. Complete sensory block was defined by anesthetic block (Grade 2) on all nerve territories. Duration of sensory block was defined as time interval between the end of administration of local anesthetic and complete resolution of anesthesia on all nerves. Complete motor block was defined as absence of voluntary movement on fingers (Grade 2). Duration of motor block was defined as the time interval between the end of local

anesthetic administration and the recovery of complete motor function of the hand and forearm. Patients were monitored for Heart Rate(HR), systolic arterial blood pressure(SBP), diastolic arterial blood pressure(DBP), Arterial oxygen saturation(SpO_2) at an interval of 5 minutes intra operatively and every 15 minutes post operatively.

Pain was assessed using the Visual Analog Scale (VAS) (0-10). Nursing staff administered IV Supridol (tramadol, Neon Laboratories, Mumbai) 100 mg when the VAS >4. The time between the end of local anesthetic administration and the first analgesic request was noted as the duration of analgesia.

All raw data were analyzed by SPSS (statistical package for social sciences) version 16.0 (SPSS inc ILLINOIS, USA, 2008). Categorical variables were analyzed using Pearson's Chi square test. Normally distributed numerical variables were analyzed using unpaired "t" test. Skewed numerical variables within the group were analyzed using Man-Whitney "U" test. All tests were two tailed. Significance was defined as P<0.05.

RESULTS

Seventy (70) patients posted for upper limb surgeries were assessed for suitability to enroll in the study. 7(seven) patients declined to participate in the study. 3 patients were excluded as they were found to be on anticoagulation drugs. The remaining 60 patients fulfilling the inclusion criteria were randomly assigned to the two study groups.

Both groups were comparable in terms of age, height and weight (2-tailed independent sample "t" test) and sex distribution (Chi-square test). The surgical characteristics were also similar in both the groups in the Chi-square test (Table 1).

Table1: Demographic characteristics of the two study groups

Variable	Group-L (n=30) X±SD	Group-LD (n=30) X±SD
Age(Years)	32.56± 10.06	30.34±12.98
Height(Cm)	170.34±10.08	167.45±11.08
Weight(Kg)	70.34 ±12.30	71.36±9.38
Type of Surgery(Bone/Soft Tissue)	12/18	15/15

The baseline haemodynamic parameters were comparable in both groups. SBP levels in group LD at 15, 60, 90, 120 minutes were significantly lower than in group L (P<0.05)(Mann-Whiteny U test) as shown in Fig 1. DBP levels in group LD at 60, 90, 120 minutes were significantly lower than those in group L (p<0.05) (Fig-2). HR levels in group LD, except basal measurements were significantly lower than in group L (P<0.05) (Fig-3).

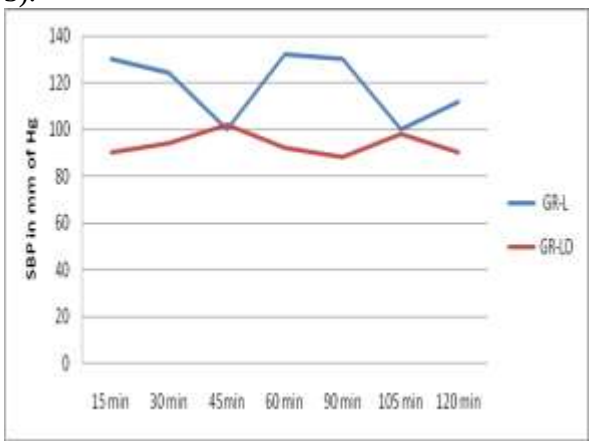

Fig. 1: *Systolic blood pressure (SBP) between the groups (GR-L = group receiving levobupivcaine, GR-LD= group receiving levobupivacaine and dexmedetomidine). Significant difference at 15, 30, 90 and 120 minutes intraoperative*

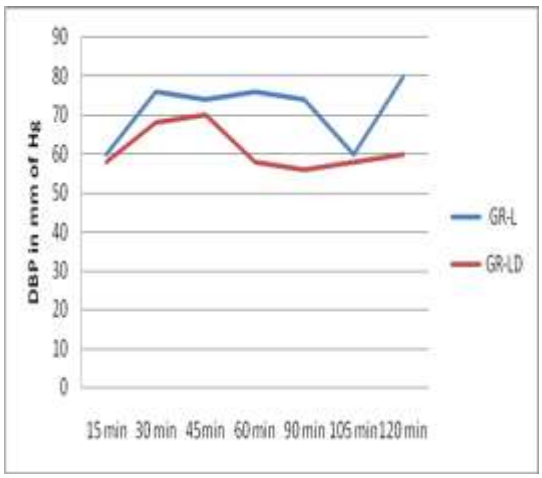

Fig. 2*: Diastolic blood pressure at 60, 90 and 120 minutes showed significant statistical difference between the two study groups. L=levobupivacaine; LD=levobupivacaine & dexmedetomidine DBP=Diastolic blood pressure*

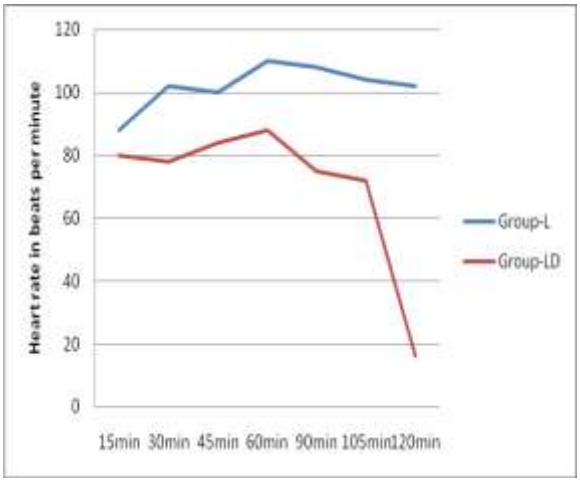

Fig. 3*: Excluding basal heart rate the heart rate in group-LD was significantly lower than group-L L---Levobupivacine LD----Levobupivacine & Dexmeditomidine.*

Sensory and motor blockade duration were longer in group LD than group L (P<0.01) (Mann-Whiteny U test). Duration of analgesia was significantly longer in group LD (997±154.23minutes) than in group L (801.13±200.08minutes) (P<0.05) (Mann-Whiteny U test) as can be seen in Table-2. No side effects-including nausea, vomiting, hypotension, and hypoxemia—were reported in either group.

Table 2: Duration of sensory and motor block, duration of postoperative analgesia in the two study groups

	Group L (n=30) (X±SD)	Group-LD (n=30) (X±SD)
Duration of motor block (minutes)	512± 60.13	840±50.23
Duration of sensory block (minutes)	645± 70.11	898±32.33
Duration of analgesia(minutes)	801.13±200.08	997±154.23

DISCUSSION

In this study we demonstrated that in patients undergoing supraclavicular brachial plexus block addition of dexmedetomidine to levobupivacaine prolongs the duration of sensory and motor blockade as well as time to rescue analgesia. The mechanism by which α2 adrenergic receptor agonists produce analgesia and sedation is not fully understood but is likely to be multifactorial. Peripherally, α2agonists produce analgesia by reducing release of norepinephrine and causing α2 receptor-independent inhibitory effects on nerve fiber action potentials. Centrally, α2 agonists produce analgesia and sedation by inhibiting substance P release in the nociceptive pathway at the level of the dorsal root neuron and by activating α2 adrenoceptors in the locus coeruleus (7, 8).

A study by ***Brumett et al (9)*** showed that dexmedetomidine enhances duration of bupivacaine anaesthesia and analgesia of sciatic nerve block in rats without any damage to nerve. Histopathological evaluation of the nerve axon and myelin were normal in both groups were normal at 24 hours and 14 days. In another study by same authors perineural demedetomidine added to ropivacaine for siatic nerve block in rats prolonged the duration of analgesia by blocking the hyperpolarization –activated cationic channel (10). This shows peripheral action of dexmedetomidine was caused by activation of hyperpolarization activated cation current which prevents the nerve from returning from hyperpolarized state to resting membrane potential for subsequent firing. ***Kousugi et al*** in their study found high concentrations of dexmedetomidine inhibit compound action potentials in frog siatic nerves without α2 adrenorecptors activation in a concentration dependent manner and reversibly (11).

The efficacy of perineural dexmedetomidine for analgesia has been established. This effect is dose dependent and the effect is peripheral (not caused by centrally mediated or systemic analgesia).

However all studies carried out so far to peripheral action of α2 agonists were animal studies. Very few human trials have been conducted. Several studies have found dexmedetomidine to be safe and effective in various neuraxial and regional anesthesia techniques including intrathecal and I.V. regional anesthesia (5,12,13). A dexmedetomidine – lidocaine mixture has been used to provide Bier"s block and was shown to improve the quality of anesthesia and tourniquet pain and reduce postoperative analgesic requirement (12,13). Keeping these facts in mind we decided to compare the effects of addition of

dexmedetomidine with levobupivacaine in peripheral nerve block.

Some studies have shown that addition of clonidine to local anesthetics in brachial plexus block have extended the duration of anesthesia and increased the quality of analgesia, (14) but ***Erlacher et al*** failed to find any advantage of addition of clonidine 100µ to 0.75% 40ml of ropivacaine . They concluded that ropivacaine itself having vasoconstrictor properties adding α2 adrenergic agonist did not increase the effect (15).

Motor and sensory block was significantly prolonged on addition of dexmedetomidine which provided for better patient compliance in the postoperative period. ***Swami et al*** in their study showed significant increase in duration of analgesia on addition of dexmedetomidine to bupivacine 0.25% in brachial plexus block (16). We were concerned with minimal patient discomfort in the postoperative period due to prolongation of motor block.

None of the patients in group LD required any sedation which can be explained on the basis of some amount of systemic absorption of the drug (17). As α2 agonists produce sedation by central action by inhibition of substance P release in the nociceptive pathway at the level of dorsal root neuron and by activation of α2 adrenoreceptors in locus coeruleus.

We were unable to use ultrasound guided blocks due to its unavailability in our institution at the time of our study which could have helped us to lower doses and volume of local anesthetic. Although clonidine still continues to be used widely as compared with dexmedtomidine probably due to its lower cost but we would like to suggest this new α2 receptor agonist as a better alternative. We admit that further trials are necessary to determine the cost effectiveness of the drug. To conclude 100µg of dexmedetomidine when added to levobupivacine 0.5% in supraclavicular brachial plexus block prolongs the duration of motor and sensory block and extends the analgesia period.

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