



A comparative study of ropivacaine alone *versus* ropivacaine with dexmedetomidine in supraclavicular brachial plexus block: A randomized double blind controlled study

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Abstract

Background and Aims: Supraclavicular brachial plexus block is frequently used procedure to provide anaesthesia and good post-operative analgesia for surgery on upper limb. The purpose of this study was to compare the, sedative and analgesic effects of ropivacaine alone *versus* ropivacaine given along with dexmedetomidine.

Materials and Methodology: This prospective, randomized and double-blinded study included total 60 patients of either sex with age between 18-60 years posted for various elective upper limb surgery and randomly allocated into 2 equal groups of 30 each. Control Group-R received injection ropivacaine (0.75%) 30 ml plus 1 ml normal saline and Group-RD received injection ropivacaine (0.75%) 30 ml plus dexmedetomidine 25 µg (1 ml) for supraclavicular brachial plexus block using the peripheral nerve stimulator. Sensory and motor block evaluated with different time unsets.

Results: There was no significant difference in the study groups with regards to demographic profile and duration of surgery. The onset of sensory and motor blockade was faster in Group-RD than Group-R. {Onset of sensory block: (Group-R=12.90±4.029 min and Group-RD=9.30± 5.861 min) ($p<0.001$), Onset of motor block: (Group-R=22.80±5.359 min and Group-RD=15.37±6.525 min) ($p<0.001$). Also total duration of sensory blockade {Group-R=393.70±88.318 mins, Group-RD=624.60±197.77 mins (p value<0.001)}, motor blockade {Group-R=339.40±78.16 mins, Group-RD=539.90±213.05 mins ($p <0.000$)}. All the results showed significant difference in both the groups.

Conclusion: Dexmedetomidine in a dose of 25 µg added to ropivacaine in supraclavicular brachial block for upper limb surgery significantly shortens the onset time and prolongs the duration of sensory and motor block without producing sedation in patients.

Keywords: ropivacaine, dexmedetomidine, adjuvant, supraclavicular brachial plexus block

Introduction

Supraclavicular brachial plexus block via Winnie's approach is a very popular mode of anaesthesia for various upper limb surgeries. This approach is attractive due to its effectiveness in terms of cost and performance, margin of safety along with good postoperative analgesia.

Supraclavicular route for brachial plexus block was first introduced by kullenkampff in 1911 which was later modified as Winnie block. The brachial plexus are blocked at the level of distal trunk and proximal division where they are compact in structure so just 30ml volume of local anaesthetic solution is adequate in an adult person. It achieves ideal operating conditions for forearm surgeries [1].

Various local anesthetics have been used to provide brachial plexus block. Ropivacaine, a long-acting amide local anaesthetic related structurally to bupivacaine, has been used for supraclavicular block in upper limb surgery. It provides pain relief with less motor blockade and is less cardiotoxic than bupivacaine, which makes it a more suitable agent for supraclavicular brachial plexus block.

Dexmedetomidine belongs to imidazole subclass of α_2 agonists [1]. Drug which has $\alpha_2:\alpha_1$ selectivity of 1600:1 which is 8 times that of clonidine. It has central action of sedation, hypnosis and analgesia by acting on locus caeruleus of brain stem. Several hypothesized mechanisms of action have been

suggested to explain the analgesic effect of α_2 -adrenoceptor agonists. Some of these include vasoconstriction around the injection site, direct suppression of impulse propagation through neurons as a result of a complex interaction with axonal ion channels or receptors, local release of enkephalin-like substances a decrease in localized inflammatory mediators and an increase in anti-inflammatory cytokines through a α_2 -adrenoceptor-mediated mechanism [2]. It also has supra spinal analgesic action via noradrenergic neurons by hyperpolarisation. It inhibits norepinephrine release in descending medullospinal tract.

The purpose of this study is to compare the hemodynamic, sedative, and analgesic effects of ropivacaine alone *versus* ropivacaine given along with dexmedetomidine. The present study was carried out on patients undergoing elective upper limb surgery during the period from December 2015 to June 2017. For a period of 18 months.

The study was carried out to compare sensory and motor effects of ropivacaine alone and ropivacaine along with dexmedetomidine in supraclavicular brachial block in upper limb surgery. Institutional Ethics Committee (IEC) approval was obtained. It was prospective, randomized and double-blinded study. The study included total 60 patients belonging to ASA grade I, II & III of either sex with age between 18-60 years posted for various elective upper limb surgery. After

observing results of various similar studies, it was considered that a clinically significant benefit of using dexmedetomidine would be a prolongation in sensory block duration of 15% (minimum) compared with the control group.

Material and Methods

Source of data

60 patients admitted to Shadan Institute of Medical Sciences, satisfying the inclusion and exclusion criteria undergoing elective upper limb surgery were included in the study, after obtaining the ethical committee clearance.

Sample size

Sample size calculation was done based on a pilot study in which the duration of sensory blockade in Group R (control group) and Group RD (study group) was 338.0 ± 25.167 and 480.50 ± 111.229 minutes respectively and duration of motor block in Group R and Group RD was 301.05 ± 23.633 and 420.0 ± 103.667 minutes respectively and duration of analgesia in Group R and Group RD was 349.0 ± 36.463 and 566.0 ± 84.520 minutes respectively. It was estimated that a minimum of 26 patients in each group would be required to have a 92% power to detect a significant difference in the duration with 95% confidence interval. Taking into considerations any dropouts we had taken 30 patients in each group for the study

Statistical analysis

Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are presented as Mean \pm SD and results on categorical measurements are presented in Number (%).

1. Proportions were compared using Chi-squares test of significance.
2. The student 't' test was used to determine whether there was a statistical difference between study groups in the parameters measured.

In the above tests the "p" value of less than 0.05 was accepted as indicating statistical significance. Data analysis was carried out using statistical package for social science (SPSS) and Microsoft word and Excel have been used to generate graphs, tables etc.

Duration of study

The study was conducted from December 2015 to June 2017.

Type of Study

A prospective randomized double blind study was conducted in patients of either sex requiring elective upper limb surgeries after obtaining an informed consent.

Inclusion criteria

1. Age : 18-70 years
2. American society of anesthesiologists (ASA) physical status I – III.
3. Elective upper limb surgeries.

Exclusion Criteria

1. Patient refusal for procedure

2. ASA IV and V
3. Any bleeding disorder or patient on anticoagulants
4. Severe respiratory disease
5. Neurological deficits involving brachial plexus
6. Patients with allergy to local anesthetics
7. Local infection at the injection site
8. Patients on any sedatives or antipsychotics
9. Body mass index (BMI)>35.
10. Cardiac arrhythmias
11. Advanced heart block and/or severe ventricular dysfunction
12. Those on other vasodilators or negative chronotropic agents
13. Altered sensorium and/or CNS disorders
14. Pregnant and nursing women

60 patients scheduled for elective upper limb surgery were randomized and divided into two equal groups in a double blind fashion.

Group R (Control): Patients in this group (n=30) received 30 millilitres (mL) of 0.5% Ropivacaine + 1mL saline.

Group RD (cases): Patients in this group (n=30) received 30 mL of 0.5% Ropivacaine + 1 microgram (μ g)/kilogram (kg) Dexmedetomidine reconstituted to 1ml.

Drug solution used and dosage

1. Ropivacaine 0.75% ampoule was used. 20ml of this was diluted to 30ml with 10ml of 0.9% normal saline to make it 0.5%. Ropivacaine was used in a dose not exceeding 3mg/kg.
2. Dexmedetomidine (100 μ g/mL : 1mL) was used. Dose of 1 μ g/kg taken by 1mL tuberculin syringe and reconstituted to 1ml was then added to the ropivacaine solution. Drug solutions were prepared by an independent Anesthesiologist not involved in the study.

Instruments

A set containing following was used:

1. Insulated stimulator needle: Stimuplex® A 22G 50mm (B Braun, Germany).
2. Peripheral nerve stimulator: SenStim® MedilogiX.
3. ECG electrode.
4. Two 20 ml syringes
5. One tuberculin syringe
6. Sterilize gauze pieces, one sterile gauze holding forceps, sterile bowl for povidone iodine and one sterile drape.

Technique of supraclavicular brachial plexus block

All the patients received premedication with 150 mg of ranitidine and 8 mg of ondansetron orally on the morning of surgery. An intravenous access was obtained on the opposite limb and an intravenous drip was started before undertaking the procedure which continued throughout the length of the surgery. Baseline parameters noted. Continuous Vital parameters were observed and documented from the Philips VM8 monitor throughout the procedure and oxygen was administered at a rate of 5L/min through an oxygen mask. Intraoperative sedation was maintained with intravenous

midazolam 1 mg, given prior to starting the procedure.

1. The supraclavicular brachial plexus block was performed by the classical approach using a single-injection, nerve-stimulator technique. The patient was kept in the supine position without a pillow, arms at his/her sides adducted and head turned to side opposite to the one being blocked. The patient was asked to flex the elbow and rest the forearm on the abdomen. The wrist was supinated so the palm of the hand faced the patients face.
2. Part of the neck was aseptically cleaned and draped.
3. The lateral (posterior) border of the sternocleidomastoid muscle (SCM) was identified and followed distally to the point where it met the clavicle. The point of needle entrance was about 1 inch (2.5 cm) lateral to the insertion of the SCM to the clavicle or one "thumb breadth" lateral to the SCM and 2 cm posterior to the midpoint of the clavicle. Palpation of the subclavian artery at this site confirms the landmark. The palpating index finger was placed at this site.
4. Local infiltration of 1ml of 1% lignocaine was given at the proposed puncture site
5. A stimplex ® A 22G 50mm insulated needle was used to perform this technique. The needle was connected to peripheral nerve stimulator (PNS) by the electrode and was properly grounded with the help of an ECG lead. The electrical stimulation was started with an intensity of 2.0mA and a pulse width of 100s. Once the desired response was obtained-that is a muscle twitch of the fingers that is clearly visible – the current strength was reduced in increments of 0.2mA gradually to 0.6mA. If the desired response persisted at 0.6mA the drug solution was injected. If the response as obtained at 0.4mA also, then the needle was repositioned to get a response at 0.6mA but not at 0.4mA
6. If there was no adequate response, the needle was moved anteriorly or posteriorly along the first rib to elicit a response.
7. Following the injection, the area was massaged to help the solution to track along the plexus.
8. During the conduct of the block and thereafter, the patient was observed vigilantly for any complications of the block and for the toxicity of the drugs injected

Prevention of deleterious effects

Following precautions were taken during conduct of the block

1. Repeated aspiration before and after every 3-5ml injection to prevent intravascular injection.
2. Injection would be stopped if early signs of toxicity appeared.

The following parameters were studied

Onset and duration of sensory block

Sensory block was assessed by pinprick test using the blunt end of a 26-gauge needle at each minute after completion of drug injection in the dermatomal areas corresponding to median nerve, ulnar nerve, radial nerve and musculocutaneous nerve till complete blockade.

Sensory block was assessed by a 3-point scale

1. Normal sensation
2. loss of sensation of pinprick (analgesia)
3. Loss of sensation of touch (anesthesia).

Onset time was defined as the time interval between the end of total local anesthetic administration and complete sensory block (score 2). Duration of sensory block was defined as the time interval between the end of local anesthetic administration and the complete resolution of anesthesia (score 0).

Onset and duration of motor block

Motor blockade was assessed by Modified Bromage Scale [9,10].

1. Normal motor function.
2. Ability to move only fingers.
3. Complete motor block with inability to move elbow, wrist and finger.

Motor block onset time was defined as the time interval between the end of total local anaesthetic administration and complete motor block (MBS score 2). Duration of motor block was defined as the time interval from the onset to the recovery of complete motor function (MBS score 0).

Other variables that were recorded are

1. Age
2. Gender
3. Weight
4. Height
5. Body mass index (BMI).
6. Coexisting diseases
7. ASA status
8. Medications patient is receiving
9. Type of surgery
10. Duration of surgery
11. Post-operative infection
12. Adverse Perioperative event

The above assessments were made by the principal investigator who was blinded to the drugs used in the study.

Results

This study was carried out on a total number of 60 patients operated under Supraclavicular brachial plexus block. Demographic data, Block data comprising Onset time and duration of sensory and motor blockade and duration of analgesia, VAS scores, modified bromage score, postoperative analgesia and side effects were compared between Ropivacaine and normal saline group (Group R) Vs Ropivacaine and Dexmedetomidine group (Group RD).

Demographic data

There was no significant difference in the patient characteristics including age, gender, height, weight, body mass index, ASA grade, type of surgery and duration of surgery as summarized in Table 1.

Table 1: Comparison of demographic variables

Parameters	Group R (Mean ± SD)	Group RD (Mean ± SD)	P value
Age (years)	39.1 ± 14.4	39.67 ± 15.24	0.933
Gender (Male / Female)	18/12	18/12	1.000
Weight (kg)	62.133 ± 7.491	63.80 ± 10.791	0.296
Height (m)	1.62 ± 0.073	1.64 ± 0.081	0.240
BMI (kg/m ²)	23.481 ± 2.743	23.72 ± 3.966	0.629
ASA Grade (I/II/III)	15/2/13	15/5/10	0.432
Type of surgery orthopaedic/plastic	24/6	25/5	0.766
Duration of surgery	98.67 ± 38.213	92.00 ± 38.341	0.354

Block data

Comparison of mean time of onset of sensory block (mins) between the study groups:

Table 2: Comparison of mean time of onset of sensory block between the groups

Mean time of onset of sensory block (mins)	Group R (Mean ± SD)	Group RD (Mean ± SD)	p value	Remark
	12.90 ± 4.029	9.30 ± 5.861	0.009	Significant

The chart below compares the time taken for onset of sensory blockade in the two groups. Onset of blockade was faster in Group RD (9.30±5.861) compared to Group R (12.90±4.029) mins: this difference was statistically significant (p=0.009).

Comparison of Mean Onset time of sensory block (min) between the study groups

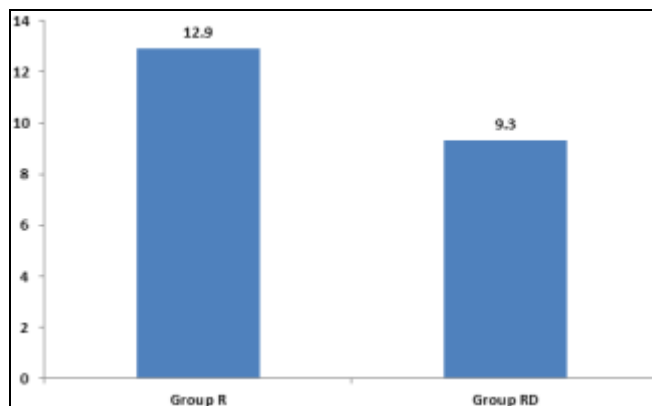


Fig 1: Showing the mean time of onset of sensory block between the groups

Comparison of mean time of onset of motor block (mins) between the study groups

Table 3: Comparison of the mean time of onset of motor block between the groups

Mean time of onset of motor block (mins)	Group R (Mean ± SD)	Group RD (Mean ± SD)	p value	Remark
	22.80 ± 5.359	15.37 ± 6.525	<0.001	Significant

The chart below compares the time taken for onset of motor

blockade in the two groups. Onset of blockade was faster in Group RD (15.37 ± 6.525 mins) compared to Group R (22.80 ± 5.359): this difference was statistically significant (p<0.001).

Comparison of Mean Onset of Motor Block (Min) between the study groups

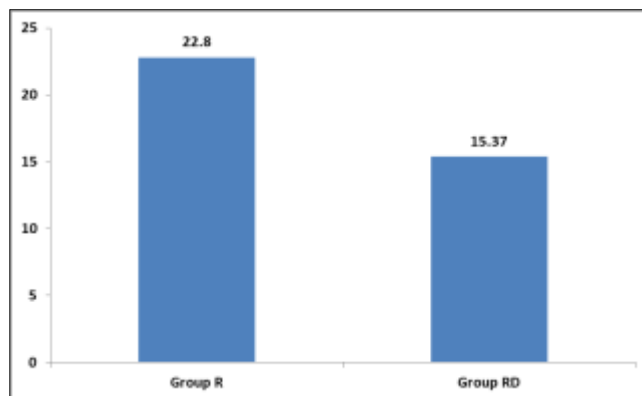


Fig 2: showing the mean time of onset of motor block between the groups

Comparison of mean duration of sensory block between the groups

Table 4: Comparison of the mean duration of sensory block between the groups

Mean duration of sensory block (mins)	Group R (Mean ± SD)	Group RD (Mean ± SD)	p value	Remark
	393.70 ± 88.318	624.60 ± 197.779	<0.001	Significant

The chart below compares the mean duration of sensory blockade in the two groups. Duration of sensory blockade was prolonged in Group RD (624.60 ± 197.779) compared to Group R (393.70 ± 88.318): this difference was statistically significant (p<0.001).

Comparison of Mean Duration of Sensory Block between the study groups

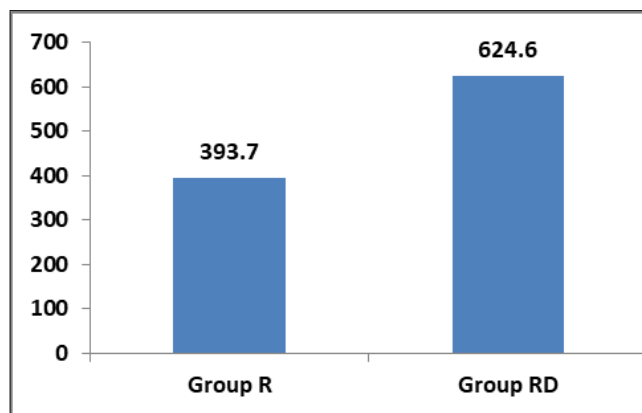


Fig 3: Bar diagram showing the mean duration of sensory block between the groups

Comparison of mean duration of motor block between the groups

Table 5: Comparison of the mean duration of motor block between the groups

Mean duration motor block (mins)	Group R (Mean \pm SD)	Group RD (Mean \pm SD)	P value	Remark
	339.40 \pm 78.166	539.90 \pm 213.05	<0.001	Significant

The chart below compares the mean duration of motor blockade between the two groups. Duration of motor blockade was prolonged in Group RD (539.90 \pm 213.05) compared to Group R (339.40 \pm 78.166): this difference was statistically significant. ($p < 0.001$)

Comparison of Mean Duration of Motor Block between the Study Groups

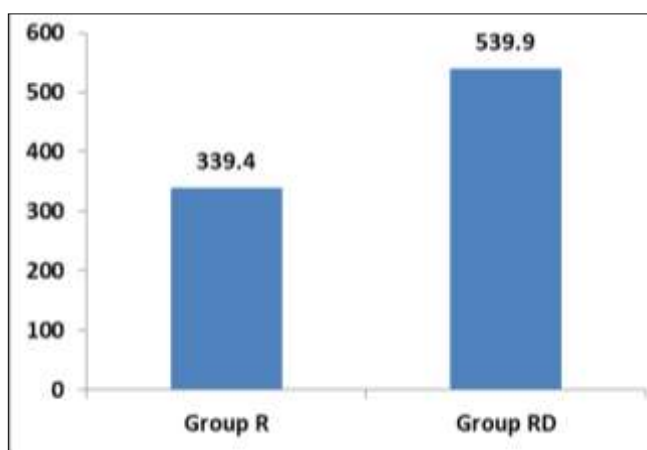


Fig 4: showing the mean duration of motor block between the groups

Discussion

Although general anesthesia continues to be used for most of the surgical procedures, regional anesthesia has been increasing in popularity in recent years. This is mainly because of the fact that the regional anesthesia techniques can be utilized for analgesia not only during the operative period, but during the postoperative period as well and avoids complications of general anesthesia.

The brachial plexus block consists of injecting local anesthetic drugs in the fascial spaces surrounding the nerve plexus, thereby blocking the autonomic, sensory and motor fibres supplying the upper extremity. It is a simple, safe and effective technique of anesthesia having distinct advantages over general anesthesia. A regional technique should always be considered whenever general condition of the patient is poor, or the patient is not adequately prepared or in the presence of associated condition like uncontrolled diabetes, cardiovascular or respiratory diseases. It is also useful when the patient prefers to retain his consciousness during surgery and when it is important for the patient to remain ambulant early.

Here we have selected supraclavicular approach to brachial plexus block. Supraclavicular brachial plexus block is widely employed regional nerve block to provide anesthesia and

analgesia for upper extremity surgeries. Supraclavicular block provides a rapid, dense and predictable anesthesia of entire upper extremity in the most consistent manner of any brachial plexus technique. It is the most effective block for all the portions of the upper extremity and is carried out at the 'division' level of the brachial plexus; with high volume the 'trunk' level of the plexus may also be blocked in this approach.

The alleviation of the suffering is of primary concern. Any method of postoperative pain relief must meet three basic criteria. It should be effective, safe and feasible. Currently available local anesthetics can provide analgesia for limited period of time when used as single injection. To extend the analgesic period beyond the operating rooms, various methods have been tried with the aim of prolonging the local anesthetic action, like continuous infusion of local anesthetics via indwelling catheters or use of different additives to local anaesthetics.

This study was a randomized, controlled, prospective, double blinded study. Sixty patients posted for upper limb surgeries were given brachial plexus block by supraclavicular approach. The patients were randomly allocated into two groups using standard randomization code. The Group R (control group) received ropivacaine 0.5% 30ml and 1ml of normal saline. The Group RD (cases or study group) received ropivacaine 0.5% 30ml and 1 μ g/kg of dexmedetomidine reconstituted in 1ml.

Peripheral action of dexmedetomidine

Dexmedetomidine is an α_2 selective agonist. It acts in a manner similar to Clonidine which is also a α_2 selective agonist.

A study by Brummet *et al* [1]. Showed that dexmedetomidine enhances duration of bupivacaine anesthesia and analgesia of sciatic nerve block in rats without any damage to the nerve. The histopathological evaluation of these nerve axons and myelin were normal in both control and dexmedetomidine plus bupivacaine groups.

The maximum effect of Clonidine was only 20%. On the other hand, adrenaline, noradrenaline and α_1 agonist phenylephrine and beta agonist isoprenaline had no effect on CAPs [2].

The efficacy of peripheral perineural dexmedetomidine added to bupivacaine and ropivacaine for sciatic nerve blocks in rats has been established [3, 4]. The increase in duration of analgesia is dose dependent [3] and the effect is peripheral (i.e., not caused by centrally mediated or systemic analgesia) [4].

However all the studies carried out so far to prove the peripheral action of α_2 agonists were animal studies. There are very few human studies, i.e., greater palatine and axillary brachial plexus nerve blocks have subsequently demonstrated that increased duration of sensory blockade can be achieved by adding dexmedetomidine to bupivacaine and levobupivacaine, respectively [5, 6]. Keeping these facts in mind this study was decided to study the action of dexmedetomidine on a less cardiotoxic local anesthetic like ropivacaine in supraclavicular brachial plexus block, so that by increasing the duration of analgesia with a single shot block we can achieve a longer duration of post-operative analgesia without significant clinical side-effects and hence can avoid continuous catheterization.

In this study, there was no statistically significant difference among the demographic data, duration of surgery and type of surgery between the study groups. The onset of sensory and motor block was earlier and there was prolonged duration of sensory and motor block and duration of analgesia in the group receiving dexmedetomidine.

Esmanoglu *et al* [5] added dexmedetomidine to levobupivacaine for axillary brachial plexus block and showed that it shortens the onset time of both sensory and motor block, prolongs the duration of block and the duration of postoperative analgesia. This may be because peripheral α_2 agonist produces analgesia by reducing release of norepinephrine, leading to α_2 receptor independent inhibitory effects on nerve fibre action potentials. In this study there was early onset and prolongation of duration of sensory and motor block [7, 8]. It was also found that there was lesser pain scores and hence prolonged duration of analgesia in those who received dexmedetomidine with ropivacaine for the block. All these findings were statistically significant.

From this study, we would like to suggest that dexmedetomidine can be safely used with local anesthetic in peripheral nerve blocks; however study to determine any toxic effects on human nerves is needed.

Conclusions

Dexmedetomidine in a dose of 25 μg added to ropivacaine in supraclavicular brachial block for upper limb surgery significantly shortens the onset time and prolongs the duration of sensory and motor blocks without producing sedation in patients. Total number of rescue analgesics required in post-operative period is also less with use of dexmedetomidine as an adjuvant to ropivacaine.

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