International Journal of Medical and Health Research
ISSN: 2454-9142
Received: 13-11-2018; Accepted: 15-12-2018
www.medicalsciencejournal.com
Volume 5; Issue 3; March 2019; Page No. 74-78

A comparative on analgesic effect and safety of ropivacaine VS ropivacaine plus dexmedetomidine in supraclavicular brachial plexus block: A randomized controlled double blind study in tertiary care centre

Dr. Zameeruddin[1*], Dr. Mohammad Imranullah Khan[2]
[1] Associate Professor, Department of Anaesthesia, Shadan Institute of Medical Sciences, Hyderabad, Telangana, India
[2] Post graduate, Department of Anaesthesia, Shadan Institute of Medical Sciences, Hyderabad, Telangana, India

Abstract
Dexmedetomidine as an adjuvant to local anesthetics in peripheral nerve blocks has been used in only a few studies.
Aims: We aimed at assessing and compare the analgesic and adverse effect of ropivacaine vs ropivacaine plus dexmedetomidine in supraclavicular brachial plexus block.
Settings and Design: Random, controlled, and double blind.
Materials and Methods: Sixty American Society of Anesthesiologist grade I, II and III patients of either sex scheduled for Elective upper limb surgery under supraclavicular brachial plexus block were divided into two equal groups in a prospective randomized double-blind controlled manner. For block patients in Group R received 0.5% ropivacaine (30cc), and Group RD 0.5% ropivacaine with 50 μg dexmedetomidine (30cc) saline.
Results: Demographic profile and surgical characteristics were similar in all the two groups.
The duration of analgesia was significantly longer in group R when compared to group RD.
Conclusions: Dexmedetomidine as an adjuvant to 0.5% ropivacaine in ultrasound guided brachial plexus block shortens the sensory as well as motor block onset time prolongs sensory and motor block duration and also increases the duration of analgesia. The action of dexmedetomidine most probably is local rather than centrally mediated.

Keywords: dexmedetomidine, ropivacaine

Introduction
Brachial plexus block has evolved as an important tool in the anaesthesiologist's armamentarium as a safe alternative to general anesthesia for upper limb surgery and for relief of perioperative pain. Its increased popularity is because of advancements in regional anesthesia techniques in terms of local anesthetic drugs, newer adjuvant drugs and use of ultrasound for safe and successful conduct of block. It helps in reduced hospital stay, less financial burden and also leads to avoidance of undesirable side-effects of general anesthesia. Since the introduction of first brachial plexus block using cocaine by Halstead (1884) the technique of brachial plexus block has evolved from classical blind technique to use of nerve stimulators and ultrasound guidance for supraclavicular brachial plexus block [1]. Many additives to local anesthetics such as opioids, clonidine, neostigmine and tramadol etc. have been used to increase the duration of the block, to improve postoperative pain management [2] and to avoid the need for placing catheter for continuous local anesthetic drug infusion. Dexmedetomidine a newer α2-adrenoreceptor agonist is currently in focus for its sedative, anxiolytic and analgesic properties. Pre- and intraoperative intravenous dexmedetomidine administration has shown to prolong the duration of sensory block with local anesthetics during peripheral nerve blocks.
Due to unique pharmacologic properties and fewer side effects, ropivacaine is being preferred by an increasing number of anaesthesiologists for peripheral nerve blocks. However, there are very few published studies on dexmedetomidine in combination with ropivacaine [6, 11]. The current study was designed with aim to evaluate the effect of adding dexmedetomidine to ropivacaine 0.5% in supraclavicular brachial plexus block in terms of, duration of postoperative analgesia and to test the hypothesis whether the effect of ropivacaine vs ropivacaine plus dexmedetomidine, is due to local action on nerve plexus or is centrally mediated.

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±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 milliliters (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 (μg)/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 (100μg/mL : 1mL) was used. Dose of 1μg/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 stimuplex ® 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 100□s. 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

Intravenous paracetamol 1 gram was given 6th hourly for the first 24 hours. Intramuscular tramadol 50 mg was given as rescue analgesic if VAS>3. Inadequate sensory and motor blockade beyond 30mins following the infiltration was considered as unsuccessful block.

Management of unsuccessful block

In the circumstance of inadequate or patchy action of the block, the block was supplemented with general anesthesia. mIf in case surgery was unduly prolonged and the effect of the block wore off, rescue analgesia was given in the form of intravenous Fentanyl 1 µg/kg and infusion of Propofol 50-100 µg/kg/min or convert to general anesthesia.

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

Duration of analgesia or first request for analgesic

Pain was assessed using a standard 10 cm visual analogue scale (VAS) by an independent anesthesiologist.

A VAS consists of a line, often 10 cm long, with verbal anchors at either end. In the numerical scale, 0 corresponds to no pain and 10 designate the worst possible pain. The patient places a mark at a point on the line corresponding to the patients rating of pain intensity. Patients are asked to choose a point on the line that represents the intensity of their current state.

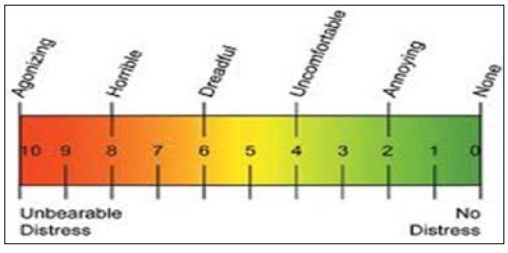

Fig 1

Time for first request for postoperative analgesic (duration of analgesia) was noted. During the intraoperative period heart rate, systolic, diastolic and mean arterial pressure were noted every 5 minutes (mins) during the first 15 mins, then every 15 mins throughout the surgery and hourly thereafter. Intravenous paracetamol 1 gram was given 6th hourly for the first 24 hours. Intramuscular tramadol 50 mg was given as rescue analgesic if VAS>3. Inadequate sensory and motor blockade beyond 30mins following the infiltration was considered as unsuccessful block.

Possible side effects of brachial plexus block:

Incidence of nausea, vomiting, Horner's syndrome, phrenic nerve palsy, pneumothorax, respiratory depression and signs and symptoms of local anesthetic toxicity were looked for and noted, if any.

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 and 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). Comparison of mean Visual Analog Score (VAS) between the groups at different time intervals.

Table 1: Comparison of mean vas between the groups at different time intervals

	Group R (Mean ± SD)	Group RD (Mean ± SD)	p value
Baseline	3.33±2.476	3.5±2.196	0.784
5 MIN	2.77±2.112	2.7±1.841	0.897
10 MIN	2.23±1.775	2.2±1.424	0.936
15 MIN	1.73±1.596	1.23±1.357	0.196
30 MIN	1.03±1.402	0.43±0.858	0.050
45 MIN	0.87±1.306	0.37±0.85	0.084
60 MIN	0.87±1.306	0.37±0.85	0.084
75 MIN	0.87±1.306	0.33±0.802	0.062
90 MIN	0.87±1.306	0.3±0.75	0.044
105 MIN	0.83±1.315	0.4±0.894	0.141
120 MIN	0.97±1.326	0.3±0.75	0.020
180 MIN	1.3±1.442	0.3±0.75	0.001
240 MIN	2.03±1.691	0.3±0.75	<0.001
300 MIN	2.33±1.988	0.5±1.009	<0.001
360 MIN	2.43±1.736	1.37±1.426	0.012
420 MIN	3.2±1.73	1.83±1.84	0.004
480 MIN	3.73±1.617	2.03±1.956	0.001

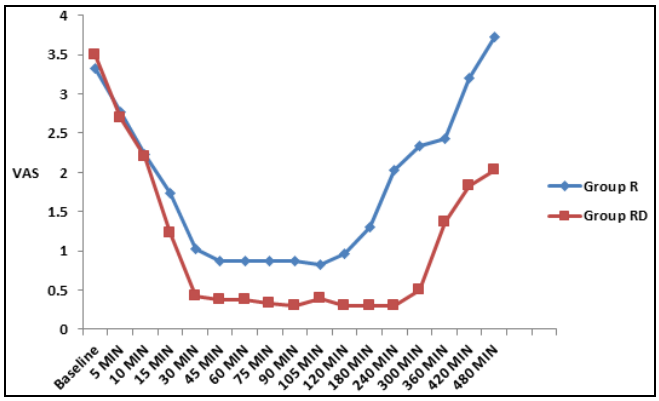

Fig 2: Line diagram comparing the mean of VAS between the groups at different time intervals

There was no statistically significant difference in mean VAS between both the groups at baseline (p=0.784), 5 minutes (p=0.897), 10 minutes (p=0.936), 15 minutes (p=0.196), 30 minutes (p=0.050), 45 minutes (p=0.084), 60 minutes (p=0.084), 75 minutes (p=0.062), and 105 minutes (p=0.141). There was a statistically significant difference at 90 minutes (p=0.044) and from 120 minutes onwards and thereafter (p<0.05) during follow up. Dexmedetomidine group had lower VAS compared to the control group. Comparison of mean modified bromage score (MBS) between the groups at different time intervals

Table 2: Comparison of mean MBS between the groups at different time intervals

	Group R (Mean ± SD)	Group RD (Mean ± SD)	p value
Baseline	0	0	
5 MIN	0.5±0.572	0.77±0.43	0.046
10 MIN	1.13±0.346	1.17±0.461	0.753
15 MIN	1.3±0.466	1.67±0.547	0.007
30 MIN	1.93±0.254	1.93±0.254	1.000
45 MIN	2±0	2±0	
60 MIN	2±0	2±0	
75 MIN	2±0	2±0	
90 MIN	2±0	2±0	
105 MIN	2±0	2±0	
120 MIN	1.97±0.183	2±0	0.321
180 MIN	1.93±0.254	2±0	0.155
240 MIN	1.73±0.64	2±0	0.026
300 MIN	1.33±0.758	1.8±0.407	0.004
360 MIN	0.77±0.679	1.63±0.669	<0.001
420 MIN	0.27±0.521	1.23±0.858	<0.001
480 MIN	0.1±0.305	0.8±0.847	<0.001

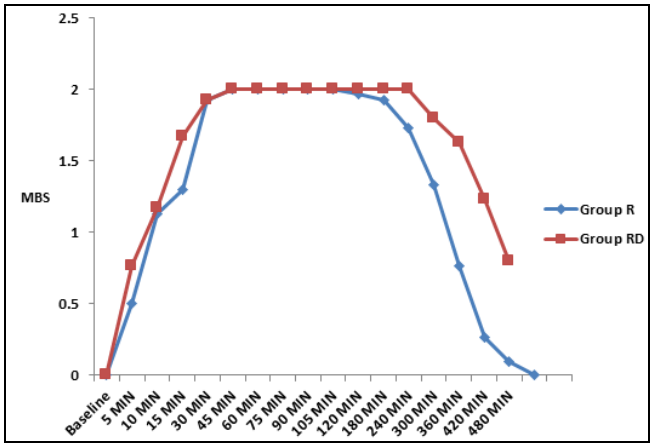

Fig 3: Line diagram comparing the mean of MBS between the groups at different time intervals

There was no statistically significant difference in mean MBS between both the groups at baseline (p=1.0), 10 minutes (p=0.897), 30 minutes (p=1.0), 45 minutes (p=1.0), 30 minutes (p=0.050), 45 minutes (p=1.0), 60 minutes (p=1.0), 75 minutes (p=1.0), 90 minutes (p=1.0), 105 minutes (p=1.0), 120 minutes (p=1.0), and 180 minutes (p=1.0), there was a statistically significant difference at 5 minutes (p=0.046) and from 240 minutes and thereafter (p<0.05) during follow up. Dexmedetomidine group had lower VAS compared to the control group.

Complications during the procedure

Table 3: Complications during the study

Complications	Group R	Group RD
Hypotension (SBP > 20% fall below the baseline)	0	3(10.00%)
Bradycardia (HR < 50/min)	0	1(3.33%)

3 patients in Dexmedetomidine group and none in control group developed hypotension during the study. 1 patient in Dexmedetomidine group and none in control group developed bradycardia during the study

Discussion

Apart from sedative, analgesic, hemodynamic-stabilizing properties, and sympatholytic pharmacologic effects, the alpha (α)-2-adrenergic receptor (α2-AR) agonists have been used to increase the duration of thermal anti-nociception and analgesia in some animal studies [4, 5]. Animal studies have proven the combination of dexmedetomidine with ropivacaine to be safe and neuro-protective. The use of dexmedetomidine decreases inflammation around peripheral nerves, thereby decreasing the potential for peripheral nerve injury [12]. In human beings, the beneficial effects of adding dexmedetomidine to local anesthetics during regional anesthesia and some peripheral nerve blockade procedures have proved to be efficacious for the surgical patients [6, 7, 11]. To best of our knowledge, this is probably the first human study showing that the addition of dexmedetomidine to ropivacaine in ultrasound-guided supraclavicular brachial plexus block shortens the sensory and motor block onset time, prolongs sensory and motor block duration and also prolongs the duration of analgesia.

The duration of analgesia, when only local anaesthetic is used is very short and does not extend into post-operative period for more than 3-4 hrs. Various drugs have been tried as adjuvant to local anaesthetics for prolonging the analgesia and improving the quality of block. Dexmedetomidine has been introduced in India in parenteral form and the effectiveness of the same for supraclavicular brachial plexus block has not been investigated in India, as very few studies have been done regarding the same. Hence, we selected dexmedetomidine as an adjuvant to ropivacaine in our study.

Ropivacaine has been found to be equally effective as bupivacaine for brachial plexus block by various authors [8, 9] Hence, ropivacaine was selected as local anaesthetic for our study.

In our study we used only 25 µg dexmedetomidine as adjunct to ropivacaine, because there are more chances to have bradycardia and hypotension with higher doses of dexmedetomidine [11].

Various authors have used different volumes of ropivacaine for brachial plexus block. We used 30 ml of local anesthetic solution for brachial plexus block basing on few papers.

Duration of analgesia

Some studies reported the duration of analgesia and had complete data to pooling. The result indicated that dexmedetomidine as an adjuvant prolonged the duration of analgesia significantly by an average of 303.04 minutes compared with the control group (MD, 303.04 minutes;

95%CI 228.84–377.24 minutes, I2=86%; P<.00001) (Fig. 1). The subgroup analysis was not conducted because of the not enough data in other subgroups.

Adverse effect

The major postoperative adverse events were bradycardia and hypotension, while postoperative drowsiness, dyspnea and Horner syndrome were also reported. As the main adverse events, statistic difference was not observed in the subgroup.

Conclusion

Thus, we conclude that in supraclavicular brachial plexus block addition of ropivacaine vs ropivacaine plus dexmedetomidine shortens the sensory and motor block onset time, prolongs both sensory and motor block duration. It also significantly delays the first demand for analgesia supplementation, decreases 24 h analgesic consumption and is not associated with any major side-effect. The action of dexmedetomidine is most probably peripheral than
Centrally mediated.

References

1. Halstead C. Great moments in the history of anaesthesiology. In: A Practice of Anesthesia. 7th ed. London, UK: Lioyd-Luke, 2003, 5.
2. Murphy DB, McCartney CJ, Chan VW. Novel analgesic adjuncts for brachial plexus block: a systematic review. Anesth Analg. 2000; 90:1122-8.
3. Rutkowska K, Knapik P, Misiolek H. The effect of dexmedetomidinesedation on brachial plexus block in patients with end-stage renal disease. Eur J Anaesthesiol. 2009; 26:851-5.
4. Brummett CM, Norat MA, Palmisano JM, Lydic R. Perineuraladministration of dexmedetomidine in combination withbupivacaine enhances sensory and motor blockade in sciatic nerve block without inducing neurotoxicity in rat. Anesthesiology. 2008; 109:502-11.
5. Brummett CM, Padda AK, Amodeo FS, Welch KB, Lydic R. Perineural dexmedetomidine added to ropivacaine causes a dose-dependent increase in the duration of thermal antinociception in sciatic nerve block in rat. Anesthesiology. 2009; 111:1111-9.
6. Zhang Y, Wang CS, Shi JH, Sun B, Liu SJ, Li P, *et al*. Perineural administration of dexmedetomidine in combination with ropivacaine prolongs axillary brachial plexus block. Int J Clin Exp Med. 2014; 7:680-5.
7. Marhofer D, Kettner SC, Marhofer P, Pils S, Weber M, Zeitlinger M. Dexmedetomidine as an adjuvant to ropivacaine prolongs peripheral nerve block: A volunteer study. Br J Anaesth. 2013; 110:438-42.
8. Kanazi GE, Aouad MT, Jabbour-Khoury SI, Al Jazzar MD, Alameddine MM, Al-Yaman R, *et al*. Effect of lowdose dexmedetomidine or clonidine on the characteristics of bupivacaine spinal block. Acta Anaesthesiol Scand. 2006; 50:222-7.
9. Agarwal S, Aggarwal R, Gupta P. Dexmedetomidine prolongs the effect of bupivacaine in supraclavicular brachial plexus block. J Anaesthesiol Clin Pharmacol. 2014; 30:36-40.
10. Esmaoglu A, Yegenoglu F, Akin A, Turk CY. Dexmedetomidine added to levobupivacaine prolongs axillary brachial plexus block. Anesth Analg. 2010; 111:1548-51.
11. Swami SS, Keniya VM, Ladi SD, Rao R. Comparison of dexmedetomidine and clonidine (a2 agonist drugs) as an adjuvant to local Anesthesia in supraclavicular brachial plexusblock: A randomised double-blind prospective study. Indian J Anaesth. 2012; 56:243-9.
12. Brummett CM, Amodeo FS, Janda AM, Padda AK, Lydic R. Perineural dexmedetomidine provides an increased duration of analgesia to a thermal stimulus when compared with a systemic control in a rat sciatic nerve block. Reg Anesth Pain Med. 2010; 35:427-31.