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**Original Research Article**

# Comparison of effects of dexmedetomidine and clonidine as adjuvant to bupivacaine 0.25% in ultrasound guided supraclavicular brachial plexus block

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## ABSTRACT

**Background:** Ultrasound guided brachial plexus block is the preferred technique for surgeries on upper limb. Adjuvants are usually added to peripheral nerve blocks to increase their analgesic efficiency and duration. We compared analgesic effects of dexmedetomidine 1mcg/kg and clonidine 1mcg/kg as adjuvant to a low volume of bupivacaine in USG guided supraclavicular brachial plexus block.
**Methods:** A prospective, randomized controlled, double blind study planned after permission from institutional ethics committee. Sixty ASA grade I, II patients, 18-60 years undergoing upper limb orthopedic surgery included. Group 1 (Control group) received 20 ml of 0.25% bupivacaine. Group 2 (Dexmedetomidine group) received 20ml of bupivacaine + dexmedetomidine (10 ml of 0.5% bupivacaine + 1µg/kg of dexmedetomidine, diluted with 0.9% NS to 20 ml) Group 3 (Clonidine group) received 20 ml of 0.25 bupivacaine + clonidine (10ml of 0.5% bupivacaine+1µ g/kg of clonidine, diluted with 0.9% NS to 20 ml) in USG guided supraclavicular brachial plexus block. Continuous variables analyzed with analysis of variance or Kruskal-Wallis test and categorical variables with Fisher's exact test.
**Results:** Pain free period was 864.90±357.16 minutes: dexmedetomidine group; 584.59±172.38 minutes: clonidine group, 431.78±138.40 minutes: control group with $p< 0.001$. VRS (verbal rating score) was significantly higher in control group as compared to dexmedetomidine at 4 hours but the pain scores were comparable between all the groups after 8 hours of block.
**Conclusions:** Dexmedetomidine as an adjuvant to bupivacaine provides prolonged anaesthesia, better pain relief in early postoperative period with haemodynamically stable, calm patients compared to clonidine and control group.

**Keywords:** Clonidine, Dexmedetomidine, Supraclavicular block, USG guided supraclavicular block

## INTRODUCTION

The use of USG (ultrasound) guided peripheral nerve block is a relatively new technique that is rapidly gaining popularity over more traditional techniques of peripheral nerve stimulators and parasthesia.[1] Use of ultrasound not only avoids the injury to the nerves associated with blind paraesthesia technique but also decreases the total dose

required to block the plexus. Supraclavicular nerve block provides anaesthesia of the entire upper extremity in the most consistent and time-efficient manner.[2] Alpha-2 adrenergic receptor agonists have been the focus of interest for their sedative, analgesic, perioperative sympatholytic and cardiovascular stabilizing effects with reduced anaesthetic requirements.[3] The concurrent injection of $\alpha_2$ adrenergic agonist drugs has been suggested to improve the nerve block characteristic of local anaesthetic solutions through either local vasoconstriction and facilitation of C-fibre blockade or a spinal action caused by slow retrograde axonal transport or simple diffusion along the nerve.[3]

Clonidine, an $\alpha_2$-adrenergic receptor agonist, has potent central and peripheral antinociceptive properties. Alpha 2 adrenoceptors are located on primary afferent terminals implicated in analgesia. It supports the analgesic action at peripheral sites.[4] Dexmedetomidine, a selective α2-adrenoceptor agonist, has been used as an adjuvant during regional and local anesthesia.[5,6] Animal and human studies have shown safety and efficacy of adding dexmedetomidine to local anaesthetics in various regional anaesthetic procedures, such as subarachnoid, epidural, and caudal injections, yet other investigations have reported reduced or negative analgesic effects when using dexmedetomidine.[7,8] We hypothesized that use of dexmedetomidine as adjuvant in the dose of 1 µg/ kg in 20 ml bupivacaine 0.25% in ultrasound guided supraclavicular brachial plexus block will provide better analgesia and longer duration of block as compared to clonidine or control hence we planned a study to compare the analgesic effect of dexmedetomidine with clonidine or control when given with bupivacaine for ultrasound guided supraclavicular brachial plexus block.

## METHODS

A prospective, randomized controlled, double blind study was carried out during the time period of September 2014 to September 2015 after getting approval from Institutional Ethics Committee and written informed consent from the patients (CTRI/2015/05/005825). Sixty patients, in the age group of 18-60 years belonging to ASA physical status I and II, who were to undergo open reduction and internal fixation for fractures of lower end humerus and forearm bones were included. Patients who had BMI > 30, local infections, anatomic deformities, heart rate less than 50bpm, heart block, coagulation disorder and allergy to local anaesthetics, dexmedetomidine or clonidine were excluded.

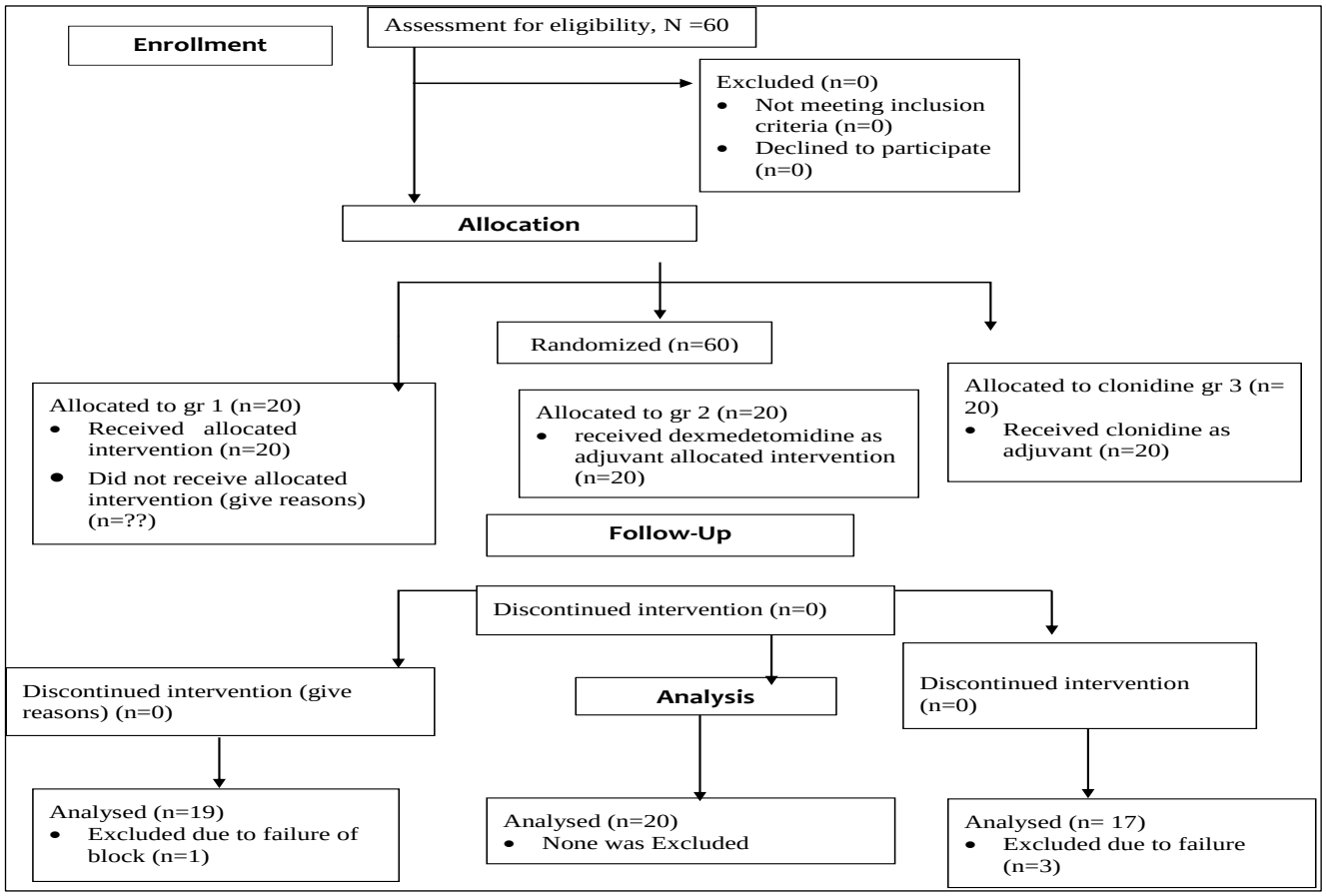


**Figure 1: Consort flow chart.**

Randomization was done by computer generated randomized number table. Random number was enclosed in a sealed opaque envelope and opened by one of the investigators to know the study drug/combination to be administered just before the block. Observer anesthesiologist was blind to the test drug/combination administered. Patients were educated about the 11-point Verbal Rating Score (VRS) one day prior to surgery where 0 is no pain and 10 is worst imaginable pain. All patients were premedicated with oral alprazolam 0.25mg the night prior and in the morning of the surgery. According to the random number, the patient was allocated to one of the three groups-

- Group 1 (Control group) received USG guided supraclavicular brachial plexus block with 20 ml of 0.25% bupivacaine.
- Group 2 (Dexmedetomidine group) received USG guided supraclavicular brachial plexus with 20 ml of 0.25% bupivacaine +1µ g/kg of dexmedetomidine (10 ml of 0.5% bupivacaine+1µ g/kg of dexmedetomidine, diluted to total of 20 ml with 0.9% normal saline)
- Group 3 (Clonidine group) received 20 ml of 0.25% bupivacaine +1µ g/kg of clonidine (10 ml of 0.5% bupivacaine+1µ g/kg of clonidine, diluted to total of 20 ml with 0.9% NS) in USG guided supraclavicular brachial plexus block.

Standard monitoring was attached, peripheral intravenous line established by 18G cannula in contralateral hand on arrival to operation theatre. Patients were monitored with ECG (electrocardiograph), heart rate, NIBP (non - invasive blood pressure) and $SpO_2$ (pulseoxymeter). Patients placed in supine position with head turned away from the side to be blocked. Heart rate, systolic and diastolic blood pressure and $SpO_2$ were recorded at 1-minute interval for 10 minutes after administration of supraclavicular block. Thereafter these were recorded at 10 minutes interval till the end of the surgery and for 24 hours at 0, 1, 2, 4, 8, 12, 18 and 24 hours interval after surgery. Ultrasound guided supraclavicular brachial block was performed under all aseptic precautions with 22 G echogenic needle using linear probe of 8-12 Hz with a Micromaxxsonosite (Sonosite, WA, USA) ultrasound machine. Data was collected every 5 minutes for first 30 minutes, 45 minutes, 60 minutes and every 30 minutes till completion of surgery and thereafter. Sensory block evaluated for each nerve using ice to test cold, comparing anaesthetized arm with contralateral arm at each minute after completion of drug injection in the dermatomes corresponding to median nerve, ulnar nerve, radial nerve and musculocutaneous nerve till complete blockade.

- Grade 1- No difference between two sides
- Grade 2- Some difference between two but cold still sensed in blocked arm
- Grade 3- Complete sensory loss on anaesthetized limb.

Motor block was assessed by thumb abduction (radial nerve), thumb adduction (ulnar nerve), thumb opposition (median nerve), and flexion of elbow (musculocutaneous nerve) with modified Bromage Scale with onset at grade 2 and peak motor block at grade 3.

- Grade 1- normal motor function with full flexion and extension of elbow, wrist and fingers
- Grade 2- reduced motor strength with ability to move fingers only
- Grade 3- complete motor block with inability to move fingers

The pain free period as time interval between time of test drug administration up to first rescue analgesic demand in minutes recorded. Pain assessment was done using VRS intra-operatively every 15 minutes and for 24 hours at 0, 1, 2, 4, 8, 12, 18 and 24 hours interval after surgery. Sedation was graded using Modified Ramsay Sedation Scale every 15 minutes with Grade 1- wide awake, Grade 2- drowsy, Grade 3- asleep but arousable with verbal stimulus, Grade 4- arousable with mild physical stimulus, Grade 5- not arousable with mild physical stimulus. Injection diclofenac 75 mg i.v (intravenous) was administered as an infusion in 100 ml Normal Saline at VRS>3. Total rescue analgesic requirement was recorded after 24 hours study period. The failure of block was defined as inadequate sensory and motor blockade beyond 30 minutes following the block.

In case of failure the block was supplemented with more drug infiltration in block or general anaesthesia was administered to complete the surgical procedure. The time 0 started when patient was shifted to PACU (postanesthetic care unit). If heart rate was< 50bpm or 20 % of the baseline, injection atropine was given. Injection mephenteramine as 3mg bolus given if systolic blood pressure of mean arterial pressure decreased to less than 20% of the baseline. Sample size calculation was done on basis of previous study.[9] The primary outcome was pain free period and assuming an increase in the duration of pain free period by 30% and assuming 90% study power and 5% an error, the minimum effect size was calculated to be 16 patients per group. Therefore 20 patients in each group were planned to overcome attrition loss.

Data was collected and entered in MS Excel 2010. Statistical analysis was performed using SPSS software 17 (SPSS, Inc., Chicago, IL). The One-Sample Kolmogorov-Smirnov Test was employed to determine whether data sets differed from a normal distribution. Normally distributed data was analyzed using a repeat-measures general linear model analysis of variance (ANOVA), whereas non-normally distributed data were analyzed using the Mann-Whitney U-test and categorical data was analyzed using the Chi-square test. For comparison between two groups post hoc test was applied in normally distributed data. A value of $P<0.05$ was considered significant.

## RESULTS

A total of sixty patients were recruited. There was failure of block in two patients and were given general anaesthesia. In another two patients, the effect was inadequate so were supplemented with more drug. Fifty-six patients were analyzed and the demographic data was comparable as regards to the age, sex, height and weight (Table 1). The pain free period was maximum in the dexmedetomidine group (864.90±357.16 minutes) followed by (584.59±172.38 minutes) in clonidine group and (431.78±138.40 minutes) in control. This was statistically significant in dexmedetomidine group as compared to clonidine and control group ($p < 0.001$). The difference was also significant in between clonidine group and control group $p< 0.001$) (Table 2).

**Table 1: Demographic data.**

| Variable | Group 1 control group mean±SD, n=17 | Group 2 dexmedetomidine group mean±SD, n=20 | Group 3 clonidine group mean±SD, n=19 | p value |
|---|---|---|---|---|
| Age (years) | 41.30 ±16.34 | 36.26± 12.36 | 35.06±12.61 | 0.344 |
| Weight (Kg) | 60.89±8.83 | 57.65±9.16 | 57.67±14.18 | 0.575 |
| Height (cm) | 158.63±5.98 | 159.05±5.42 | 159.53±5.88 | 0.899 |
| Sex (male/female) | 16/1 | 19/1 | 17/2 | 0.382 |
| ASA status (I/II) ¶ | 17/0 | 20/0 | 18/1 | 0.362 |

Value expressed as mean±SD, Independent t-test, ¶-expressed as number of patients in each group and analysed by Chi square test.

Total motor blockade was more in the dexmedetomidine (597.05±150.84 minutes) group as well as clonidine (405.47±134.05 minutes) group as compared to the control group (342.50±135.94 minutes), difference being statistically significant between dexmedetomidine and clonidine. ($p< 0.001$) (Table 2).

**Table 2: Comparison of sensory, motor blockade and pain free period in three groups.**

| Variable | Group 1 (control) mean±SD n= 17 | Group 2 (dexmedetomidine) mean±SD, n= 20 | Group 3 (clonidine) mean±SD, n= 19 | p value |
|---|---|---|---|---|
| Duration of sensory block (minute) | 369.50±133.79 | 644.40±162.47 | 445.76 ±137.92 | <0.001 |
| Duration of motor block (minute) | 342.50±135.94 | 597.05±150.84 | 405.47±134.05 | <0.001 |
| Pain free period (minute) | 431.78±138.40 | 864.90±357.16 | 584.59±172.38 | <0.001 |

**Table 3: Rescue analgesia requirement among the three groups.**

| | Group 1 (control) n=17, mean±SD | Group 2 (Dexmedetomidine) n=20, mean±SD | Group 3 (clonidine) n=19, mean±SD | P value |
|---|---|---|---|---|
| Total dose of diclofenac (in mg) | 133.33 ±32.08 | 60.00±39.24 | 79.41±18.19 | < 0.001 |

The sensory blockade was (644.40±162.47 minutes) in dexmedetomidine group, (445.76±137.92 minutes) in clonidine group and (369.50±133.79 minutes) in control group, the difference being statistically significant ($p< 0.001$) (Table 2, Figure 2). The block was significantly prolonged in dexmedetomidine group as compared to clonidine group ($p< 0.001$). The requirement of the rescue analgesic in the form of injection diclofenac was maximum in control group (133.33±32.08 mg) as compared to the dexmedetomidine group (60.00±39.24 mg) and clonidine group (79.41±18.19 mg) (Table 3).

VRS was significantly higher in control group as compared to dexmedetomidine at 4 hours, but the pain scores were comparable between all the groups after 8 hours of block (Figure 2). There was a statistically significant decrease in heart rate in both the clonidine group and dexmedetomidine as compared to control at 9 minutes ($p=0.025$) and 10 minutes ($p= 0.045$) of giving block but in only one case it decreased to 47 minutes and injection atropine was given. Heart rate was lower in dexmedetomidine group at 20 minutes ($p =0.026$*) and

60 minutes (p= 0.022*) as compared to control but none of cases had heart rate less than 58/minutes (Figure 3).

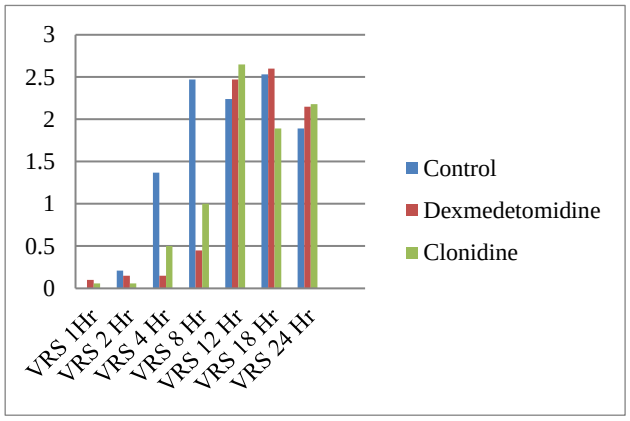


**Figure 2: Comparison of VRS for pain among three groups.**

There was statistically significant difference in systolic blood pressure (SBP) in clonidine and dexmedetomidine group as compared to control group in initial 6 minutes to 9 minutes but in none of cases the SBP was below 100 mm of Hg and no intervention was needed in any of cases. Mean arterial pressure (MAP) and diastolic blood pressure (DBP) were well maintained (Figure 4). Sedation score was higher in both groups as compared to control from 5 minutes after block to 70 minutes, maximum sedation score being 3, all patients were lightly sedated and arousable on verbal command.

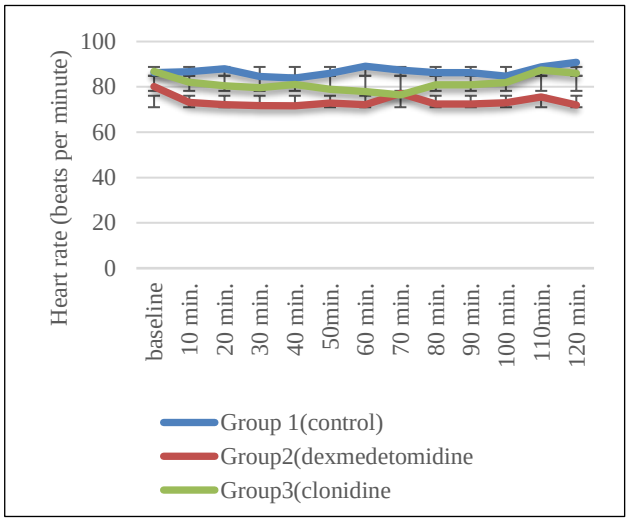


**Figure 3: Comparison of heart rate changes in three groups.**

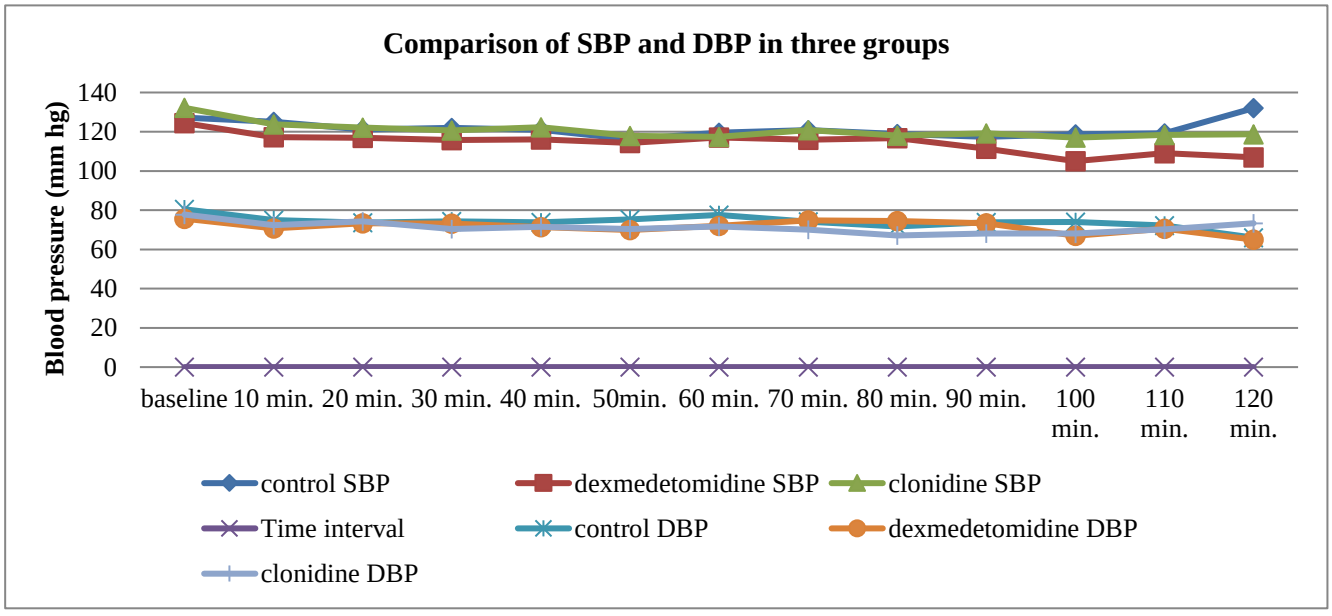


**Figure 4: Comparison of blood pressure changes in three groups.**

## DISCUSSION

The USG guided brachial block was given using 20 ml of the drug. We used 20 ml volume in present study as compared to other studies which used higher volume. In one of the recent study authors used 35 ml of drug to achieve adequate analgesia in USG guided supraclavicular block and in similar study 30 ml of volume was used to achieve the adequate effect in ultrasound guided infraclavicular block.[9,10] The reason behind using low volume was that use of ultrasound helped in direct visualisation of the bundles leading to infiltration of these bundles directly, this led to

requirement of low volume of local anaesthetic drug. Similar low volume was used by authors in another study where 2 to 4 ml of drug was used to surround each nerve in axillary brachial plexus block under ultrasound guidance and achieved adequate blockade.[11]

The pain free period was significantly more in the dexmedetomidine group as compared to the clonidine and control group and this increase may be due to the use of 1 mcg/kg of the drug. The increase in pain free interval was beyond the pharmacological effects of either of the drugs individually and may be explained by direct modulation of activity of sensory nerve fibres. The alpha 2 action of these two drugs is multifactorial both at spinal and supraspinal level and peripheral $\alpha_2$ adrenoceptors may also mediate the antinociception.[12] $\alpha_2$ blockers by acting at any of these sites, reduce nociceptive transmission, leading to analgesia. The activation of inwardly rectifying G1-protein-gated potassium channels resulting in membrane hyperpolarization and decreasing the firing rate of excitable cells in the central nervous system is considered to be a significant mechanism of the inhibitory neuronal action of $\alpha_2$-adrenoceptor agonists.[13] So, the direct peripheral action of dexmedetomidine on nerves in block may be responsible for the prolongation of pain free duration.

The sensory blockade was maximum in the dexmedetomidine group with the duration of 644.40±162.47 minutes which was slightly more than 413.97±87.13 minutes in a study by Swamy SS et al.[9] Similarly, the motor blockade was maximum with dexmedetomidine (597.05±150.84 minutes) as compared to 472.24±90.06 minutes in the same study. The sensory and motor block were 179.4±14.4 minutes and 155.5±15.8 minutes in a study which can be due to use lower dose of dexmedetomidine in dose of 0.75 mcg/kg.[10] It has been seen that the prolongation of the block is directly proportion to the dose of the drug used.

The sensory and motor blockade in the clonidine group were 445.76±137.92 minutes and 472.24±90.06 minutes as compared to that in another study with sensory blockade at 227.00±48.36 minutes and motor blockade at 292.67±59.13 minutes The sensory and motor block was 279.1±28.98 minutes and 330.4±31.68 minutes in a similar study where authors used 30 $\mu g$ of clonidine with 0.5% bupivacaine for supraclavicular brachial plexus block and stated that it prolongs postoperative analgesia without added problems apart from some sedation in the early postoperative period but they concluded that this may not be the ideal dose.[9,14] So, we used 1$\mu g$ /kg dose of clonidine in present study and the increased duration may be explained by the increased amount of drug used by us.

VRS score was better with dexmedetomidine than the control group at 4 hours but the pain scores were comparable between all the groups after 8 hours of block. This was in accordance with another study comparing these two agents although the authors used 0.5mcg/kg of both the drugs.[15]

The rescue analgesic requirement was maximum in control group as compared to both dexmedetomidine and clonidine group. Five of the patients in the dexmedetomidine group did not require any analgesic in first 24 hours of the block indicating the better analgesia. Clonidine group also received less analgesic as compared to control. The findings were consistent with a recent review.[11] There was decrease in the heart rate with both clonidine and dexmedetomidine which was clinically not significant. This decrease was attributed to alpha 2 agonist actions of both the drugs. These observations were consistent with the reviews done by different authors.[7,8,16]

Similarly, reduction of SBP was seen both with clonidine and dexmedetomidine but was not clinically detrimental for the patient and attributed to the decreased bleeding in the surgical field. Patients were mildly sedated and arousable on command in all the other studies and was independent of local anaesthetic used.[15] In present study also, patients were mildly sedated to grade 2. It contributed to successful surgery under regional with a calm patient, decreasing the need for supplemental anxiolytics.

The strength of the study is that block was performed under direct USG visualisation reducing chances of inadvertent intravascular infiltration and the amount of drug needed. There was an adequate and prolonged block with calm, stable patient with low dose of local anaesthetic, thereby avoiding side effects due to large volume and dose of bupivacaine. The limitation of the study was that the study was carried on small number of cases. Further study with larger sample size is needed for making strong recommendations.

## CONCLUSION

The use of dexmedetomidine to bupivacaine 0.25% results in the prolongation of the pain free period, duration of motor blockade and sensory blockade as compared to clonidine or control providing a haemodynamically stable, calm patient. Ultrasound guided supraclavicular block using low volume bupivacaine with 1mcg/kg dexmedetomidine resulted in adequate blockade and post-operative analgesia. It also led to minimum side effects attributable to the high volume and doses of bupivacaine. Hence, use of dexmedetomidine as adjuvant to bupivacaine in USG guided blocks is beneficial for intraoperative and postoperative analgesia and can be used for long regional surgeries for ultrasound guided block.

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## REFERENCES


1. Rupera KB, Khar BN, Shah VR, Parikh BK. Supraclavicular brachial plexus block: ultrasonography guided technique offer advantage over peripheral nerve stimulator guided technique. National J Med Res. 2013;3:241-4.
2. Singh S, Aggarwal A. A randomized controlled double-blinded prospective study of the efficacy of clonidine added to bupivacaine as compared with bupivacaine alone used in supraclavicular brachial plexus block for upper limb surgeries. Indian J Anaesth. 2010;54:552-7.
3. 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.
4. Erlacher W, Schuschnig C, Orlicek F, Marhofer P, Koinig H, Kapral S. Clonidine as adjuvant for mepivacaine, ropivacaine and bupivacaine in axillary, perivascular brachial plexus block. Can J Anesth. 2001;48:522-5.
5. Yoshitomi T, Kohjitani A, Maeda S, Higuchi H, Shimada M, Miyawaki T. Dexmedetomidine enhances the local anesthetic action of lidocaine via an alpha-2A adrenoceptor. Anesth Analg. 2008;107:96-101.
6. Brummett CM, Norat MA, Palmisano JM, Lydic R. Perineural administration of dexmedetomidine in combination with bupivacaine enhances sensory and motor blockade in sciatic nerve block without inducing neurotoxicity in rat. Anesthesiol. 2008;109:502-11.
7. Saadawy I, Boker A, Elshahawy MA, Almazrooa A, Melibary S, Abdellatif AA, et al. Effect of dexmedetomidine on the characteristics of bupivacaine in a caudal block in Pediatrics. Acta Anaesthesiol Scand. 2009;53:251-6.
8. Sebastian D, Ravi M, Dinesh K, Somasekharam P. Comparison of dexmedetomidine and clonidine as adjuvant to ropivacaine in supraclavicular brachial plexus nerve blocks. IOSR-JDMS. 2015;14:91-7.
9. Swami SS, Kenya VM, Ladi SD, Rao R. Comparison of dexmedetomidine and clonidine as an adjuvant to local anaesthesia in supraclavicular brachial plexus block: randomized double blind prospective study. Indian J Anaesth. 2012;56:24.
10. Ammar AS, Mahmoud KM. Ultrasound guided single injection infraclavicular brachial plexus block using bupivacaine alone or combined with dexmedetomidine for pain control in upper limb surgery: A prospective randomized controlled trial. Saudi J Anaesth. 2012;6:109-14.
11. Harper GK, Stafford MA, Hill DA. Minimum volume of local anaesthetic required to surround each of the constituent nerves of the axillary brachial plexus, using ultrasound guidance: a pilot study. Br J Anaesth. 2010;104:633-6.
12. Nakamura M, Ferreira SH. Peripheral analgesic action of clonidine: Mediation by release of endogenous encephalin like substances. Eur J Pharmacol. 1988;146:223-8.
13. Birnbaumer L, Abramowitz J, Brown AM. Receptor effector coupling by G proteins. Biochem Biophys Acta. 1990;1031:163-224.
14. Chakraborty S, Chakrabarti J, Mandal M C, Hazra A, Das S. Effect of clonidine as adjuvant in bupivacaine-induced supraclavicular brachial plexus block: A randomized controlled trial. Indian J Pharmacol. 2010;42:74-7.
15. Chaudhary SK, Verma RK, Rana S, Singh J, Gupta B, Singh Y. Ultrasound-guided femoro-sciatic nerve block for post-operative analgesia after below knee orthopaedic surgeries under subarachnoid block: Comparison between clonidine and dexmedetomidine as adjuvants to levobupivacaine. Indian J Anaesth. 2016;60:484-90.
16. Patil KN, Singh ND. Clonidine as an adjuvant to ropivacaine induced supraclavicular brachial plexus block for upper limb surgeries. J Anaesthesiol Clin Pharmacol. 2015;3:365-9.


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