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Original Research Article

A Randomized Controlled Double-Blinded Comparative Study of Ropivacaine Alone Versus Ropivacaine with Dexmedetomidine in Ultra Sound Guided Supraclavicular Brachial Plexus Block

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Conflict of interest: Nil

Abstract:

Background: Pain is "an unpleasant sensory or emotional experience associatedwith actual or potential tissue damage or described in terms of such damage".

Objective: to compare the effectiveness of ropivacaine alone and its combination with dexmedetomidine in brachial plexus block through supraclavicular route, with the help of ultrasound guidance.

Methods: The present study was carried out on patients undergoing elective upper limb surgery at Tirumala Hospital, Vizianagaram in the department of Anaesthesiology during the period from May- 2013 to May-2014.

Results: There was no significant difference in the study groups with regards todemographic 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=14.133± 1.676 min & group-RD =12.667± 1.213min) (p=0.000), Onset of motor block : (group-R =25.967± 2.748min & group-RD=23.333± 3.467min)(p=0.002)} Also total duration of sensory blockade {Group R=547.833± 26.152mins, Group RD =811.667± 25.405 mins (p value = 0.000)}, motor blockade {Group R=509.667± 24.703 mins, Group RD = 760.667 ± 28.062mins(p value = 0.000)} and number of rescue injections in 24 hours {Group R= 2.733± 0.450, Group RD=1.400± 0.498 (p value = 0.000)} was significantly different in two groups. There was good haemodynamic stability in both groups.

Conclusions: Dexmedetomidine in a dose of 25µg added to ropivacaine insupraclavicular 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.

Keywords: Ropivacaine, dexmedetomidine, brachial plexus block, supraclavicular route, ultrasound guidance.

Introduction

Pain is an unpleasant effect associated with significant psychological and physiological changes during surgery and post-operative period. Regional anaesthetic techniques have specific advantages both for standalone anaesthesia and as analgesic supplements for intraoperative and postoperative care. Supraclavicular brachial plexus block is preferred for its rapid onset, reliable anesthesia and as a safe technique for any surgery in the upper extremity that does not involve the shoulder.

Various approaches [1] of brachial plexus block have been used for upper limb surgeries, among these approaches supraclavicular and infraclavicular techniques are more effective in producing complete anaesthesia of all the branches of the brachial plexus as the narrowest part of the plexus is encountered by these techniques. Supraclavicular approach is easier than the infraclavicular approach as the plexus is more superficial above the clavicle. Regional anesthesia works well when local anesthetic is put in the right place in right volume. The first brachial plexus block was performed under direct visualization after surgical exposure. The technique has slowly evolved from landmark guided percutaneous localization of brachial plexus to use of electrical nerve stimulation and ultrasound guidance. The use of ultrasound to guide localization and anaesthetizing brachial plexus allows limiting complications.

Various local anesthetics have been used to produce 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. A variety of adjuvant has been studied for brachial plexus blockade including opioid and non-opioid agents. Dexmedetomidine has been already used

for intravenous regional anesthesia (Bier's block) [2]. Dexmedetomidine has shown greater affinity as an alfa-2 adrenoreceptor agonist than clonidine. The effect of Dexmedetomidine when added to lidocaine for intravenous regional anaesthesia, demonstrate that addition of 1 mcg/kg dexmedetomidine to lidocaine improves quality of anaesthesia and intraoperative as well postoperative analgesia without causing side effects. [3]

Dexmedetomidine, an alpha-2 adrenoreceptor agonist was introduced into clinical practice as a short term sedative (<24 hrs) and has been targeted for use in the perioperative period. Dexmedetomidine has not been associated with respiratory depression, despite frequently profound levels of sedation. It decreases sympathetic tone with attenuation of neuroendocrine and haemodynamic responses to anaesthesia and surgery, reduces anaesthetic requirement, causes sedation & analgesia. Because of arousable sedation, lack of respiratory depression & analgesia sparing effect, dexmedetomidine might prove useful in postoperative period for patient undergoing surgical procedures that are associated with significant pain. Thus using the new armamentarium, we attempt to compare the effectiveness of ropivacaine alone and its combination with dexmedetomidine in brachial plexus block through supraclavicular route, with the help of ultrasound guidance.

Materials and Methods

The prospective, randomized and double blinded study was carried out on patients undergoing elective upper limb surgery at Tirumala Hospital, Vizianagaram in the department of Anaesthesiology during the period from May- 2013 to May-2014. Institutional Ethical Committee approval was obtained. The study included total 60 patients belonging to ASA grade I and II of either sex with age between 18-60 years posted for various elective upper limb surgery. Sample size was decided in consultation with a statistician.

We calculated a sample size that would permit a type I error of $\alpha = 0.005$ and power of 80%. Enrollment of 25 patients in each group was required. Considering the dropouts, 30 patients were selected in each of the group Informed consent was taken from each patient who meets inclusion criteria's.

Patients meeting the inclusion criteria during the preanesthetic evaluation were randomly assigned into two groups of 30 each with the help of a computer-generated table of random numbers by simple randomization method. Total 31 milliliter of solution for supraclavicular brachial plexus blockade was administeredas follows-

Group-R: Ropivacaine alone: Patients of this group received injection Ropivacaine (0.75%) 30 milliliters + 1 milliliter normal saline.

Group-RD: Ropivacaine with Dexmedetomidine

Patients of this group received injection Ropivacaine (0.75%) 30 milliliter + Dexmedetomidine 25 microgram diluted in 1 milliliter normal saline.

Pre-anaesthetic evaluation was done on the evening before surgery.

A routine examination was conducted:

The following investigations were done in all the patients: Haemoglobin estimation, Urine examination for albumin, sugar and microscopy, Standard 12 lead ECG, X-ray chest, Fasting and post prandial blood sugars, Blood urea and serum creatinine. All patients included in the study were premedicated with tablet Alprazolam 0.5 mg and Ranitidine 150 mg orally at night before surgery and were kept nil orally 11 pm onwards.

All patients were premedicated with I.V 1 mg Midazolam 20 minutes before giving the block. The patients were connected with monitor to record heart rate (HR), noninvasive measurement of systolic blood pressure (SBP), diastolic blood pressure (DBP), continuous electrocardiogram (ECG) monitoring and haemoglobin oxygen saturation (SpO2). The baseline systolic BP, diastolic BP and heart rate were recorded. The patients and the observing anaesthesiologist as well as the physicians and nurses of the acute pain service were blinded to the study drug used. The patients were placed in dorsal recumbent position with the head turned away from the site of injection.

The injection site was infiltrated with 1 ml of lidocaine 2% subcutaneously. A nerve stimulator was used to locate the brachial plexus. The location end point was a distal motor response with an output lower than 0.6 mA. During injection, negative aspiration was performed after every 6.5–7.0 ml to avoid intravascular injection.

Sensory and motor block along with monitoring of vitals was determined every 5 minutes in first 30 minutes and then every 15 minutes during 1st hour followed by every second hourly during 24 hours. Any hypersensitivity reaction for the drugs, evidence of pneumothorax, and other adverse events were also monitored. To evaluate duration sensory block and motor block, patients were asked to inform the time when incisional discomfort as a sensation of pain began and also the time when full power returned to the shoulder. In the postoperative period, when the patient complained of pain at the operative site, Injection Diclofenac 75 mg I/M was given. Patients were followed up for 24 hrs for any side effects. Patients were explained about the 10-point visual analogue scale (VAS) with which the severity of postoperative pain was

determined: 0 corresponding to "no pain" and 10, corresponding to "worst imaginable pain".

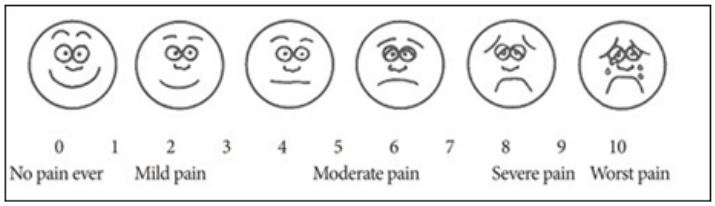

Figure 1: VAS score by visual analogue scale

Assessment of motor blockade was done by Bromage three point score:

0 - normal motor function with full flexion and extension ofelbow, wrist and fingers

1 - Decrease motor strength with ability to move fingers and/orwrist only

2-complete motor blockade with inability to move fingers

Assessment of sedation was done by Ramsay Sedation Scale:

1. Patient is anxious and agitated or restless, or both
2. Patient is cooperative, oriented and tranquil
3. Patient responds to commands only
4. Patient exhibits brisk response to light glabellar tap or loud auditory stimulus
5. Patient exhibits a sluggish response to light glabellar tap or loud auditory stimulus
6. Patient exhibits no response to light glabellar tap or loud auditory stimulus

These outcomes were assessed by an anaesthesia registrar blinded to groupallocation.

Haemodynamic parameters were recorded at 0,5,10,15,20,25,30,45 minutes, 1st hr, 2nd hr and thereafter every second hourly till 24 hrs. Postoperatively, all patients received routine analgesic intramuscular injection Diclofenac 75 mg when they started feeling pain (VAS>3). Time for first dose of rescue analgesic in postoperative period and total rescue analgesic requirement in 24 hours were recorded. The maximum pain scores and Ramsay sedation score at different time intervals (at 0,5,10,15,20,25,30,45 minutes, 1st hr, 2nd hr and thereafter every second hourly till 24 hrs in postoperative period) for each patient were recorded.

Incidences of nausea and vomiting, respiratory depression and sedation were noted. All the parameters were recorded as per the proforma and subjected to statistical analysis**.**

Statistical Analysis: Data were expressed as mean values ± standard deviation/ standard error, percentages (%), and numbers (n). The statistical analysis was performed by a statistician using Windostat Version 9.2 in Vishakapatnam, Andhra Pradesh. Two statistical tests were primarily used to analyze the data.

Results:

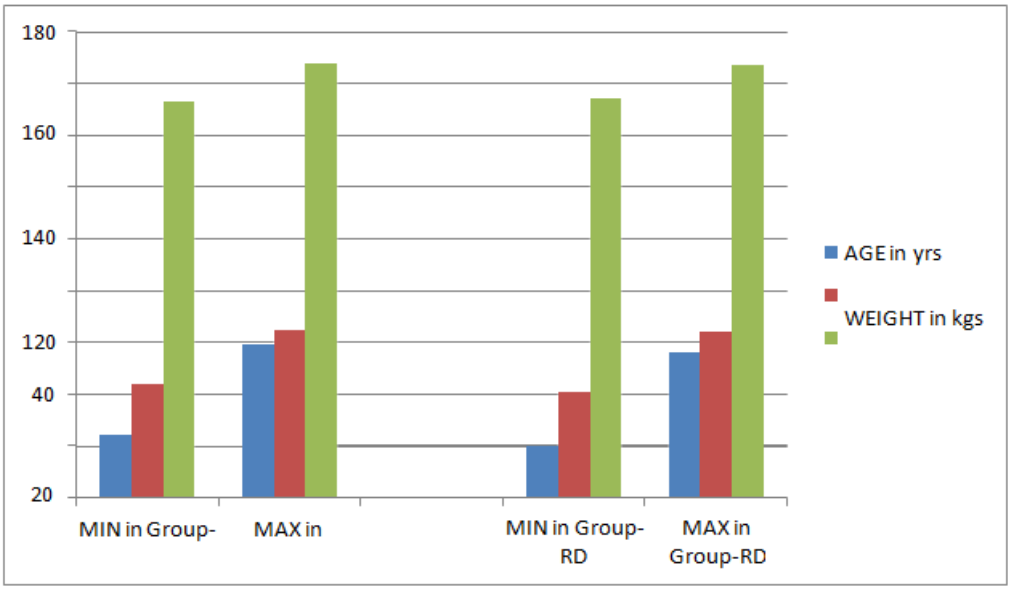

Figure 2: Comparison of Maximum and Minimum values of Age, Weight & Height

Our study was conducted on 60 patients who were randomly allocated into group-R and group-RD consisting of 30 patients each. Minimum age recorded in our study was 20 years and maximum age was 59 years. The mean age of patient in group R was 38.233±11.482 years while the mean age of patient in group RD was 35.633±9.44628 years. The P value was 0.352 which signifies that the two groups were comparable with regards to age.

Mean weight of patients in group-R was 58.1 ± 6.284 kgs and mean weight of patients in group-RD was 58.4 ± 5.577. The P value was 0.850 which is not significant showing that the groups are comparable with regards to Weight.

Mean height of patients in group-R was 159.5 ± 4.447 cms while mean height of patients in group-RD was 159.8 ± 3.682 cms. The P value was 0.786 which was again insignificant and group I and II are comparable withregards to height. Thus the patients in our study group were comparable with respect to Age, Weight and Height eliminating bias (if any) which can occur due to these factors.

Table 1: Comparison of Sex and ASAPS in two Groups

Groups	Sex		ASAPS	
	Male	**Female**	**I**	**II**
Group R (n=30)	17	13	17	13
	56.67%	43.33%	56.67%	43.33%
Group RD (n=30)	14	16	17	13
	46.67%	53.33%	56.67%	43.33%
P Value	0.446		1.000	

T-test is applied. P value is significant if less than 0.05. In Group R, 56.67% patients were male and the remaining 43.33%cases were female. In Group II, 46.67% cases were male and 53.33% cases were female. Difference between them was comparable in both groups. In Group R, 56.67% patients were ASAPS I and the remaining 43.33% cases were ASAPS II. In Group RD also 56.67% cases were ASAPS I and 43.33% cases were ASAPS II. There was statistically no difference between two groups. Thus the patients in our study groups were comparable with respect to Sex and ASAPS eliminating bias (if any) which can occur due to these factors.

Table 2: Comparison of duration of surgery

Duration Of Surgery (In Min)	Group R	Group RD	
	Mean ± SD	**Mean ± SD**	**P Value**
	101.633 ±	103.500±	0.822
	31.012	33.040	

The total duration of surgery was also comparable in both groups with mean duration in group R 101.633 ± 31.012 mins and group RD 103.500± 33.040 mins. The P value was insignificant (0.822). Thus there was no significant difference among the two groups with respect to the duration of surgery.

Table 3: Comparison of onset of sensory block

Onset of Sensory block (In Min)	Group R	Group RD	
	Mean ± SD	**Mean ± SD**	**P Value**
	14.133±	12.667±	0.000
	1.676	1.213	

Onset time is the time from the completion of injection of study drug to first loss of pinprick sensation in any of the dermatomes C5-T1. In group R, it was 14.133± 1.676 min and 12.667± 1.213 min in group RD. This shows that ropivacaine with dexmedetomidine provides faster sensory block than ropivacaine alone.

Table 4: Comparison of onset of motor block

Onset of motor block (In Min)	Group R	Group RD	P Value
	Mean ± SD	**Mean ± SD**	
	25.967±2.748	23.333±3.467	0.002

The total time required to achieve complete paralysis of the upper limbwas considered as onset of motor block. In group R, it was 25.967± 2.748 min and 23.333± 3.467 min in group RD. P value is 0.002 which is a significant. This shows that ropivacaine with dexmedetomidine provides faster motor block than ropivacaine alone.

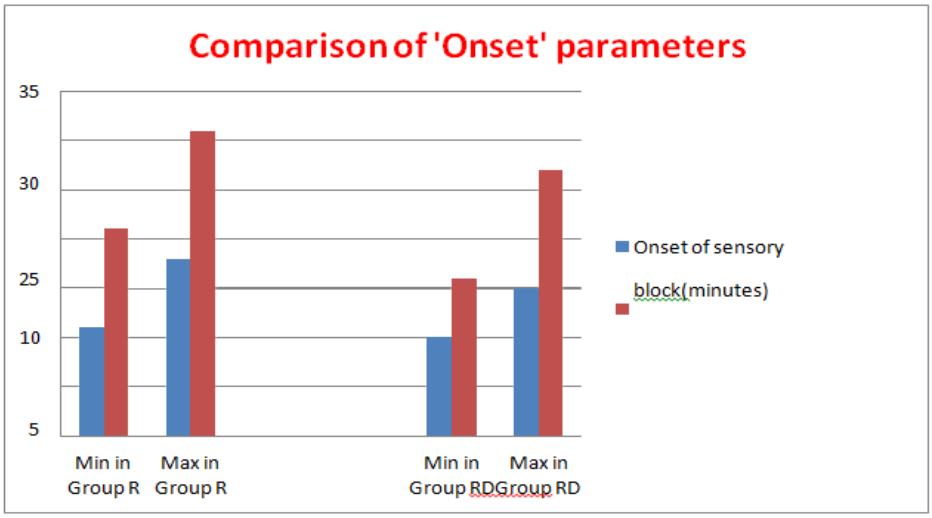

Figure 3: Comparison of 'Onset' parameters

In present study, the minimum time of onset of sensory block was 10 min and maximum time was 18 minutes. Minimum time of onset of motor block was16 min and maximum time was 31 minutes.

Table 5: Comparison of Duration of motor block

Duration of motor block (In Min)	Group R	Group RD	
	Mean ± SD	Mean ± SD	P Value
	509.667±	760.667±	0.000
	24.703	28.062	

The above mentioned values compare the duration of motor blockade in the two groups. Duration of motor blockade was longer in group RD (760.667± 28.062min) compared to group R (509.667± 24.703min) and this difference was statistically significant.

Table 6: Comparison of Duration of Sensory block

Duration of sensory block (In Min)	Group R	Group RD	
	Mean ± SD	Mean ± SD	P Value
	547.833±26.152	811.667±25.405	0.000

The above mentioned values compare the duration of sensory blockade in the two groups. Duration of sensory blockade was longer in group RD (811.667± 25.405min) compared to group R (547.833± 26.152min) and this difference was statistically significant.

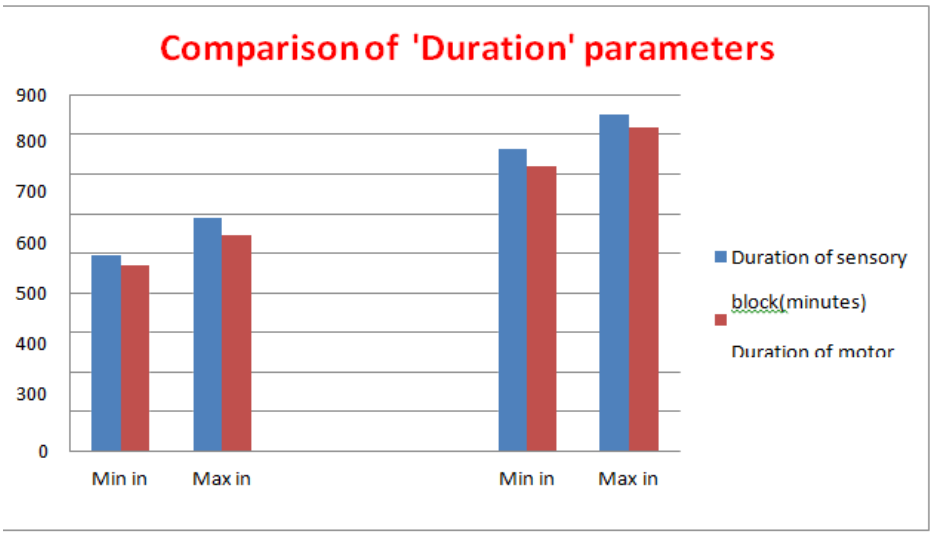

Figure 4: Comparison of 'Duration' parameters

In present study, the minimum duration of sensory block was 495 min and maximum time was 850 minutes. Minimum duration of motor block was 470 min and maximum time was 820 minutes.

Haemodynamic variables:

Haemodynamic parameters (HR, SBP, and DBP) were recorded at 0,5,10,15,20,25,30,45 minutes, 1st hr, 2nd hr and thereafter every second hourly till 24 hrs to record any incidence of bradycardia or hypotension.

ANOVA test was used to compare HR, SBP, and DBP over different intervals of time.

Heart Rate:

- Heart rate in Group R and Group RD were comparable. The difference was statistically not significant. (P=0.476)
- There was no fall or rise in heart rate more than 15 beats than previousobservation.

Blood Pressure: SBP in Group R and Group RD were comparable. The difference was statistically not significant (P=0.416).

Diastolic Blood Pressure: DBP in Group R and Group RD were comparable. The difference was statistically not significant (P=0.784). Thus in the present study we found that there was no significant difference among the two groups in total 24 hours of duration with respect to parameterslike HR, SBP, and DBP.

VAS scores: Visual analogue scale (VAS) scores were also recorded at 0,5,10,15,20,25,30,45 minutes, 1st hr, 2nd hr and thereafter every hourly till 24 hrs. ANOVA was applied for statistical analysis of VAS scores in the two groups over the various time intervals.

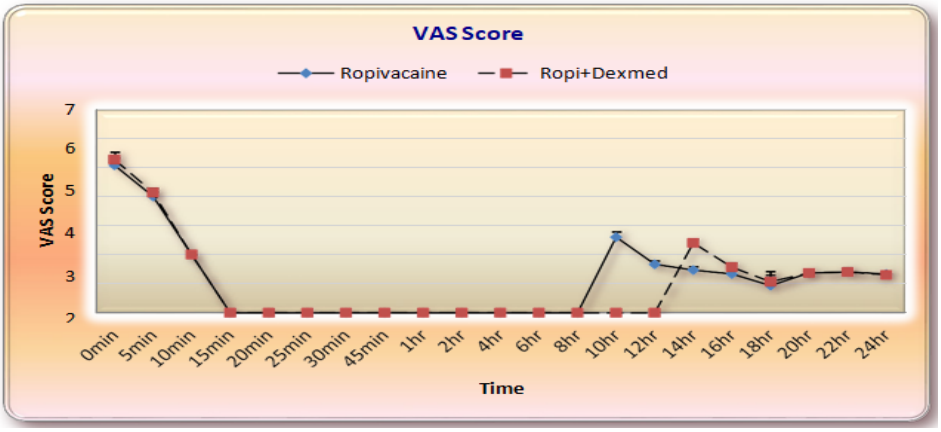

Figure 5: VAS Score

VAS scores at different time intervals: Patients in Group RD had 0 VAS score for a longer duration than those in Group R. Differences in VAS scores of the two groups was statistically significant.(P=0.000). Thus in our present study we found that VAS scores were significantly higher in Group R as compared to Group RD.

Ramsay Sedation Score: The Ramsay sedation score was used to assess sedation at 0 hour and then at different specific intervals up to 24 hours. ANOVA was applied to establish statistical significance between the differences in sedation scores in the two groups over time.

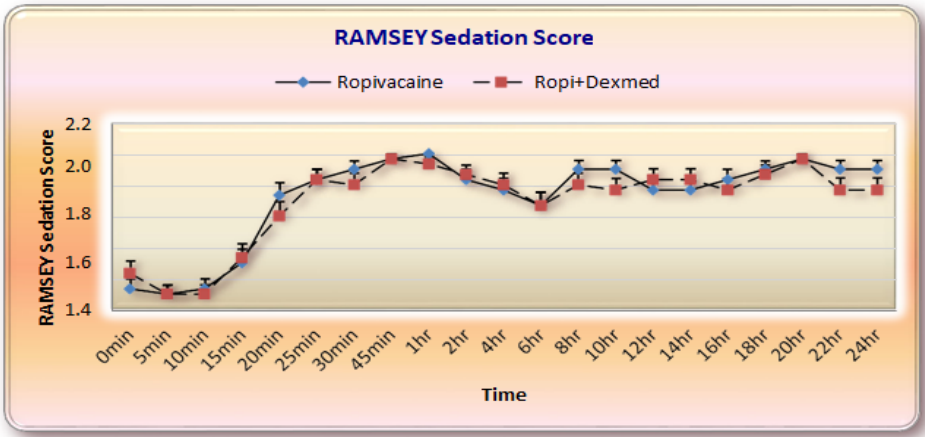

Figure 6: RAMSEY Sedation Score

Ramsay sedation scores at different time intervals: The mean Ramsay sedation (RSS) scores of Group R was almost equal to Group RD. ANOVA established that the difference was not significant (P=0.169). During this study, no patient was reported to be "excessively somnolent" or "difficult

to arouse."

Discussion

In our study, the drugs selected for brachial plexus block were Ropivacaine and Dexmedetomidine. There have been a few clinical studies evaluating the effect of mixing dexmedetomidine with local anesthetics during placement of peripheral nerve blockade. Peripheral analgesic effects of dexmedetomidine have enabled an overall improved blockade quality when added to local anesthetics in a peripheral nerve block model and are thought to be mediated by α2-receptor binding. [4] In a randomized double-blind trial performed by Esmaoglu et al., [5] dexmedetomidine added to levobupivacaine for axillary brachial plexus blockade shortened the block onset time, prolonged the duration of motor and sensory effects, and extended postoperative analgesia. In addition, dexmedetomidine mixed with lidocaine has been reported to decrease tourniquet pain, improve block quality, and prolong postoperative analgesia during intravenous regional anesthesia. [6]

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 hours. 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.

Bupivacaine is being regularly used for brachial plexus block for upper limb orthopaedic surgeries in most of the hospitals. Ropivacaine, another local anaesthetic with structural similarity to bupivacaine without its cardiotoxic effects has been introduced to Indian market already. Ropivacaine has been found to be equally effective as bupivacaine for brachial plexus block by various authors. [7,8] Hence Ropivacaine was selected as local anaesthetic for our study.

Doses of the drugs selected: Ropivacaine was found to have similar potency at higher doses and less potency than Bupivacaine at lower doses as found by Andrea Casati et al. [9]

The potency ratio being 1.5:1 between Ropivacaine and Bupivacaine respectively, Bupivacaine 0.5% would be of the same potency as Ropivacaine 0.75%. Hence it appears that Ropivacaine 0.75% would be as effective as Bupivacaine 0.5% for brachial plexus block.

Various authors have used different volumes of Ropivacaine for brachial plexus block. Stephen M Klein et al [10] and Vaghadia et al [11] used 20 ml of local anesthetic solution for brachial plexus block. Hence 0.75 % Ropivacaine 20 ml volume was selected for our study.

Gandhi R et al [12] found that dexmedetomidine gives better hemodynamic stability and greater postoperative analgesia. Dexmedetomidine 30 microgram for supraclavicular brachial plexus blockade was administered The conclusion of the study was that Dexmedetomidine is a useful drug for combination with bupivacaine, as it prolongs the duration of analgesia in supraclavicular brachial plexus block. Only two cases of bradycardia and two cases of hypotension were noticed in dexmedetomidine group patients with 30 microgram dose of dexmedetomidine.

Esmaoglu et al [5] found that in patients undergoing axillary brachial plexus block, 100microgram dexmedetomidine, added to levobupivacaine, shortens sensory and motor block onset time and extends block durations. Dexmedetomidine may lead to side effects such as hypotension and bradycardia with increased dosage, along with its effects such as sedation and anxiolysis. In this study the incidence of bradycardia was high.

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

Onset of sensory block: In our study, we observed that onset time was 14.133± 1.676 min in group R and 12.667± 1.213 min in group RD. (P value<0.05) Here onset time is the time from the completion of injection of study drug to loss of pinprick sensation.

This observation well matches with study of Sandhya Agarwal 13, onset of sensory 13.20±1.848min and 19.04±3.195 min in dexmedetomidine group and control group respectively.

Similar observation was made by Aliye Esmaoglu [5], where the onset time of sensory block was much faster in dexmedetomidine group, 9.03 ±1.15 min compared to that of placebo (10.46 ± 1.30 min). This shows that ropivacaine with dexmedetomidine provides faster sensory block than ropivacaine alone.

Onset of motor block: In our study, we observed that onset of motor block was earlier in study group of dexmedetomidine having the mean value of 23.333± 3.467min and in comparison; the control group had a mean value of 25.967± 2.748min. Which is statistically significant (p = 0.002).

This observation matches well with the study conducted by Sandhya Agarwal [13], who had earlier onset of motor blockade in dexmedetomidine group compared to control group, 16.3±1.7min and 22.7±2.8 min respectively. Similar observation was

made by Aliye Esmaoglu [5], where the onset time of motor block was much faster in dexmedetomidine group compared to that of placebo.

Duration of motor block: The duration of motor block, in our study was 760.667± 28.062min with dexmedetomidine group-RD and 509.667± 24.703 min for control group-R, which is statistically significant (p= 0.000).

This observation matches well with the study conducted by Rachana Gandhi [12], who had longer duration of motor blockade in dexmedetomidine group compared to control group, 660.2 ± 60.4min and 100.7 ± 48.3min respectively.

Similar observation was made by Aliye Esmaoglu [5], where the duration of motor block was much longer in dexmedetomidine group-RD773.00 ±67.62 min compared to that of placebo group-R(575.00 ±65.00 min). This observation also well matches with study of Sandhya Agarwal [13], duration of motor block 702.0±111.6min and 208.0±22.7 min indexmedetomidine group-RD and control group-R respectively. This shows that dexmedetomidine also prolongs total duration ofmotor block if added to local anaesthetics.

Duration of sensory block/ duration of analgesia: In our study duration of sensory blockade is the time from the onset of sensory blockade to till the patient's complaints of pain at the site of surgery and rescue analgesia was given. So it is also considered as "duration of analgesia" in our study.

The duration of sensory blockade, in our study was 811.667± 25.405 min with dexmedetomidine group-RD and 547.833± 26.152 min for control group- R, which is statistically significant (p=0.000).

Aliye Esmaoglu [5] in his study, found that the duration of sensory block was longer in dexmedetomidine group compared with placebo 887 ± 66.23min versus 673.00 ±73.77min .These observation were similar to our study. In a study conducted by Rachana Gandhi [12] the duration sensory block was 732.4 ± 48.9min in the dexmedetomidine group, compared with 146.5 ± 36.4min in the control group.

This shows that dexmedetomidine prolongs sensory block of supraclavicular brachial plexus block very significantly.

Ramsay sedation scale Score: Sedation in our study was assessed by Ramsay sedation scale. Patients from both the study groups were not sedated at any specific time during 24 hours. Their sedation score were either 1 or 2. The mean Ramsay sedation scores of Group R was almost equal to Group RD.

This shows that dexmedetomidine at low doses if used in supraclavicular blockwill not produce any sedation in patients.

Total requirement of rescue analgesia in 24 hours: As we have already seen that dexmedetomidine prolongs total duration of sensory block means it extends total duration OD analgesia too. Because of this, patient may require less number of rescue analgesic injections in post-operative period. In our study we found that total number of rescue analgesic injections in 24 hours was higher in group-R (2.733± 0.450) than in group-RD (1.400± 0.498).

Haemodynamic variables: There was no any incidence of fall in blood pressure more than 20mmhg compare to baseline reading. No patient had bradycardia or tachycardia. This shows that dexmedetomidine is not producing its well-known side effects like bradycardia and hypotension if it is used in small doses(less than 30 microgram) as an adjuvant with local anesthetics in supraclavicular brachial plexus block.

Conclusion

Dexmedetomidine in a dose of 25µg added to Ropivacaine in supraclavicular brachial plexus 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 postoperative period is also less with use of Dexmedetomidine as an adjuvant to Ropivacaine.

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