Supraclavicular Brachial Plexus Block: Comparison of Varying Doses of Dexmedetomidine with Ropivacaine

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Citation

Shakya S, Singh J, Ghimire A, Shrestha B. Supraclavicular Brachial Plexus Block: Comparison of Varying Doses of Dexmedetomidine with Ropivacaine. *Kathmandu Univ Med J.* 2021;75(3):345-50.

ABSTRACT

Background

Alpha-2 adrenergic receptor agonists have been the focus of interest nowadays as an adjuvant to local anesthesia due to its excellent sedative, analgesic, antihypertensive, anesthetic sparing and hemodynamic stabilizing properties. The ideal dose of dexmedetomidine for brachial plexus block is matter of debate.

Objective

To find the appropriate minimal dose of dexmedetomidine with desired clinical effects and minimal side-effects, we compared different doses (25 mcg, 50 mcg, 75 mcg and 100 mcg) of dexmedetomidine as an adjuvant to ropivacaine.

Method

One hundred fifty patients of ASA I and II, aged (18-60) years, weighing (50-60) kilograms undergoing upper limb surgeries under brachial plexus block were enrolled in this prospective, double blind, randomized control study. Patients in all group received 19 ml of 0.5% ropivacaine in common. In addition; group RD25, RD50, RD75 and RD100 received 25 mcg, 50 mcg, 75 mcg and 100 mcg of dexmedetomidine diluted in 1 ml of normal saline (NS) respectively whereas group RD00 received only 1 ml of NS. The duration of analgesia was the primary outcome whereas block characteristics, hemodynamic parameters, oxygen saturation, sedation score and adverse effects were taken as secondary outcome. Statistical analysis was done using ANOVA test, Chi-square test and Scheffe's multiple comparison tests.

Result

The demographic profile and baseline hemodynamic variables were comparable in all five groups. Increasing dose of dexmedetomidine showed significant improvement in block characteristics but associated with increase in sedation and incidence of bradycardia.

Conclusion

We conclude that dexmedetomidine 50 mcg would be an appropriate dose as adjuvant to local anesthesia in brachial plexus block.

KEY WORDS

Analgesia, Brachial plexus block, Bradycardia, Dexmedetomidine, Ropivacaine

INTRODUCTION

Brachial plexus block, supraclavicular approach under ultrasound guidance provides fast, complete and dense analgesia for upper limb procedure.[1] The effect tends to wear off rapidly due to high vascularity of the site. Different novel analgesic adjuvant to brachial plexus block like buprenorphine, dexamethasone, magnesium, and midazolam had been used.[2-5] Alpha-2 adrenergic receptor agonists have been the focus of interest nowadays due to its excellent sedative, analgesic, antihypertensive, anesthetic sparing and hemodynamic stabilizing properties. Some alpha-2 adrenergic agonist (clonidine and dexmedetomidine) had been used efficaciously and safely as an adjuvant to local anesthetic agents in regional nerve blocks.[6,7]

The ideal dose of dexmedetomidine for brachial plexus block is matter of debate. There are no studies suggestive of appropriate dose of dexmedetomidine as an adjuvant in brachial plexus block. Wide range of dose of dexmedetomidine has been used in different studies and have shown that increasing the dose of dexmedetomidine had improved block characteristics but also increases incidence of side effects like bradycardia, hypotension, increase sedations. So, to minimize the side effects of dexmedetomidine and also to find the most appropriate minimal dose of dexmedetomidine with desired clinical effects; we compared different dose of dexmedetomidine as an adjuvant to local anesthetics.

METHODS

After approval from the institutional review committee (protocol approval number 123/19) and with informed written consent from patients, 150 patients of ASA I and II, age between (18-60) years, weighing (50-60) kilograms undergoing upper limb orthopedic surgeries under brachial plexus block were enrolled in this prospective, double blind, randomized control study from 1st September, 2019 to 30th March, 2020. Patient on adrenergic agonist or antagonist therapy, known sensitivity to local anesthesia or dexmedetomidine, second and third degree heart block, bradycardia (with HR less than 50 bpm), hypotension (MBP less than 65 mmHg), patients with brachial plexus injury, renal and hepatic insufficiency, uncontrolled diabetes and hypertension, pregnant and lactating women, alcohol and drug abuse, psychiatric disorders, neuromuscular disorder and coagulopathy, patchy or inadequate anesthesia requiring conversion to general anesthesia or when additional opioid or sedation required, any position other than supine position during the surgery and patient refusal were excluded from the study.

These patients were allocated into five different groups using sealed envelope technique to ensure concealment of allocation sequence. The envelope was opened by the person not involved in the study who then prepared the drug solution according to randomization. The anesthesiologist performing the block and observing the patient was blinded to treatment groups. Data collection was done by anesthesiologist who was unaware of the group allocation. Patient was randomly assigned to one of the five groups. The 10 cm visual analogue scale (VAS) (0-no pain and 10-worst pain) was explained during pre-operative visit. All patients received tablet lorazepam 2 mg orally on the night before surgery. Patients in group RD00 received 19 ml of 0.5% ropivacaine plus 1 ml of normal saline (total 20 ml). Patients in group RD25 received 19 ml of 0.5% ropivacaine plus 25 mcg of dexmedetomidine diluted in 1 ml of normal saline (total 20 ml). Patients in group RD50 received 19 ml of 0.5% ropivacaine plus 50 mcg of dexmedetomidine diluted in 1ml of normal saline (total 20 ml). Patients in group RD75 received 19 ml of 0.5% ropivacaine plus 75 mcg of dexmedetomidine diluted in 1 ml of normal saline (total 20 ml). Patients in group RD100 received 19 ml of 0.5% ropivacaine plus 100 mcg of dexmedetomidine diluted in 1 ml of normal saline (total 20 ml). We had selected the patient with weight between 50-60 kgs to make the dose of dexmedetomidine correspond to 0.5 mcg/kg [25 mcg], 1 mcg/kg [50 mcg], 1.5 mcg/kg [75 mcg] and 2 mcg/kg [100 mcg].

After shifting the patients to the operation theatre, noninvasive monitors such as blood pressure (BP), Oxygen saturation (SpO_2), electrocardiogram (ECG) were applied, and their baseline values were recorded. Intravenous (IV) assess was established using 18G cannula and IV fluid (Ringer's lactate) was started at 100 ml/hr. Under all aseptic condition, supraclavicular brachial plexus block was performed with the help of ultrasonography (USG) and 22G, 100 mm needle (stimuplex, B/Braun, Germany). Sensory and motor blockades were assessed for every 2 mins after completion of injection till 30 mins and then every 2 hourlies until the effect of block. For sensory loss assessment, we used pinprick test with a 3-point scale: 0-no block, 1-analgesia [loss of sensation to pinprick] and 2-loss of touch in the distribution of median, ulnar, radial and musculocutaneous nerve.[8] Motor blockade was assessed by modified Bromage scale for upper extremities using 3-point scale: 0-complete movement of finger and wrist, 1-ability to move the fingers only, 2-inability to move fingers.[9] Onset of sensory blockade was defined as the interval between the end of injection and sensory block evidence by loss of sensation to pinprick or by score of 1. Onset of motor blockade was defined as the interval between the end of injection and complete paralysis of wrist or score of 1. Duration of sensory and motor block was taken as time interval between the onset of block and complete recovery of sensory and motor functions on all four nerve territories (Grade 0). Duration of analgesia was taken as time interval between the onset of sensory block and the first dose of rescue analgesia given to the patient. A complete block was defined as block with grade 2 score. Patients with score of 0, 1 was considered having incomplete block and was excluded from the study.

Post-operative pain assessment using VAS was done for every 2 hours till the block last. Post-operative heart rate (HR), systolic (SBP), diastolic (DBP) and SpO_2 was recorded for every 5 mins for 15 mins, every 15 mins till 2 hrs, every 2 hourly till 6 hours, every 6 hourlies till the effect of block. Rescue analgesia was provided with inj. Ketorolac 30 mg intravenous when VAS > 3 cm. The incidence of side effects (bradycardia, hypotension and sedation) was recorded. Sedation was assessed using 4-point sedation score (0-awake, 1-drowsy, 2-sleeping but arousable on verbal command, 3- sleeping and arousable only on tactile stimulation). Bradycardia was defined as decrease in HR by 30% from baseline value and/or an absolute HR < 50 beats per minute; which was manage by 0.6 mg IV bolus of atropine. Hypotension was defined as fall in blood pressure by 30% from baseline and/or an absolute MBP < 65 mmHg; which was manage by IV crystalloids (200 ml of Ringer lactate/normal saline) or increments of mephentermine 3 mg IV.

A pilot study was done with 20 patients (4 in each group). Sample size calculation was done using duration of analgesia as the primary end point. To detect an observed difference of 130 mins in duration of analgesia between groups with type I error of 5% and power of 80%, the minimum sample size required was 21.125. We included 30 patients in each group (total 150 patients) for better validation of results. Data was checked, entered and analyzed using SPSS version 24 for windows (IBM corp., Armonk, NY, USA). Quantitative data were expressed as mean + standard deviation, and for qualitative data; number, ratio and percentages were used. ANOVA test was used to compare demographic variables (age, weight, blood pressure, heart rate, SpO_2, onset and duration of sensory and motor block, duration of analgesia). Intergroup comparison was done with Scheffe's multiple comparison test. Chi-square test was used to compare gender, ASA grade, sedation score and complications. The p-value < 0.05% was considered significant.

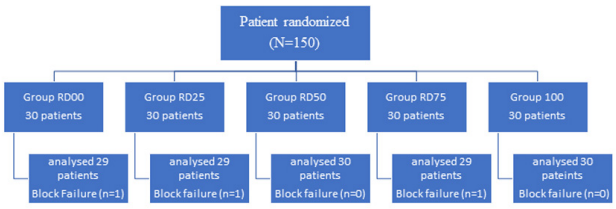

Figure 1. Consort diagram showing the number of patients included and analyzed.

RESULTS

Demographic variables such as age, weight, male to female ratio and ASA grade were comparable between all groups (table 1; p-value > 0.05). Baseline hemodynamic parameters such as HR, SpO_2, SBP and DBP were also comparable between all groups (table 2; p-value > 0.05).

Table 1. Demographic variables

Variables	RD00	RD25	RD50	RD75	RD100	P value
Age(years)	34.6 ± 12.6	36.4 ± 14.3	35.5 ± 12.7	35.6 ± 10.7	34.7 ± 13.4	0.980
Weight(kgs)	55.6 ± 3.9	56.1 ± 4.6	55.6 ± 3.3	55.7 ± 3.2	55.9 ± 3.7	0.769
Male: Female Ratio	19:10	18:11	21:9	19:10	17:13	0.866
ASA grade I: II	27:2	28:1	29:1	28:1	27:3	0.729

P-value < 0.05 – significant; P-value < 0.001 – highly significant : ANOVA test, Chi-square test

Table 2. Baseline hemodynamic parameters (Mean ± SD)

Variables	RD00	RD25	RD50	RD75	RD100	P value
Baseline HR (bpm)	76.1 ± 11.7	81.0 ± 16.8	72.6 ± 11.4	70.5 ± 13.7	76.5 ± 12.8	0.072
Baseline SpO_2(%)	96.8 ± 1.0	97.4 ± 1.7	97.5 ± 2.0	97.5 ± 1.7	97.2 ± 1.6	0.602
Baseline SBP	138.8 ± 16.1	135.6 ± 24.1	130.3 ± 17.0	139.4 ± 22.8	133.8 ± 15.4	0.518
Baseline DBP	78.2 ± 8.3	82.1 ± 12.4	83.1 ± 12.5	81.7 ± 11.7	80.1 ± 11.2	0.619

P-value <0.05 – significant; P-value <0.001 – highly significant: ANOVA test

Compared to RD00, RD25 group showed no significant differences in onset of sensorimotor block, duration of sensorimotor block and duration of analgesia (table 4; p-value > 0.05). In RD50 group, there was statistically significant shortening of onset time of sensorimotor block and prolongation of duration of both sensorimotor block and analgesia compared to RD00 and RD25 group (table 4; p-value < 0.05). Whereas compared to RD75 and RD100 group, RD50 group showed no significant change in onset of sensorimotor block but there was statistically significant prolongation of duration of both sensorimotor block and analgesia (table no. 4). Group RD75 and RD100, with comparison to RD00 and RD25; there was statistically shortening of onset time of sensorimotor block and prolongation of duration of both sensorimotor block and analgesia (table 4, p-value < 0.05).

There was a significant increase in sedation score with increase in dose of dexmedetomidine (table 5, p-value < 0.05). Statistically significant decrease in HR was noted from 5 minutes to 4 hours, whereas decrease in SBP and DBP was noted from 15 minutes to 120 minutes with increase dose of dexmedetomidine (Table not showed). Bradycardia developed in eight patients in RD100 group and six patients in RD75 group which was treated with atropine but was not observed in other three groups. None of the patients in any group, developed hypotension, fall in saturation and hypoxia.

Table 3. Comparison of block parameters (Mean ± SD)

Variables	RD00	RD25	RD50	RD75	RD100	P value
Onset of sensory block (Mins)	17.52 ± 3.0	16.4 ± 3.4	10.6 ± 2.6	9.0 ± 3.4	7.9 ± 3.6	0.000*
Onset of Motor block (Mins)	22.2 ± 3.9	20.2 ± 3.1	14.0 ± 2.4	12.6 ± 3.6	11.6 ± 4.6	0.000*
Duration of sensory block (Mins)	643.6 ± 150.1	674.2 ± 140.1	888.0 ± 163.7	1037.7 ± 122.0	1183.6 ± 238.8	0.000*
Duration of Motor block (Mins)	552.5 ± 150.7	601.0 ± 124.7	753.5 ± 157.0	884.4 ± 99.9	1015.1 ± 197.5	0.000*
Duration of Analgesia (Mins)	700.0 ± 167.2	717.4 ± 128.6	973.6 ± 177.6	1156.5 ± 123.7	1313.5 ± 231.9	0.000*

P-value < 0.05 – significant; P-value < 0.001 – highly significant: ANOVA test

Table 4. Pair wise comparison of block parameters (Scheffe's multiple comparison test)

Variables		RD00 & RD25	RD00 & RD50	RD00 & RD75	RD00 & RD100	RD25 & RD50	RD25 & RD75	RD25 & RD100	RD50 & RD75	RD50 & RD100	RD75 & RD100
Onset of sensory block	P value	0.797	0.000*	0.000*	0.000*	0.000*	0.000*	0.000*	0.451	0.066	0.793
Onset of motor block	P value	0.334	0.000*	0.000*	0.000*	0.000*	0.000*	0.000*	0.722	0.176	0.886
Duration of sensory block	P value	0.977	0.000*	0.000*	0.000*	0.000*	0.000*	0.000*	0.024*	0.000*	0.030*
Duration of motor block	P value	0.824	0.000*	0.000*	0.000*	0.000*	0.000*	0.000*	0.028*	0.000*	0.028*
Duration of Analgesia	P value	0.997	0.000*	0.000*	0.000*	0.000*	0.000*	0.000*	0.003*	0.000*	0.000*

P-value < 0.05 – significant; P-value <0.001 – highly significant: Scheffe's multiple comparison test

Table 5. Comparison of sedation score

Sedation Score	RD00	RD25	RD50	RD75	RD100	P-value
0	22(75.8)	5(17.2)	0	0	0	0.000*
1	6(20.6)	19(65.5)	15(50)	5(17.2)	4(13.3)	
2	1(3.4)	5(17.2)	11(36.6)	15(51.7)	16(53.3)	
3	0	0	4(13.3)	9(31)	10(33.3)	

P-value <0.05 – significant; P-value <0.001 – highly significant: Chi-square test

DISCUSSION

Peripheral nerve blocks have been evolved as alternative to general anesthesia in upper limb surgeries. Our study was created to find the most appropriate minimal dose of dexmedetomidine as an adjuvant to local anesthetic drug with desired clinical effects and minimal side effects. Results of this prospective, randomized double blind comparative study demonstrated that adding 50 mcg dexmedetomidine to 0.5% ropivacaine shortened the onset of sensorimotor block, prolonged the duration of both sensorimotor block and analgesia with no side effects. Whereas, addition of 75 mcg or 100 mcg of dexmedetomidine was associated with bradycardia and caused more sedation.

Dexmedetomidine is highly selective (8 times more selective than clonidine) and a specific alpha-2 adrenergic agonist, having analgesic, sedative, antihypertensive and anesthetic-sparing effects when given by systemic route.[10] Dexmedetomidine added to local anesthetics in regional anesthesia techniques enhances the quality and duration of analgesia.[11,12] The mechanism by which dexmedetomidine affects the nerve block is multi-factorial. Peripherally, it acts by inhibiting the release of nor-epinephrine and also by direct effect on nerve action potential. Centrally, it acts by activation of α2-adrenoreceptors of locus coeruleus and by inhibiting the release of substance P.[13] Dalle et al., had proposed that alpha 2 agonists, by enhancing activity dependent hyperpolarization generated by Na/K pump during repetitive stimulation, increases the threshold for initiating action potential causing blockade of conduction.[14] Kosugi et al., in their study found Dexmedetomidine in high concentrations, inhibit CAPs in frog sciatic nerves without a2 adrenoreceptor activation. Also, Dexmedetomidine decreased the peak amplitude of CAPs reversibly and in a concentration dependent manner. Their action was not antagonized with alpha 2 adrenoreceptor antagonist like Yohimbine and Atipamezole.[15] Swami et al., Agarwal et al., compared equal doses (1 mcg/kg) of clonidine and dexmedetomidine in peripheral nerve block and concluded that that dexmedetomidine is more efficient than clonidine in improving block characteristics.[16,17] Dose of dexmedetomidine as adjuvant to local anesthetic ranges of 0.5-2 mcg/kg has been used in various studies.18 Even the dose of 150 mcg of dexmedetomidine has been associated with minimal side effects.[19] However, some studies have also shown that dexmedetomidine even at 30 mcg can cause significant compromise which challenges its use in peripheral nerve blocks in day care surgeries.[8] Brummet et al. demonstrated a dose dependent increase in sensory and motor blockade duration in rat sciatic nerve with dexmedetomidine as adjuvant to bupivacaine and found that even a very high dose of 40 mcg/kg did not cause any neurotoxicity.[20]

Various studies had been done using different doses of dexmedetomidine as adjuvant to local anesthetics and showed wide ranges of results. In our study, dose of dexmedetomidine equal to or more than 50mcg had faster onset of sensorimotor block which was comparable to result shown by various studies.[17,21-31] In contrast, Gandhi et al. used 30 mcg of dexmedetomidine which showed delay

in onset of sensorimotor block and Marhofer et al., Pillai et al. used lower dose (20 mcg) of dexmedetomidine which showed faster onset of sensorymotor block.[8,13,20,23] Similarly, Rancourt et al. used 1 mcg/kg of dexmedetomidine and Das et al. used 2 mcg/kg of dexmedetomidine and showed no change in onset of sensorimotor block.[19,32] Our study showed no significant difference in onset time of sensorimotor block between three groups (RD50, RD75 and RD100) which was similar to the result shown by Sinha et al, and Singh et al.[33,34] In contrast, some studies showed significant difference in onset of sensorimotor block between 1 mcg/kg and 2 mcg/kg.[21,35-39] Faster onset of sensorimotor block associated with higher dose of dexmedetomidine might be due to its peripheral direct effect on nerve action potentials.[14]

In our study, we observed that dose of dexmedetomidine less than 50 mcg did not prolonged the duration of both sensorimotor block and analgesia. Intergroup comparison showed no statistically significant difference in duration of block and analgesia between RD00 and RD25 group. Balakrishnan et al. also showed similar finding with the lower dose (30 mcg) of dexmedetomidine.[21] Whereas, Gandhi et al. and some studies showed significant prolongation of duration of sensorimotor block and analgesia even with lower dose (0.5 mcg/kg) of dexmedetomidine.[8,13,22,23] In our study, we observed that dose of dexmedetomidine equal to or more than 50 mcg prolonged the duration of both sensorimotor block and analgesia. Inter group comparison showed dose dependent increase in the duration of sensorimotor block and analgesia. These results were comparable with the findings of various studies.[21-23,35-38] In contrast, Sinha et al., Singh et al. showed no difference in duration of sensorimotor block and analgesia between 1 mcg/kg and 2 mcg/kg dose of dexmedetomidine.[33,34] Prolongation of duration of sensorimotor block and analgesia associated with dexmedetomidine might be due to its both peripheral and central effects.[13,14]

Our study showed statistically significant increase in the sedation score with the increment dose of dexmedetomidine which was comparable with results in other studie.[21,22,35,38,39] In this study, baseline hemodynamic parameter like SBP, DBP, O_2 saturation were all comparable between all groups. Statistically significant differences were observed in HR (from 5 minutes to 4 hours) and in SBP, DBP (from 15 minutes to 120 minutes) time interval. Eight patients in group RD100 and six patients in group RD75 developed bradycardia which was managed with atropine. Bradycardia reported with higher dose of dexmedetomidine were also shown in the various studies.[21,27,29,33-35,39] Hypotension was not observed in our study which was also not observed in some studies, whereas study by Zhang et al. and other studies had shown hypotension with higher dose.[21,33-35,39] In this study, we had not observed transient rise in BP initially followed by decrease in both HR and BP whereas it was observed in the study done by Balakrishnan et al. Zhang et al.[21,35] This can be explained by the biphasic response to high dose (1-4 mcg/kg) of dexmedetomidine due to initial stimulation of α2B receptors of vascular smooth muscles.[40]

Fall in saturation and Hypoxia was not observed in our study whereas study shown by Kumari et al. fall in saturation was observed and was easily managed by administering oxygen via venti-mask at 4-5 L/min and there were no significant episodes of hypoxemia.[38]

From our study, we found that higher dose of dexmedetomidine as an adjuvant to local anesthesia in brachial plexus block was associated with improved block parameters, more sedation and hemodynamic changes.

Our study was conducted only in otherwise healthy patients. The effects of dexmedetomidine in patients with renal, hepatic or cardiac compromise cannot be concluded from our study. We did not study the plasma levels of the drug after the block; therefore, we cannot say whether the effect was due to perineural action or systemic absorption. Type and site of the surgeries were varied and was single center study. Time of tourniquet application were not monitored.

CONCLUSION

We compared the clinical effects of varying dose of dexmedetomidine as adjuvant to ropivacaine in USG guided supraclavicular brachial plexus block in this double blind, prospective, randomized comparative study. We observed that the dose of 25 mcg of dexmedetomidine had no any significant improvement in block parameters. With 50 mcg, 75 mcg and 100 mcg of dexmedetomidine, we found faster onset of sensorimotor block and prolongation of duration of both sensorimotor block and analgesia. Both 75 mcg and 100 mcg dose of dexmedetomidine was associated with improved block parameters but also associated with increased incidence of bradycardia, increased sedation and undesirable prolongation of motor block. Thus, we conclude that dexmedetomidine with dose of 50 mcg when used as adjuvant to local anesthesia in peripheral nerve block has longer duration of analgesia, significant improvement in block qualities and no side effects.

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