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Effect of Dexmedetomidine as an adjuvant to ropivacaine on the quality of block and post-operative analgesia in supraclavicular brachial plexus block

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Abstract
Background: Dexmedetomidine has been used as an adjuvant added to local anesthetic to prolong analgesia following peripheral nerve blockade. We aimed at assessing the effect of dexmedetomidine as an adjuvant to ropivacaine in supraclavicular brachial plexus block.
Materials and Methods: 80 patients of ASA grade I and II of age between 20-60 years of either sex were randomized into two equal groups. Group C received 0.5% ropivacaine (30cc) and Group D received 0.5% ropivacaine with 1 μg/kg dexmedetomidine (30cc).
Results: Baseline data was comparable. Sensory and motor block onset was earlier; sensory and motor blockade was prolonged in Group D. Analgesia duration was longer in Group D. Postoperative VAS at 12 h was significantly lower in Group D.
Conclusion: It can be concluded that dexmedetomidine as an adjuvant to 0.5% ropivacaine in supraclavicular brachial plexus block shortens the sensory as well as motor block onset time, prolongs the sensory and motor block duration and time to first analgesic use, and decreases total analgesic use with no side-effects.

Keywords: Dexmedetomidine, Ropivacaine, supraclavicular brachial plexus block

Introduction

Till now general anesthesia was the only option available for surgeries of the upper limb and alleviation of pain, but now brachial plexus block is evolving, which has given the anesthesiologists a safe alternative to general anesthesia. In 1884, Halstead used cocaine for brachial plexus block for the first time, since then there is a significant evolution in brachial plexus block. At that time blind techniques were used, then nerve stimulators came and at present the supraclaviclar brachial plexus block is performed under the ultrasound guidance [1].

With the development in regional anesthesia techniques i.e. the use of local anesthetic medications, newly developed adjuvant drugs and the help of ultrasound has made this technique very safe and effective. Hospital stay has reduced along with cost, and also the side-effects that are seen with general anesthesia are not seen with this technique.

Brachial plexus block has proven to help not only in the intraoperative management, but postoperatively also it provides a long duration of analgesia, keeping the patient relieved from pain. This reduces the need for additional analgesic medication and thus improving the overall patient satisfaction [2].

Ropivacaine is a local amino-amide anesthetic that blocks the peripheral afferents acting on voltage dependent Na+ channels. It is less cardiac and central nervous system toxic than other local anesthetics such as bupivacaine that are long-acting [3].

The reduced lipid solubility of ropivacaine offers greater sensory and motor blockade compared to bupivacaine and levobupivacaine, and prompt motor functions recover more quickly.[4-7] Catheter-based procedures allow for continuous pain relief during the perioperative period, but they also present problems related to patient management, displacement of the catheter postoperatively, and the potential for increased infection.[8]

While an increasing number of randomised controlled trials (RCTs) have shown that adjuvants added to ropivacaine in BPB, such as dexmedetomidine, opioids, clonidine and neostigmine, can extend the analgesic time and decrease analgesic intake after surgery, the anaesthetic effect is therefore better than ropivacaine alone [7-11].

Dexmedetomidine is highly selective (eight times more selective than clonidine) [12]. a specific and potent alpha2-adrenergic agonist with systemic analgesic, sedative, antihypertensive, anxiolytic, and anaesthetic sparing effects.[13] During peripheral nerve blockade[14] and regional anesthesia[15] procedures, the addition of dexmedetomidine to local anaesthetics can also prove effective for surgical patients as it has also been shown to extend the block length and post-operative analgesia [16, 17].

The aim of this study was to see how adding dexmedetomidine as an adjuvant to 0.5 percent ropivacaine affected the onset and duration of sensory and motor block, the quality of the block, and the duration of postoperative analgesia in supraclavicular brachial plexus block.

Materials and Methods

The present prospective, randomized, double-blind controlled trial was carried out after obtaining the approval from the ethics committee of our institution. Eighty patients of American Society of Anesthesiologist (ASA) grades I to II aged between 20 to 60 years of either sex, satisfying the inclusion criteria undergoing elective upper limb surgery below mid-humerus level under supraclavicular brachial plexus block were included after voluntary written informed consent.

The patients were randomized into two groups (Group R and Group R+D) using computer generated numbers. Group R patients received 0.5% ropivacaine (30 cc) and 0.5% ropivacaine with 1 µg/kg dexmedetomidine (30cc) in Group R+D for the same block. Both the patients and the anesthesiologist were blinded to the drug being administered.

Exclusion criteria

Patients with preexisting peripheral neuropathy of upper limb, diabetes, long-term analgesic therapy, bleeding diathesis, local skin site infections, patients on adrenoreceptor agonist or antagonist therapy, history of severe cardiac, respiratory, hepatic or renal disease, pregnancy and known hypersensitivity to the study drugs, were omitted from the study. Patients having a history of significant neurological, psychiatric, or neuromuscular disorders were also excluded.

During the preoperative assessment, history of drug allergy, past surgical history or any long-term medication were inquired. Then general and systemic examination and airway assessments were carried out. Patients were kept on nil by mouth (fasting) for over a 6-hour duration prior to the surgery. All patients were given tabl*et al*prazolam 0.25 mg as a premedication for alleviating anxiety and apprehension, if any. The patients likewise received tablet Ranitidine 150 mg in the night before and on the morning of surgery with sips of water.

After preoperative evaluation, patients were explained about the procedure and also the 10 cm VAS (Visual Analogue Scale) (0, no pain and 10, worst pain imaginable).

All patients underwent routine investigations Hb%, Total leukocyte count, differential leukocyte count, erythrocyte sedimentation rate, platelet count, blood sugar, blood urea, serum creatinine and liver function tests. A 12 lead electrocardiography (ECG) and chest X-rays were also recorded.

Standard ASA monitors such as ECG, pulse oximeter, and non-invasive blood pressure were attached in the operating room, and baseline parameters were registered. In the nonoperative arm, a 20 G cannula was used to gain intravenous access. Ringers' lactate was infused intravenously (i.v.) and oxygen was administered at a rate of 3 L/min via a face mask. Prior to surgery, all patients received an injection of midazolam 0.03 mg/kg.

An experienced anesthesiologist, different from the one who carried out the intra- and post-operative assessments, delivered the brachial plexus block through the supraclavicular approach. The anesthesiologist was also blinded from the treatment groups. After proper explanation of technique and positioning, under all aseptic precautions, interscalene groove was identified where a mark was made approximately 1.5-2.0 cm posterior to the mid-clavicle point. Nerve locater connected to a 22-gauge 5 cm insulated stimuplex® needle was used for nerve localization. The stimulation frequency was set at 1 Hz and the intensity of the stimulating current was initially set to deliver 1.5 mA and was then gradually decreased. When an output current of less than 0.5 mA elicited a mild distal motor response in the forearm and hand, the needle location was deemed appropriate. On negative completion of injection until 30 minutes, then every 30 minutes until the end of surgery, then hourly until the block had fully worn off, then hourly until 12 hours.

Pinpricks in the dermatomal areas conforming to the median nerve, radial nerve, ulnar nerve, and musculocutaneous nerve have been used to determine sensory blockade of each nerve. The onset time of motor blockade was described as the time interval between the end of the local anaesthetic injection and paresis in all nerve distributions.

The time period between the start of sensory block and the first post-operative pain was used to determine the length of sensory block. The time interval between the onset of motor block and complete recovery of motor functions was known as the period of motor block. After 30 min, if the block was adequate, surgery commenced. Injection diclofenac sodium (rescue analgesic) 75 mg was given intravenously when VAS ≥3 cm. Number of injection diclofenac given to each patient during first 24 hour of the post-operative period was recorded.

In the recovery room, anesthesiologist who was also blinded to the treatment groups, carried out the observations. In the recovery room, subjective VAS (scale of 10) was evaluated, then every 15 minutes for first 1 hour, then every 1 hourly for next 4 hours and then every 4 hourly till 12 hours.

Nausea, vomiting, tachycardia (>20% above baseline value), bradycardia (<50 beats per minute), hypotension (<20% below baseline value), hypertension (>20% above baseline value), hypoxemia (SpO_2 <90%), sedation or any other side effect if any, during 24 h postoperative period were assessed. Five score sedation scale was used for assessment of sedation, where a score of 1 = Alert and wide awake, 2 = Arousable to verbal command, 3 = Arousable with gentle tactile stimulation, 4 = Arousable with vigorous shaking, and 5 = Unarousable.

Statistical Analysis

IBM SPSS version 18.0.0.0 (Statistical Package for Social Sciences) software was used to analyse the results. For demographic data, hemodynamic parameters, the onset and length of sensory and motor blockade, and the duration of analgesia, an unpaired t-test was used. Categorical variables were analyzed using the Pearson's Chi-square test.

Normally, distributed continuous variables were analyzed using the independent sample *t*-test and $P < 0.05$ was considered as statistically significant.

Results

In the present study 40 patients were enrolled into two randomized groups – Group R (n=40) and Group R+D (n=40).

The mean age in Group R was 38.20 ± 14.49 years and in Group R+D was 35.00 ± 12.31. The mean age in both the groups were comparable (p=0.291).

The mean weight in Group R was 62.93 ± 6.81 kg and in Group R+D was 62.50 ± 7.74 kg, which was statistically comparable (p=0.795). In both the groups, there was no statistically significant difference in ASA status.

At preoperative time, the mean heart rate was comparable between the two groups (80.93 ± 9.29 in Group R vs. 81.65 ± 7.85 in Group R+D, p value = 0.707), while after giving the drugs, the mean heart rate was significantly lower in Group R+D in comparison to Group R (74.43 ± 9.70 vs. 79.40 ± 8.84, p value = 0.019). (Table 1)

The mean systolic and diastolic blood pressure before the surgery and after administration of drug was comparable between the two groups ($p>0.05$).

Mean sensory block onset (min) was significantly faster in the Group R+D in comparison to the Group R (4.53 ± 1.87 min vs. 13.43 ± 1.75 min, p value = 0.001) and duration of sensory block was significantly longer in the Group R+D in comparison to Group R (649.75 ± 69.75 min vs. 466.48 ± 65.34 min, p value = 0.001). (Table 2)

Also, mean motor block onset (min) was significantly quicker in the Group R+D in comparison to the Group R (7.25 ± 2.26 min vs. 17.05 ± 1.99 min, p value = 0.001) and duration of motor block was significantly longer in the Group R+D in comparison to Group R (567.30 ± 69.29 min vs. 409.18 ± 53.17 min, p value = 0.001). (Table 2)

The mean duration to first analgesic requirement was significantly longer in Group R+D in comparison to Group R (663.00 ± 74.11 min vs. 475.28 ± 73.56 min, p value = 0.001). (Table 3)

The total analgesic requirement was significantly lower in Group R+D in comparison to Group R (0.68 ± 0.62 mg vs. 2.65 ± 0.48 mg, p value = 0.001).

The mean VAS was comparable between the two groups till 2 hours, after 2 hours, it was significantly lower in the Group R+D in comparison to Group R ($p<0.05$). (Table 4)

In Group R+D, only 1 (2.5%) patient experienced longer sedation, while 7 (17.5%) patients experienced hypotension. Though none of the patients required intervention for the management of hypotension. (Figure 1)

Table 1: Comparison of mean heart rate between the two groups at preoperative and after drug

Heart Rate	Group R [Mean±SD]	Group R+D [Mean±SD]	't' value	P value
Preoperative	80.93 ± 9.29	81.65 ± 7.85	-0.377, df=78	0.707, NS
After drug	79.40 ± 8.84	74.43 ± 9.70	2.397, df=78	0.019*

Unpaired 't' test applied. P value < 0.05 was taken as statistically significant

Table 2: Sensory and motor block onset and duration comparison between the two groups

Parameter	Group R [Mean±SD]	Group R+D [Mean±SD]	't' value	P value
Sensory block onset time (min)	13.43 ± 1.75	4.53 ± 1.87	21.981, df=78	0.001*
Sensory block duration time (min)	466.48 ± 65.34	649.75 ± 69.75	-12.129, df=78	0.001*
Motor block onset time (min)	17.05 ± 1.99	7.25 ± 2.26	20.590, df=78	0.001*
Motor block duration time (min)	409.18 ± 53.17	567.30 ± 69.29	-11.451, df=78	0.001*

Unpaired 't' test applied. P value < 0.05 was taken as statistically significant

Table 3: Comparison of time to first analgesic requirement and total analgesic requirement between the two groups

Parameter	Group R [Mean±SD]	Group R+D [Mean±SD]	't' value	P value
Time to first analgesic requirement (min)	475.28 ± 73.56	663.00 ± 74.11	-11.370, df=78	0.001*
Total analgesic need (mg)	2.65 ± 0.48	0.68 ± 0.62	15.965, df=78	0.001*

Unpaired 't' test applied. P value < 0.05 was taken as statistically significant

Table 4: Comparison of mean heart rate between the two groups at preoperative and after drug

VAS	Group R [Mean±SD]	Group R+D [Mean±SD]	't' value	P value
0 minute	0.00 ± 0.00	0.00 ± 0.00	-	-
15 minutes	0.00 ± 0.00	0.00 ± 0.00	-	-
30 minutes	0.00 ± 0.00	0.00 ± 0.00	-	-
45 minutes	0.00 ± 0.00	0.00 ± 0.00	-	-
1 hour	0.00 ± 0.00	0.08 ± 0.47	-1.000, df=78	0.320, NS
2 hours	0.00 ± 0.00	0.15 ± 0.95	-1.000, df=78	0.320, NS
3 hours	0.40 ± 0.90	0.00 ± 0.00	2.810, df=78	0.006*
4 hours	1.75 ± 1.48	0.05 ± 0.32	7.101, df=78	0.001*
8 hours	4.78 ± 2.03	1.05 ± 1.66	8.972, df=78	0.001*
12 hours	5.15 ± 0.77	2.93 ± 2.23	5.954, df=78	0.001*

Unpaired 't' test applied. P value < 0.05 was taken as statistically significant

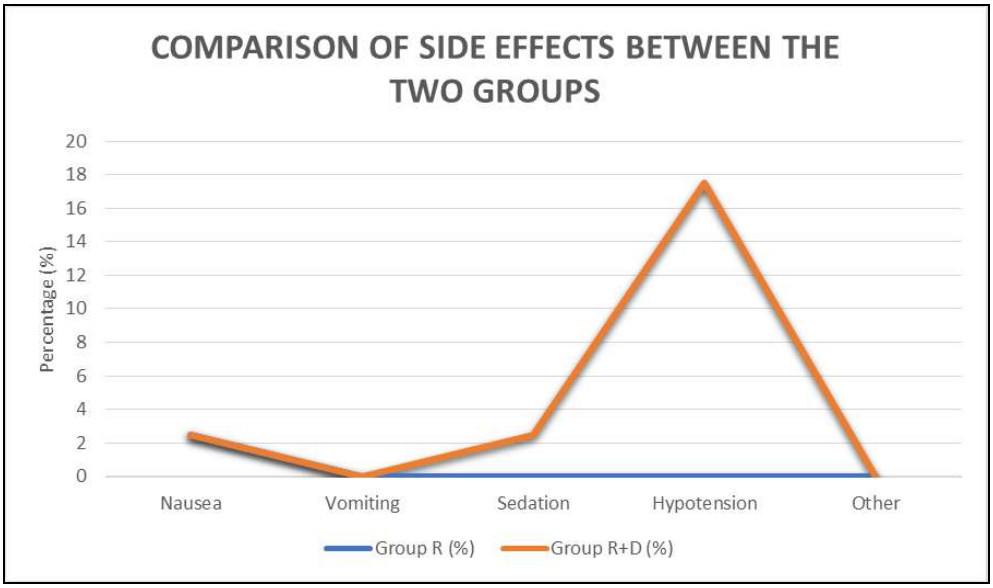

Fig 1: Line diagram showing comparison of side effects between the two groups

Discussion

The mechanism of the analgesic actions of α_2 agonists has not been fully elucidated and is probably multifactorial. A number of supraspinal and spinal sites modulate the transmission of nociceptive signals in the CNS. Peripheral α_2 adrenoceptors may also mediate the antinociception [18]. α_2 blockers by acting at any of these sites reduce nociceptive transmission, leading to analgesia. The activation of inwardly rectifying G_1 -protein-gated potassium channels resulting in membrane hyperpolarization and decreasing the firing rate of excitable cells in the CNS is considered to be a significant mechanism of the inhibitory neuronal action of α_2 -adrenoceptor agonists [19]. Reduction of calcium conductance into cells, thus inhibiting neurotransmitter release is other prominent physiologic action ascribed to α_2 adrenoceptors. This effect involves direct regulation of entry of calcium through N-type voltage-gated calcium channels and is independent of cAMP and protein phosphorylation and is mediated by G_0 proteins. These mechanisms reflect two very different ways of causing analgesia: the nerve is prevented from firing, and signal propogation to neighbours is also prevented.

We had randomized 40 patients each in Group R and Group R+D to receive 0.5% ropivacaine (30 cc) and 0.5% ropivacaine with 1 µg/kg dexmedetomidine (30cc) for the same block, respectively. The age and weight were comparable between the two groups ($p>0.05$). Das *et al.* [20] reported comparable distribution of age, sex, body weight, ASA status and duration of surgery in Group Ropivacaine+Dexmedetomidine and Group Ropivacaine. Also, in the study done by Bangera *et al.* [22] the baseline parameters of age, weight, gender and ASA grades were comparable between Group R+D and Group R ($p>0.05$), which is comparable to our study findings.

The mean heart rate preoperatively was comparable between the two groups, but after drug administration, it fell significantly in Group R+D ($p<0.05$). The mean systolic and diastolic blood pressures remained comparable between the two groups before surgery and after administration of drugs ($p>0.05$). Fritsch *et al.* [21] in their study also reported that dexmedetomidine lowered the heart rate but blood pressures were stable, which is similar to our findings. Bangera *et al.* [22] reported a significant decrease in heart rate, systolic blood pressure and diastolic blood pressure in group RD ($p<0.05$), but none of the patients had either bradycardia or hypotension requiring intervention.

The mean sensory and motor block onset times were significantly quicker in the group R+D in comparison to Group R ($p<0.05$). Das *et al.* [20] though reported earlier mean sensory and motor block onset in their study in group ropivacaine+dexmedetomidine, but the difference statistically not significant ($p>0.05$), while in our study, we found a significant difference. Fritsch *et al.* [21] in their study reported a significantly quicker sensory and motor block in group receiving dexmedetomidine ($p<0.05$). Bangera *et al.* [22] in their study also reported a significantly early onset of motor and sensory block in Group RD in comparison to Group R ($p<0.05$). Marhofer *et al.* [23] in their study also reported a significantly faster mean sensory and motor block time ($p<0.05$) in group receiving dexmedetomidine in comparison to ropivacaine alone group.

The duration of both sensory and motor block were significantly longer in the Group R+D ($p<0.05$), while Das *et al.* [20] also found significantly longer duration of sensory and motor block in ropivacaine+dexmedetomidine group ($p<0.05$). The median duration of nerve block was considerably lower in dexmedetomidine group in comparison to ropivacaine group in the study done by Fritsch *et al.* [21] Bangera *et al.* [22] in their study also reported a considerably longer duration of motor and sensory block in Group RD in comparison to Group R ($p<0.05$). Marhofer *et al.* [23] also reported a significantly longer duration of sensory and motor block in dexmedetomidine group ($p<0.05$). The results of the studies are comparable to our findings [20-23]

A significantly longer duration of analgesia was found in the Group R+D in comparison to Group R ($p<0.05$), hence the requirement of analgesia was also significantly small in Group R+D ($p<0.05$). Das *et al.* [20] also reported significantly lower requirement of analgesia in their study in group receiving dexmedetomidine. Bangera *et al.* [22] also found significantly longer analgesia duration in Group RD ($p<0.05$), which is comparable to our study findings.

The mean pain score as assessed using VAS was comparable till 2 hours of surgery, but after that time, it was significantly lower in the Group R+D ($p<0.05$). In the study

done by Fritsch *et al*. [21] the pain score was significantly lower for 14 hours after surgery in the dexmedetomidine group. Our findings are comparable.

Seven patients of Group R+D experienced hypotension, while none in the Group R. Fritsch *et al*. [21] did not report any side effects in their study in both the groups. Bangera *et al*. [22] in their study did not report any incidence of bradycardia or hypotension, while in our study we found hypotension in 7 patients. Though, no intervention was required for the management of hypotension.

The only limitation of our study was that we did not experiment with different doses of dexmedetomidine. As a result, we suggest that newer studies be performed with various doses of dexmedetomidine to determine the most effective and lowest dose for supraclavicular brachial plexus block.

Conclusion

The results of our study show that using dexmedetomidine as an adjuvant to ropivacaine in the supraclavicular brachial plexus block is very promising. Except for a substantial decrease in heart rate following drug administration, the mean systolic and diastolic blood pressures were comparable in both groups. In contrast to the ropivacaine group, the dexmedetomidine group had a significantly shorter sensory and motor block onset period and a significantly longer sensory and motor block length.

All other parameters evaluated between the ropivacaine alone and dexmedetomidine+ropivacaine groups were comparable. The only side effect associated with the addition of dexmedetomidine was hypotension, which did not require any intervention in our research.

We highly recommend the use of dexmedetomidine as an adjuvant in supraclavicular brachial plexus block for the surgeries of the upper limb.

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