

## A Comparative Study of the Efficacy of Dexmedetomidine and Clonidine as an Adjuvant to Bupivacaine in Supraclavicular Brachial Plexus Block

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### Abstract

**Background:** Supraclavicular brachial plexus block is preferable to general anesthesia in upper limb surgeries. Various adjuvants have been added to improve the quality of the block and prolong postoperative analgesia. Alpha-2 agonists are used as adjuvants to local anesthetics to extend the duration of neuraxial and peripheral nerve blocks. We compared clonidine and dexmedetomidine as an adjuvant to bupivacaine in supraclavicular brachial plexus block. **Aims:** To compare the effects of Clonidine and Dexmedetomidine when added as adjuvant to Bupivacaine on onset and duration of sensory & motor block, duration of analgesia and quality of block for Supraclavicular brachial plexus block. **Methods:** In this prospective, double-blinded study 60 ASA I-II patients were randomly divided into two groups of 30 each. First group received 30 ml bupivacaine 0.325% with Clonidine 1 mcg/kg (Group C) and second group received 30 ml bupivacaine 0.325% with dexmedetomidine 1 mcg/kg (Group D) in Supraclavicular brachial plexus. The characteristics for anesthesia and analgesia were assessed for the two groups. **Results:** Onset of sensory block was faster in Group D than in Group C, while onset of motor block was faster in Group C than in Group D, but the difference was not statistically significant. Duration of sensory block and motor block was  $234.17 \pm 24.11$  min and  $296.30 \pm 25.78$  min in Group C as compared with  $445.07 \pm 67.79$  min and  $503.10 \pm 75.67$  min in Group D. Statistically significant longer duration of sensory and motor block was observed in Group D ( $p < 0.001$ ). There was significant increase in duration of analgesia in Group D ( $477.27 \pm 70.11$  min) as compared with Group C ( $285.43 \pm 26.88$  min). In Group D, 83.3% of the patients achieved Grade IV quality of block as opposed to 43.3% in Group C ( $p = 0.006$ ). **Conclusion:** To conclude, dexmedetomidine prolongs the duration of sensory and motor block and enhances the quality of block as compared with clonidine when used as an adjuvant to Bupivacaine. The added advantage of conscious sedation, hemodynamic stability, and minimal side-effects makes it a potential adjuvant for nerve blocks.

**Keywords:** Bupivacaine; Clonidine; Dexmedetomidine; Supraclavicular brachial plexus block.

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### Introduction

Most of the upper limb surgeries are performed under brachial plexus block. Peripheral nerve

blocks provides intraoperative anesthesia and postoperative analgesia without any systemic side-effects.<sup>1</sup> Supraclavicular brachial plexus block provides safe, effective, low-cost anesthesia with good postoperative analgesia.

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Clonidine, a partial  $\alpha_2$  adrenoceptor agonist is used as adjuvant to local anesthetics to prolong the peripheral nerve block duration.<sup>2-4</sup> The  $\alpha_2 : \alpha_1$  selectivity of dexmedetomidine is eight times that of clonidine and it has high specificity for  $\alpha_2$  subtype which makes it a much more effective sedative and analgesic agent.<sup>5</sup>

Dexmedetomidine is being used for intravenous (IV) sedation and analgesia for intubated and mechanically ventilated patients in Intensive Care Units (ICUs),<sup>6,7</sup> and nonintubated patients for surgical and other procedures.<sup>8</sup> In previous clinical studies, the use of IV dexmedetomidine lead to significant opioid sparing effects and decrease in inhalational anesthetic requirements.<sup>9</sup> It has been described to improve the quality of intrathecal and epidural anesthesia.<sup>10-13</sup> This study was designed to test the hypothesis that dexmedetomidine when added as an adjuvant to bupivacaine in supraclavicular brachial plexus block increases the sensory and motor block duration, duration of analgesia and block quality when compared with clonidine.

## Materials and Methods

A prospective randomized double-blind clinical trial was carried out on sixty ASA I and II patients planned for elective upper limb surgeries under supraclavicular brachial plexus block after obtaining written informed consent and ethical committee approval. They were divided into two groups (Group C and Group D) of 30 patients each.

*Group C:* Received clonidine 1  $\mu\text{g}/\text{kg}$  + bupivacaine 0.325% (30 cc), and

*Group D:* Received dexmedetomidine 1  $\mu\text{g}/\text{kg}$  + bupivacaine 0.325% (30 cc).

Patients with significant neurological & neuromuscular deficit, cardiovascular, pulmonary, alcohol or drug abuse, pregnancy or lactating women and patients on adrenoceptor agonist or antagonist therapy or on sedatives, antipsychotic therapy were excluded from this study. Patient refusal for procedure, morbid obesity, peripheral vascular disease, coagulopathy, or known allergies were also excluded.

On arrival in the operation room, basal Heart Rate (HR), noninvasive Systolic Blood Pressure (SBP) & Diastolic Blood Pressure (DBP), and Oxygen Saturation ( $\text{SpO}_2$ ) were recorded. An 18/20 gauge (G) IV cannula was secured in nonoperated arm and Ringer's lactate was started.

Patients were allocated randomly into two groups. Anesthesiologist not involved in the study prepared the drug solutions. The anesthesiologist conducting the block and monitoring the patient was blinded to the treatment group. The same anesthesiologist collected the data who was unaware of the group allocation.

Neural localization was done by using a nerve stimulator (B Braun) connected to a 22 G, 5 cm length stimulating needle (Stimuplex, Braun). The location end point was a distal motor response with an output lower than 0.5 mA in the median nerve region. 30 mL of a solution containing local anesthetic combined with clonidine or dexmedetomidine as mentioned above was injected. Negative aspiration was done every 5 ml to avoid intravascular injection while injecting drug solution. A 3-min massage was performed to avoid an uneven drug distribution.

Sensory block was assessed in the distribution of four nerve territories of median nerve, radial nerve, ulnar nerve and musculocutaneous nerve by pin prick test using a 3-point scale. Sensory block assessment was done at each minute after completion of drug injection until total sensory blockade. Onset of sensory block was appraised when there was a dull sensation to pin prick and complete sensory block was appraised when there was complete loss of sensation to pin prick along the distribution of any of the above mentioned nerves.

Sensory block was graded<sup>25</sup> as:

*Grade 0:* Sharp pin prick felt;

*Grade 1:* Analgesia, loss of sensation of pin prick;

*Grade 2:* Anesthesia, loss of sensation of touch.

Motor block was determined by thumb abduction (radial nerve), thumb adduction (ulnar nerve), thumb opposition (median nerve), and flexion of elbow (musculocutaneous nerve) according to the modified Bromage scale<sup>14</sup> on a 3-point scale. At each minute motor block assessment was carried out by the same observer until total motor blockade after drug injection.

Motor block was graded as:

*Grade 0:* Normal motor function with full flexion and extension of elbow, wrist, and fingers;

*Grade 1:* Decreased motor strength with ability to move the fingers only;

*Grade 2:* Complete motor block with inability to move the fingers.

Sensory block onset time was defined as the time interval between the end of local anesthetic administration and complete sensory block (score 2 for all nerves). Sensory block duration was defined as the time interval between the complete sensory block and complete resolution of anesthesia on all the nerves (score 0). Motor block onset time was defined as the time interval between total local anesthetic administration and complete motor block (Grade 2). Motor block duration was defined as the time interval from complete motor block to complete recovery of motor function of hand and forearm (Grade 0).

The block was contemplated incomplete when any of the segments supplied by ulnar, radial, median and musculocutaneous nerve did not have analgesia even after 20–30 min of drug injection.

These patients were supplemented with IV fentanyl (1–2 µg/kg) and midazolam (0.02 mg/kg). We considered block failed when two or more nerves unaffected. In this case, general anesthesia was given intraoperatively.

HR, SBP, and DBP were recorded at 0, 15, 30, 60, 90, and 180 min intraoperatively and every 60 min postoperatively. The modified Ramsay Sedation Scale (RSS)<sup>15</sup> was used to assess sedation score from 1–6 as follows:

- 1 = Anxious, agitated, restless;
- 2 = Cooperative, oriented, tranquil;
- 3 = Responds to commands only;
- 4 = Brisk response to light glabellar tap or loud noise;
- 5 = Sluggish response to light glabellar tap or loud noise;
- 6 = No response to stimulus.

Blood loss was calculated by the gravimetric method and replaced if more than the allowable blood loss. Duration of surgery was noted.

The quality of operative conditions were assessed according to the following numeric scale<sup>16</sup>:

- Grade 4:* No complaint from patient (Excellent);
- Grade 3:* Minor complaint with no need for the supplemental analgesics (Good);
- Grade 2:* Complaint that required supplemental analgesia (Moderate);
- Grade 1:* Patient given general anesthesia (Unsuccessful).

The intra- and postoperative assessment was done by an anesthesiologist who was unaware of the drug used. Duration of Analgesia (DOA) is the time between the complete sensory block and the first analgesic request. Patients were assessed for duration of analgesia as per a numeric rating scale of 0 to 10. Postoperatively, numeric rating scale was recorded every 60 min until the score of 5.

The rescue analgesia was given in the form of Inj. diclofenac sodium (1.5 mg/kg) intramuscularly at the Numeric Rating Scale of 5 and the time of administration was noted. Patients were observed for any side-effects like nausea, vomiting, dryness of mouth and also observed for complications like pneumothorax, hematoma, local anesthetic toxicity and postblock neuropathy in the intra and postoperative periods.

### Statistical Methods

Descriptive and inferential statistical analysis has been used in our study. Continuous measurement results are presented on Mean ± SD (Minimum-Maximum) and results on categorical measurements are presented in percentage numbers (%). 'p - value of less than 0.05' was considered to be significant. The following assumptions on data were made - dependent variables were normally distributed, random sampling from the population was ensured and the cases of the samples were independent.

Student *t*-test (two tailed, independent) and Chi-square/Fisher Exact test were used to assess the significance of study parameters on continuous scale for inter group analysis on metric parameters and categorical scale between two or more groups respectively. Levene's test for homogeneity of variance has been performed to assess the homogeneity of variance and  $p \leq 0.01$  was considered to be strongly significant.

### Results

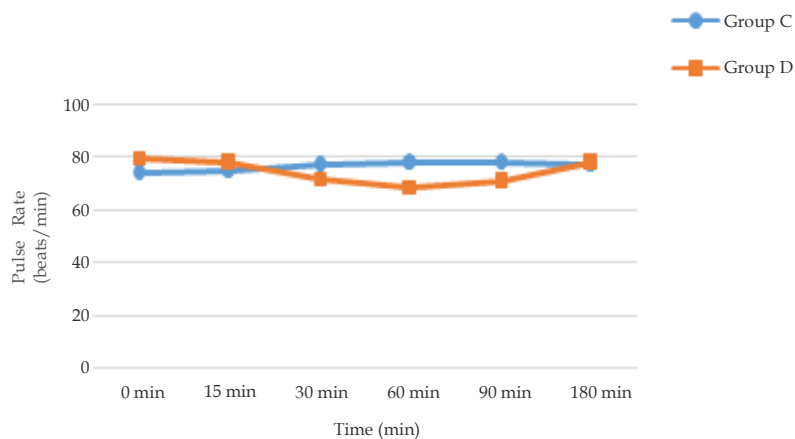
Sixty patients fulfilling the inclusion criteria were randomly assigned to one of the two groups. The demographic data and surgical characteristics were comparable in both groups, showed in Table 1, ( $p > 0.001$ ).

The baseline hemodynamic parameters were comparable in both groups. Significantly lower pulse rate was observed at 30, 60 and 90 min, but not less than 60 beats/min, in Group D as compared with Group C, showed in Fig. 1, ( $p < 0.001$ ).

**Table 1:** Demographic data

Parameters	Group C (n = 30) Clonidine Mean ± SD)	Group D (n = 30) Dexmedetomidine (Mean±SD)	p - value
Age (years)	36.87 ± 10.89	39.67 ± 11.41	0.335 (NS)
Weight (kg)	58.87 ± 7.75	60.77 ± 7.99	0.354 (NS)
Gender (M/F)	18/12	12/18	1.000 (NS)
<b>Type of surgeries</b>			
# Lower end of humerus	6	4	
# Elbow (Olecranon)	4	4	
# Radius & ulna	20	22	

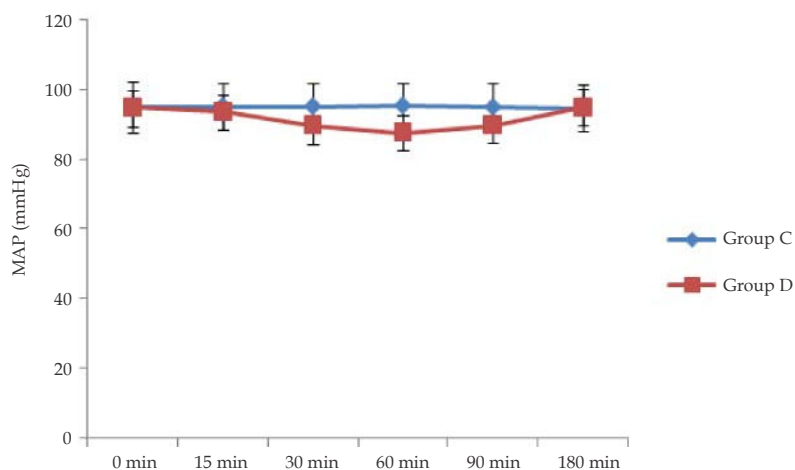
n = Number of patients; SD = Standard Deviation; p < 0.05 significant; NS= Not significant; M = Male; F = Female; Kg = Kilogram; # = Fracture.



**Fig. 1:** Comparison of Pulse rate in both the groups.

Systolic blood pressure, diastolic blood pressure and mean arterial blood pressure were found to be significantly lower than baseline from 30 to 90 min in Group D as compared with

Group C ( $p < 0.001$ ). Treatment was not required for this fall in blood pressure. The hemodynamic parameters were comparable at the end of 180 min, (Fig. 2).



**Fig. 2:** Comparison of mean arterial pressures in both the groups.

Sensory block onset was faster in Group D than in Group C, while onset of motor block was faster in Group C than in Group D, but statistically the

difference was not highly significant, Table 2, ( $p > 0.001$ ).

**Table 2:** Onset of Sensory block and Motor block

Onset of block (min)	Group C (Mean $\pm$ SD)	Group D (Mean $\pm$ SD)	<i>p</i> - value
Sensory	2.69 $\pm$ 0.55	2.82 $\pm$ 0.51	0.348 (NS)
Motor	4.95 $\pm$ 1.55	5.75 $\pm$ 1.52	0.047 <sup>+</sup>

S = Not significant; SD = Standard deviation; + : Suggestive Significance.

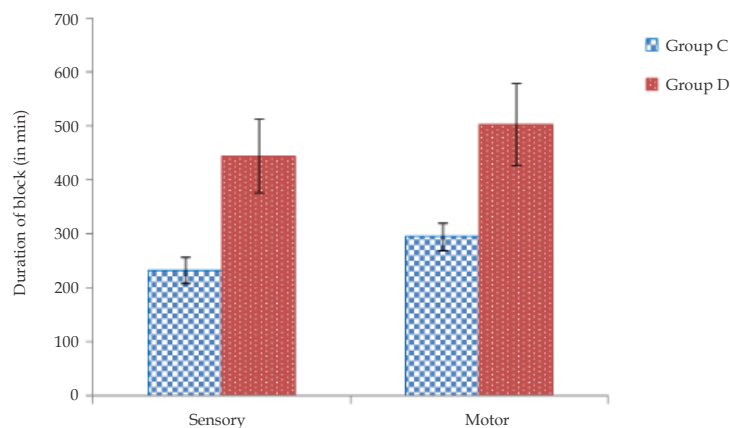
Duration of sensory block was 234.17  $\pm$  24.11 min in Group C as compared with 445.07  $\pm$  67.79 min in Group D. Statistically significant longer duration of sensory block was observed in Group D, showed in Table 3 and Fig. 3, (*p* < 0.001). The

duration of motor block was 296.30  $\pm$  25.78 min in Group C as compared with 503.10  $\pm$  75.67 min in Group D. Again, duration of motor block was significantly longer in Group D, Table 3 and Fig. 3, (*p* < 0.001).

**Table 3:** Duration of Sensory and Motor block and duration of analgesia

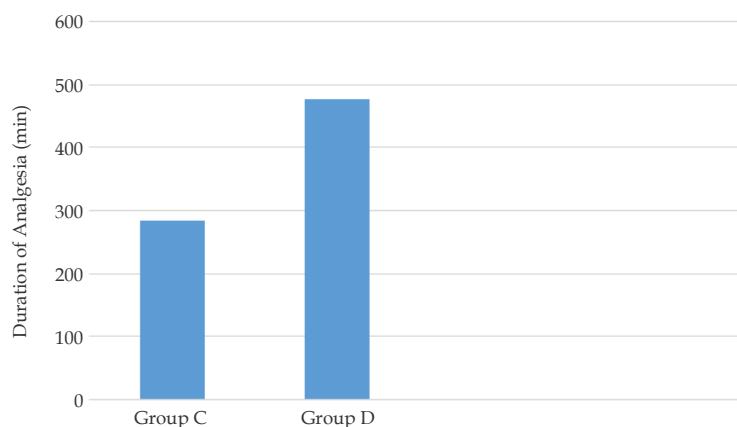
Duration (min)	Group C (Mean $\pm$ SD)	Group D (Mean $\pm$ SD)	<i>p</i> - value
Sensory	234.17 $\pm$ 24.11	445.07 $\pm$ 67.79	< 0.001*
Motor	296.30 $\pm$ 25.78	503.10 $\pm$ 75.67	< 0.001*
Analgesia	285.43 $\pm$ 26.88	477.27 $\pm$ 70.11	< 0.001*

SD = Standard Deviation; Min= Minutes; \* = Highly significant.

**Fig. 3:** Comparison of duration of block in both the groups.

There was significant increase in duration of analgesia in Group D (477.27  $\pm$  70.11 min) as compared with Group C (285.43  $\pm$  26.88 min). The

difference was statistically significant, Table 3 and Fig. 4, (*p* < 0.001).

**Fig. 4:** Comparison of duration of Analgesia in both the groups.

In Group D, 83.3% of the patients achieved Grade IV quality of block as opposed to 43.3% in Group C ( $p = 0.006$ ). 17 patients in Group C with Grade II and III block and 5 patients in Group D needed sedation or sedation with analgesia. One patient

in Group C needed general anesthesia as the block was inadequate, (Table 4).

Side-effects like nausea, vomiting, dry mouth were not reported in the postoperative period in both the groups.

**Table 4:** Quality of block

Quality of block	Group C		Group D	
	No	%	No	%
I	0	0.0	0	0.0
II	8	26.7	2	6.7
III	9	30.0	3	10.0
IV	13	43.3	25	83.3
<b>Total</b>	30	100.0	30	100.0

No: Number of patients; % = Percentage of patients.

## Discussion

In this randomized, double-blinded trial, we compared dexmedetomidine and clonidine as an adjuvant to Bupivacaine in supraclavicular brachial plexus block, and found that there was a significantly increased sensory and motor block duration in the dexmedetomidine group than in the clonidine group.

Mechanism of action of clonidine: Clonidine was used for its antihypertensive properties. The central actions are mediated through  $\alpha_2$  adrenoceptors. Specific peripheral effects of clonidine appear to be less obvious because  $\alpha_2$  adrenoceptors are not present on the axon of the normal peripheral nerve.<sup>4</sup> The mechanism of action of clonidine varies, which are centrally mediated analgesia,  $\alpha_2$   $\beta$  adrenoceptor-mediated vasoconstrictive effects, attenuation of inflammatory response and direct action on peripheral nerve.<sup>17</sup>

Dalle et al. advocated that clonidine, by enhancing the Na/K pump during repetitive stimulation, increases the threshold for initiating the action potential causing slowing or blockage of conduction.<sup>18</sup> Kosugi et al. studied the effects of various adrenoceptor agonists and antagonist on Compound Action Potential (CAP) recorded from frog sciatic nerve, and found that CAPs were inhibited by  $\alpha_2$  adrenoceptor agents so that, they are able to block nerve conduction.<sup>19</sup> The increased effect of low-dose clonidine on lidocaine-induced inhibition of action potential of C-fibers and A $\delta$  fibers (Gaumann et al., 1992;<sup>20</sup> Butterworth and Strichartz, 1993) together with synergistic mechanism of action with local anesthetics (Eledjam et al., 1991) may be the possible explanation to the direct peripheral action.<sup>21</sup>

Studies shown that clonidine as an adjuvant to bupivacaine prolongs the duration of anesthesia and analgesia in brachial plexus block,<sup>2,3</sup> but with side-effects like bradycardia, hypotension, and respiratory depression. In our study, we observed slight hypotension during 30 to 90 minutes duration.

### Mechanism of action of dexmedetomidine

As both dexmedetomidine and clonidine belong to same group i.e.  $\alpha_2$  agonist, there is similarity in the mechanism of analgesic effects. Brumett et al. showed that dexmedetomidine increases duration of bupivacaine anesthesia and analgesia of sciatic nerve block in rats.<sup>17</sup>

Another study showed that perineural dexmedetomidine added to ropivacaine for sciatic nerve block in rats prolonged the duration of analgesia by blocking the hyperpolarization-activated cation, that prevents the nerve from returning from a hyperpolarized state to resting membrane potential for subsequent firing.<sup>22</sup>

Studies have demonstrated side-effects like bradycardia, hypotension with dexmedetomidine. In our study, we observed hypotension during 30 to 90 minutes duration. Baroreceptor reflex and HR response to vasopressors is preserved with the use of dexmedetomidine which helps in the treatment of hypotension and bradycardia easily.

Esmaoglu et al. studied dexmedetomidine with levobupivacaine for axillary brachial plexus block and showed that dexmedetomidine shortens the both sensory and motor block onset, prolongs the duration of block and postoperative analgesia.<sup>23</sup> It may be because peripheral  $\alpha_2$  agonist produces analgesia by reducing release of norepinephrine,

leading to  $\alpha_2$  receptor-independent inhibitory effects on nerve fiber action potentials.<sup>16,24</sup>

Many studies were conducted for  $\alpha_2$  agonist peripheral nerve action and most of them were on animals with few human studies. A study showed increased duration of sensory blockade by adding dexmedetomidine to bupivacaine and levobupivacaine in greater palatine and axillary brachial plexus nerve blocks respectively.<sup>23,24</sup> Archana Tripathi et al.<sup>26</sup> concluded dexmedetomidine (1  $\mu\text{g}/\text{kg}$ ) as an adjuvant prolongs the duration of sensory and motor block and analgesia duration and improves the anesthesia quality when injected with bupivacaine (39 ml of 0.25%) as compared with clonidine (1  $\mu\text{g}/\text{kg}$ ) in supraclavicular brachial plexus block. Rajaclimax Kirubahar et al.<sup>27</sup> concluded that dexmedetomidine (2  $\mu\text{g}/\text{kg}$ ) as an adjuvant to bupivacaine (35 ml of 0.375%) in supraclavicular brachial plexus block shortens the onset time to sensory and motor block and prolongs the analgesia duration when compared to clonidine (2  $\mu\text{g}/\text{kg}$ ). In our study, we used low-volume of bupivacaine when compared to other studies.

In our study, we compared the addition of clonidine (Group C 1  $\mu\text{g}/\text{kg}$ ) and dexmedetomidine (Group D 1  $\mu\text{g}/\text{kg}$ ) to 30 ml of bupivacaine (0.325%) in supraclavicular brachial plexus block. The result of our study shows that all patients in both groups were comparable with respect to demographic profile, duration of surgery and type of surgery. With these doses, we had stable hemodynamics in patients, except for fall in blood pressure during 30 to 90 minutes, fall in blood pressure was more pronounced in dexmedetomidine group than compared to clonidine group.

In our study, sensory block onset was a little faster with Group D as compared with Group C which was statistically insignificant, while motor block onset was a little longer in Group D which was mildly significant statistically. The duration of analgesia was longer in Group D when compared to Group C which was statistically significant. In our study, the quality of block in 83% of the patients in Group D was Grade IV (excellent block) while only 43% in Group C achieved Grade IV quality. This improved quality of block observed in Group D might be the result of various mechanisms of nerve conduction block such as hyperpolarization,<sup>4</sup> decreased CAP<sup>19</sup> and inhibition of voltage gate of sodium pump.

In our study, there was no significant sedation observed, mild arousable sedation was observed during intraoperative and postoperative period.

From our study, we would like to suggest that dexmedetomidine can be safely used with bupivacaine in peripheral nerve blocks; Further trials are needed to determine the exact dose and effect of neurotoxicity on the human nerve.

## Conclusion

We would like to conclude that dexmedetomidine prolongs the sensory and motor block duration and escalates the quality of block when compared with clonidine as an adjuvant to Bupivacaine in peripheral nerve block. The additional benefit of hemodynamic stability, conscious sedation and minimal side-effects makes it a promisable adjuvant for nerve blocks. Further studies with large sample sizes are warranted to validate these findings.

**Support:** Nil

**Conflicts of interest:** Nil

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