Original Research Article

Indian Journal of Anesthesia and Analgesia
2018; 5(9): 1469-1475
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.5918.7

Comparison of Dexmedetomidine and Clonidine as Adjuvant to Bupivacaine in Ultrasound Guided Supraclavicular Brachial Plexus Block

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Abstract

Background and Aims: We compared analgesic effect of dexmedetomidine and clonidine as adjuvant to 30 ml solution of 0.25% bupivacaine in ultrasound guided supraclavicular brachial plexus block. *Materials and Methods:* Ninety patients scheduled for upper limb orthopedic surgeries were allocated to one of the three groups; control group B (n=30), clonidine group C (n=30), and the dexmedetomidine group D (n=30) in a randomized double blind fashion. In group B 1 ml Normal Saline; in group C 1 ml Clonidine (0.75µg/kg); and in Group D 1 ml Dexmedetomidine (0.75µg/kg); were added to 30 ml of 0.25% bupivacaine and administered during ultrasound guided supraclavicular brachial plexus block. Patients were evaluated for onset and duration of sensory and motor block along with duration of analgesia, sedation, side effects, if any. Hemodynamic parameters were also monitored. *Results:* The groups were comparable with respect to demographic parameters. Patients in group D had earlier onset as well as prolonged duration of sensory and motor block compared to group B and group C, which was statistically significant ($p < 0.001$). Mean Duration of analgesia was 301.5± 48.7 minutes in group B, 456.7±75.8 minutes in group C and 585.0±99.4 minutes in group D. On comparison duration of analgesia was significantly prolonged in group D ($p < 0.001$). *Conclusion:* Dexmedetomidine as adjuvant to local anaesthetic results in increased duration of sensory and motor block along with prolonged duration of analgesia as compared to clonidine.

Keywords: Adjuvant; Brachial Plexus Block; Bupivacaine; Clonidine; Dexmedetomidine; Ultrasound.

How to cite this article:

Dheer Singh, Ashwin Choubey, Urvashi Yadav et al. Comparison of Dexmedetomidine and Clonidine as Adjuvant to Bupivacaine in Ultrasound Guided Supraclavicular Brachial Plexus Block. Indian J Anesth Analg. 2018;5(9): 1469-75.

Introduction

Peripheral neural blockade is an integral part of composite anaesthetic care. Brachial plexus block provides intraoperative anaesthesia as well as postoperative analgesia for upper limb orthopaedic surgeries. It offers many advantages over general anaesthesia, such as better postoperative pain relief, decreased incidence of PONV along with avoidance of complication of laryngoscopy and airway instrumentation; and systemic side effects of anaesthesia drugs and systemic analgesics. Ultrasound guidance for nerve localization during brachial plexus block is associated with improved success rate and safety [1]. The distinct advantages of brachial plexus block over general anaesthesia can be extremely useful in patients with significant co-morbidities.

A variety of perineural adjuvants have been used with the aim of extending the duration of analgesia during nerve blocks [2]. Alpha-2 adrenergic receptor agonists have been used as adjuvant for

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Received on 27.05.2018, **Accepted on** 22.06.2018

their sedative, analgesic, and perioperative sympatholytic effect. Clonidine, an α2-adrenergic agonist, has been previously used in various studies and shown to prolong the duration of anaesthesia and analgesia in nerve blocks. Dexmedetomidine is a highly selective α2-adrenergic agonist. It has been reported to improve the quality of intrathecal and epidural anaesthesia. However, data of its use in supraclavicular brachial plexus block is limited.

The aim of this clinical study was to compare clonidine and dexmedetomidine, as adjuvant to bupivacaine in supraclavicular brachial plexus block, in terms of onset and duration of sensory and motor block and duration of analgesia.

Materials and Methods

After ethical committee approval and informed written consent, a double-blind randomized prospective clinical study was carried out on 90 American Society of Anaesthesiologist (ASA) Grade I and II patients of either sex, aged 18–60 years, BMI 18-30 kg/m^2, undergoing surgery for fractures of lower end humerus and forearm bones under supraclavicular block. Patients with a history of pre-existing cardiac or pulmonary diseases, on adrenoreceptor agonist or antagonist therapy, with known hypersensitivity to local anaesthetic drugs or dexmedetomidine or clonidine, bleeding disorders, pregnant women and pre-existing peripheral neuropathy, were excluded from the study. After Pre anaesthetic evaluation the patients were randomly allocated, using sequentially numbered cards in sealed opaque envelopes to one of the following groups:

Group B (n=30): Bupivacaine 0.25% (30 ml) + 1 ml Normal Saline

Group C (n=30): Bupivacaine 0.25% (30 ml) + 1 ml Clonidine (0.75μg/kg)

Group D (n=30): Bupivacaine 0.25% (30 ml) + 1 ml Dexmedetomidine (0.75μg/kg)

The local anaesthetic solution was prepared by an anaesthetist not involved in the study. The dose of clonidine and dexmedetomidine i.e. 0.75μg/kg was diluted with normal saline to total volume of 1 ml. The anaesthetist performing the block was blinded to the treatment group. All observations were carried out by a single investigator who was also blinded to the treatment group.

On arrival in the operation room, standard monitors including NIBP cuff, pulse oximeter and ECG were attached and baseline heart rate, blood pressure and oxygen saturation were recorded. An intravenous line with 18 G cannula was secured in the unaffected limb and intravenous ringer lactate infusion was started.

Sonosite Fujifilm ultrasound system with HFL38/8-12 MHZ transducer was used for ultrasound guidance following all aseptic precaution. The block was performed with the patient in supine position with patient's head turned towards contralateral side. After aseptic preparation of the skin transducer was placed in transverse plane in the supraclavicular fossa and under ultrasound guidance the brachial plexus, subclavian artery, cervical pleura, and first rib were identified. 2 ml of 2% lignocaine was injected in the skin, lateral to the transducer. The bunch of grape appearance on ultrasound was noted and the 22 G, 5 cm needle was inserted in plane towards the brachial plexus, in a lateral to medial direction. After careful negative aspiration, 31 ml of solution containing study drug was administered.

Hemodynamic variables viz heart rate and mean arterial blood pressure along with oxygen saturation were recorded at time zero and 5^{th}, 15^{th}, 30^{th}, 60^{th}, 90^{th}, 120^{th}, 150^{th} minute and 3^{rd}, 6^{th}, 12^{th} and 24^{th} hour.

Sensory and motor block evaluation was done every minute after completion of drug administration until complete sensory and motor block. Sensory block was assessed by pinprick test with a blunt 26 G hypodermic needle in the distribution of ulnar, median, radial and musculocutaneous nerves using a 3-point scale as:

0 = Normal sensation,

1 = Loss of sensation of prick (analgesia),

2 = Loss of sensation of touch (anaesthesia).

The block was considered incomplete when any of the segments supplied by median, radial, ulnar and musculocutaneous nerve did not have analgesia even after 30 minutes of drug injection. When more than one nerve remained unaffected, it was considered a failed block. In this case, general anaesthesia was given intraoperatively. Onset time for sensory block was defined as the time interval between the end of total local anaesthetic administration and complete sensory block (score 2) on all nerve territories. Duration of sensory block defined as the time interval between the end of local anaesthetic administration and the complete resolution of anaesthesia (score 0).

Motor block was evaluated by thumb abduction (radial nerve), thumb adduction (ulnar nerve), thumb opposition (median nerve), and flexion at elbow

(musculocutaneous nerve) on a 3-point scale as:

0= Normal motor function,

1= Reduced motor strength (but able to move fingers),

2= Complete motor block.

Onset time motor block was defined as time interval between the end of total local anaesthetic administration and absence of voluntary movement on hand and forearm (score 2). Duration of motor block was defined as the time interval between end of local anaesthetic administration and the recovery of complete motor function of the hand and forearm (score 0).

Sedation score was assessed according to Ramsay Sedation Scale (RSS) from 1-6, with 1 corresponding to an anxious or agitated state and 6 to no response [3].

Patient pain was evaluated by Visual Analogue Scale (VAS), a scale of zero to ten, where 0 is no pain and 10 is very severe pain. In all the three groups time to injection was considered as time zero, VAS at time zero was baseline score and was recorded in all patients. Patient's pain was evaluated at the time zero and 5^{th}, 15^{th}, 30^{th} minute and 1^{st}, 2^{nd}, 6^{th}, 24^{th} hour by a co-investigator, who was blinded to the used method and asked for their pain scores and the same co-investigator recorded all pain scores. Nursing staff was directed to administer inj. diclofenac sodium 1.5 mg/kg intramuscular when VAS ≥ 4 (rescue analgesia). Time of first request for postoperative analgesic (duration of analgesia) was recorded. Total analgesic requirement in first 24 hours was also noted.

Patients were monitored for nausea, vomiting, skin rash, 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 both intraoperatively and during 24 hour postoperative period.

Statistical Analysis

The data was recorded, summarized, tabulated and statistically analyzed using SPSS statistics program (Version 20). The statistical analysis of quantitative data (Mean± SD) between the groups was done by student 't' test. The statistical analysis of qualitative data (N%) between the groups was done by using fischer exact test. p-value <0.05 was considered to be statistically significant.

Results and Analysis

There was no statistically significant difference among the patients in the three groups with respect to age, weight, BMI, sex ratio, duration of surgery, and ASA physical status (Table 1).

The mean time for onset of sensory block was 17.7±2.2 minutes in group B, 12.0±1.2 minutes in group C, and 10.5±1.1 minutes in group D. The mean time for onset of motor block was 22.4±2.2 minutes in group B, 16.7±1.6 minutes in group C, and 14.8±1.4 minutes in group D (Table-2). The onset of sensory and motor block was earlier in group D which was found to be statistically significant when compared among group B and D (p=0.0001), and C and D (p=0.0001).

The duration of sensory block was maximum in group D (545.3±94.2min) followed by group C (419.3±74.0 min) and group B (275.7±40.6 min). The duration of motor block was also maximum in group D (508.3±95.8 min), followed by group C

Table 1: Patient profile and duration of surgery

Parameters	Group B N=30	Group C N=30	Group D N=30	P-value B vs C	B vs D	C vs D
Age	39.2 ± 12.3	36.1 ± 13.4	35.4 ± 11.9	0.35	0.23	0.83
Sex						
Male	21	20	20	1.00	1.00	1.00
Female	9	10	10			
BMI	22.3 ± 1.6	22.0 ± 1.4	21.8 ± 1.5	0.44	0.22	0.60
			ASA score			
1	28	28	28	1.00	1.00	1.00
2	2	2	2			
Duration of surgery (minutes)	119.0 ±25.5	114.0 ± 24.2	109.0 ± 21.6	0.44	0.10	0.40

(378.7±73.2 min) and group B (238.7±46.7). This was found to be statistically significant when compared among group B and C (p=0.0001), B and D (p=0.0001), and C and D (p=0.0001) (Table 2).

Mean Duration of analgesia was 301.5±48.7 minutes in group B, 456.7±75.8 minutes in group C and 585.0±99.4 minutes in group D (Table 2). It was statistically significant when compared among group B and C (p=0.0001), B and D (p=0.0001), and C and D (p=0.0001).

Mean consumption of diclofenac during 24 hours was maximum in group B, 306.7±25.4 mg. Patient in group D had significantly lower total 24 hour diclofenac consumption than group C, 190.0±54.8 mg vs 233.3±54.7 mg (p =0.003) (Table 2).

The baseline hemodynamic parameters were comparable in all the groups (Figure 1) and (Figure 2). Heart rate and Mean arterial pressure (MAP) were found to be lower in patients in group C and group D compared to group B. Patient receiving dexmedetomidine (group D) had lower heart rate and MAP than patients receiving clonidine (Group C) which was statistically significant between 30 minutes to 120 minutes (p<0.05).

Patients in group D were more sedated than group C when Ramsay Sedation score (RSS) was

Table 2: Block characteristics among the three groups

Parameters	Group B N=30	Group C N=30	Group D N=30	P value B vs C	B vs D	C vs D
Onset of Sensory Block (minutes)	17.7 ± 2.2	12.0 ± 1.2	10.5 ± 1.1	0.0001*	0.0001*	0.0001*
Onset of Motor Block (minutes)	22.4 ± 2.2	16.7 ± 1.6	14.8 ± 1.4	0.0001*	0.0001*	0.0001*
Duration of Sensory Block (minutes)	275.7 ± 46.7	419.3 ± 74.0	545.3 ± 94.2	0.0001*	0.0001*	0.0001*
Duration of Motor Block (minutes)	238.7 ± 40.6	378.7 ± 73.2	508.3 ± 95.8	0.0001*	0.0001*	0.0001*
Duration of analgesia (minutes)	301.5 ± 48.7	456.7 ± 75.8	585.0 ± 99.4	0.0001*	0.0001*	0.0001*
Total 24 Hr Analgesic consumption(mg)	306.7 ± 25.4	233.3 ± 54.7	190.0 ± 54.8	0.0001*	0.0001*	0.003*

*p value significant

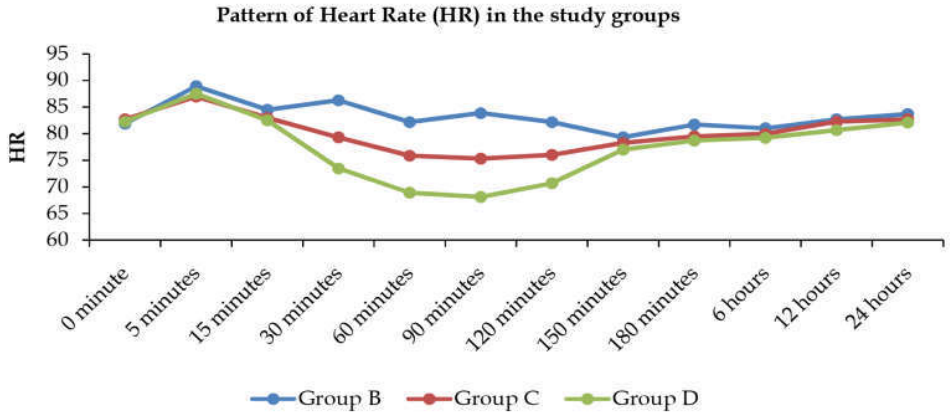

Fig. 1: Line diagram showing pattern of heart rate in the study groups

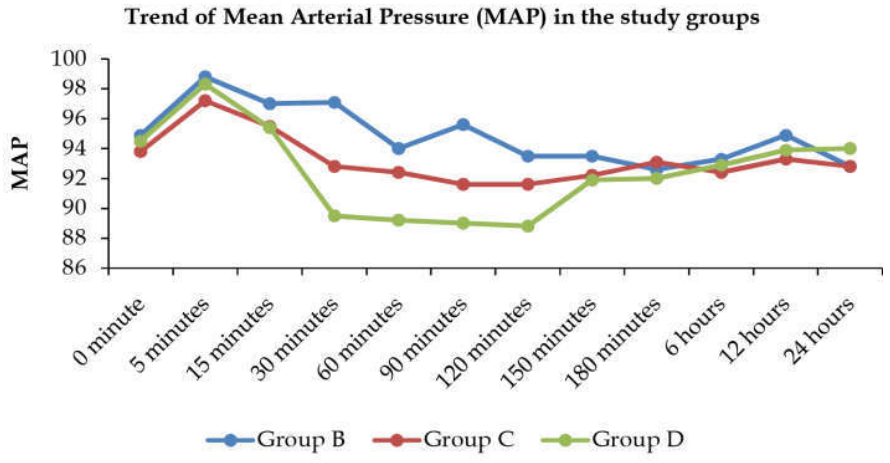

Fig. 2: Line diagram depicting trend of mean arterial pressure in the study groups

recorded at 30,60,120 and 180 minutes (Figure 3). In group C, all the patients had RSS ≤ 3 at 60 minutes while none of the patient achieved grade 4 sedation. In group D, 5 patients had grade 4 sedation, while remaining patients had RSS ≤ 3 at 60 minutes. At 360 minutes both group achieved their baseline score.

No episode of hypoxemia during 24 h period postoperatively was seen in any patient. None of the patients in group B and group C experienced any side effect. While two patients in group D experienced intraoperative bradycardia with hypotension. No episode of nausea, vomiting, or any other side-effect was observed.

Discussion

This prospective, randomized, double-blind study demonstrate that compared to clonidine (0.75 μg/kg), dexmedetomidine (0.75 μg/kg) as adjuvant to 30 ml of 0.25% bupivacaine results in faster onset and prolonged duration of both sensory and motor block in ultrasound-guided supraclavicular brachial plexus block. The duration of analgesia was also significantly prolonged in patients receiving dexmedetomidine compared to clonidine (p=0.0001). The prolonged duration of analgesia obtained in our study in dexmedetomidine group resulted in lower total 24 hour analgesic consumption compared to clonidine group and was clinically and statistically significant (p=0.003).

In animal studies, use of dexmedetomidine perineurally has been associated with decreased inflammation around peripheral nerve [4]. No neurological deficit was observed in any of our patients. No neurological deficit was reported in similar study by Swami et al. [5].

In our study, Bupivacaine dose was chosen as per recommendation in the text book and based on previous researches [6]. Clonidine as adjuvant was used at a dose of 0.75μg/kg. This dose was based on study by Singelyn et al. in which they found that 0.5 μg/kg clonidine, as adjuvant to local anaesthetic for axillary block, significantly prolonged analgesia and no additional advantage with doses higher than 1.5 μg/kg [7].

We used an equal dose of dexmedetomidine i.e. 0.75 μg/kg for comparison. Similar dose of dexmedetomidine has been used in study conducted by Ammar et al in which they tested the efficacy of adding 0.75 μg/kg of dexmedetomidine to 30 ml of 0.33% bupivacaine during ultrasound guided infraclavicular brachial plexus block [8].

Swami SS et al. in 2012 conducted a study in which they compared clonidine (1 μg/kg) and dexmedetomidine (1 μg/kg) as adjuvant to 35 ml of 0.25% bupivaciane in supralavicular brachial plexus block [5]. They concluded that dexmedetomidine when added to local anaesthetic in supraclavicular brachial plexus block significantly enhanced the duration of sensory and motor block and also the duration of analgesia compared with clonidine. The finding in their study corroborates our study. Swami SS et al. used nerve stimulation as the guidance method. Use of ultrasound guidance in our study enabled reduction in total volume of local anaesthetic as well as dose of adjuvants (0.75 μg/kg compared to 1 μg/kg).

Tripathi A et al. in 2016 compared (1 μg/kg) clonidine and (1 μg/kg) dexmedetomidine as adjuvant to 39 ml of 0.25% bupivacaine in supraclavicular brachial plexus block [9]. They observed no statistically significant difference in the onset of sensory and motor block in both the groups. However, similar to our study they found significantly increased duration of sensory and motor block, and analgesia in dexmedetomidine group.

Recently, El Boghdadly K et al. in 2017 conducted a systematic review and meta analysis to compare the efficacy of perineural Dexmedetomidine and Clonidine when added to local anaesthetic in supraclavicular brachial plexus block; in which they included 868 patients from 14 clinical studies [10]. This meta analysis was unavailable at the time we started our study. They observed that compared with clonidine, dexmedetomidine prolonged the duration of sensory and motor block, and analgesia. Dexmedetomidine also hastened the onset of sensory and motor block. Their finding further corroborates our study.

We observed that the use of alpha-2 agonists, dexmedetomidine and clonidine as adjuvant to bupivacaine in supraclavicular brachial plexus block, apart from hastening the onset of sensory and motor block also significantly prolonged the duration of sensory and motor block, as well as duration of analgesia compared to control group. The mechanism of the analgesic actions of α_2 agonists is probably multifactorial. The analgesic effect of α_2 agonists is mediated through stimulation of α_{2C} and α_{2A} receptor in dorsal horn, thus directly suppressing pain transmission by reducing the release of pronociceptive transmitters, substance P and glutamate, and

hyperpolarization of interneurons. During perineural administration the effect of dexmedetomidine and clonidine on nerves is likely elicited by prolonged hyperpolarization of unmyelinated C fibres (sensory) and to a lesser extent the A fibres (motor function). In animal models, the analgesic effect of perineural dexmedetomidine and clonidine have been shown to be caused by enhancement of the hyperpolarisation-activated cation current, which prevents the nerve from returning from a hyperpolarized state to resting membrane potential for subsequent firing [11,12].

In our study, patients receiving dexmedetomidine reported higher sedation score compared to clonidine. No patient experienced airway compromise or required airway assistance. Similar to our study Swami et al. in their study reported that the patients in dexmedetomidine and clonidine group were comfortable throughout the surgery with arousable sedative effects. α_2 agonists produce sedation by central action through activation of α_2 adrenoreceptor in locus coeruleus. The sedative effect can be explained on the basis that some amount of systemic absorption of drug could be present which can be due to lipophilic nature of clonidine and dexmedetomidine [13].

Patients receiving α_2 agonist reported lower heart rate and mean arterial pressure than control group which was statistically significant between 30 to 120 minutes. The reduction in heart rate was more profound in dexmedetomidine group. In Group D, two patients developed intraoperative bradycardia and required atropine administration, 0.6mg intravenously. Bradycardia was not reported in clonidine and control group. Some previous studies have reported the incidence of bradycardia and hypotension with α_2 adrenoreceptor agonists [14,15]. El Boghdadly K et al. in their meta analysis also reported that dexmedetomidine increases the risk of transient bradycardia. In peripheral nerve blockade the bradycardia observed can be a side effect due to systemic absorption of $\alpha_2$agonists.

The limitation of our study was small sample size. The strength of our study is that we used ultrasound guidance for supraclavicular brachial plexus block allowing us to use lesser concentration of local anaesthetic and α_2 agonists.

Furthermore, the effect of intravenous α_2 agonist and perineural administration needs to be compared and studied to delineate the action and mechanism by which α_2 agonists produce analgesia in peripheral nerve block. Further dose finding studies are required for recommendation on dose of dexmedetomidine when used perineurally as adjuvant, for maximum benefits and minimum side effects.

Conclusion

We conclude that the use of dexmedetomidine as adjuvant to local anaesthetic agent during ultrasound guided brachial plexus block provides longer duration of analgesia compared to clonidine. Dexmedetomidine holds considerable promise as an adjuvant in peripheral nerve block.

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