Original Article

Dexmedetomidine prolongs the effect of bupivacaine in supraclavicular brachial plexus block

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Abstract

Background: We compared the effects of adding dexmedetomidine to a 30 ml solution of 0.325% bupivacaine in supraclavicular brachial plexus block. Onset and duration of sensory and motor block along with the duration of analgesia were the primary endpoints.

Materials and Methods: Fifty patients posted for upper limb surgeries were enrolled for a prospective, randomized, double-blind, placebo-controlled trial. Patients were divided into two groups, the control group S and the study group SD. In group S (n = 25), 30 ml of 0.325% bupivacaine + 1 ml normal saline; and in group SD (n = 25), 30 ml of 0.325% bupivacaine + 1 ml (100 μg) dexmedetomidine were given for supraclavicular brachial plexus block using the peripheral nerve stimulator. Onset and duration of sensory and motor blocks were assessed along with the duration of analgesia, sedation, and adverse effects, if any. Hemodynamic parameters, like heart rate (HR), systolic arterial blood pressure (SBP), and diastolic arterial blood pressure (DBP) were also monitored.

Results: Demographic data and surgical characteristics were comparable in both the groups. The onset times for sensory and motor blocks were significantly shorter in SD than S group ($P < 0.001$), while the duration of blocks was significantly longer ($P < 0.001$) in SD group. Except for the initial recordings (at 0, 5, 10, and 15 min), heart rate levels in group SD were significantly lower ($P < 0.001$). SBP and DBP levels in SD group at 15, 30, 45, 60, 90 and 120 min were significantly lower than in S group ($P < 0.001$). In fact, when the percentage changes in HR/SBP/DBP were compared from 0-5/0-10/0-15/0-30/0-45/0-60/0-90/0-120 min in SD with S group, they came out to be highly significant ($P < 0.001$) in group SD. The duration of analgesia (DOA) was significantly longer in SD group than S group ($P < 0.001$). Except that, bradycardia was observed in one patient in the group SD, no other adverse effects were observed in either of the groups.

Conclusion: Dexmedetomidine added as an adjuvant to bupivacaine for supraclavicular brachial plexus block significantly shortens the onset time and prolongs the duration of sensory and motor blocks and duration of analgesia. Patients in group SD were adequately sedated (modified Ramsay Sedation Score, RSS = 2/6 or 3/6) with no adverse effects except bradycardia in one patient of group SD.

Key words: Adjuvant, dexmedetomidine, effects, supraclavicular brachial plexus block

Introduction

Many drugs have been used as adjuvants to local anesthetic agents to prolong the duration of peripheral nerve blocks. Clonidine, a partial α-2 adrenoceptor agonist has been reported to prolong the duration of anesthesia and analgesia during such blocks.[1-3] The α2:α1 selectivity of dexmedetomidine is eight times that of clonidine and its high specificity for α2 subtype makes it a much more effective sedative and analgesic agent.[4]

Dexmedetomidine is being used for intravenous regional anesthesia (Bier's block),[5,6] intravenous (i.v.) sedation and analgesia for intubated and mechanically ventilated patients in intensive care units (ICUs),[7,8] and nonintubated patients for surgical and other procedures.[9] It has been reported to improve the quality of intrathecal and epidural anesthesia.[10-13] Its use in peripheral nerve blocks has recently been described.[14-16] However, the reports of its use in supraclavicular brachial plexus block are limited.[17] In this study, we investigated whether adding dexmedetomidine to bupivacaine for supraclavicular brachial plexus block would affect the sensory and motor blocks and duration of analgesia.

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Materials and Methods

After the approval of the Hospital Ethical Committee, patients were explained about the drug and only those who gave willful written consent were included in the study. Fifty ASA physical status I and II patients, 18-60 years undergoing upper limb surgery under supraclavicular brachial plexus block were enrolled in a prospective, randomized, double-blind, placebo-controlled trial.

Exclusion criteria were patients with a history of significant neurological, psychiatric, neuromuscular, cardiovascular, pulmonary, renal, hepatic disease; alcoholism or drug abuse; pregnancy or lactating women; and patients receiving adrenoceptor agonist or antagonist therapy or chronic analgesic therapy. Also excluded were patients with morbid obesity, diabetes, peripheral vascular disease, suspected coagulopathy, or known allergies.

Patients were randomly allocated in this double blind study (using a sealed envelope technique) into two groups. Control group S (n = 25) received 30 ml of 0.325% bupivacaine with 1 ml of isotonic sodium chloride solution. Study group SD (n = 25) received 30 ml of 0.325% bupivacaine and 1 ml (100 mcg) of dexmedetomidine. The drug solutions were prepared by an anesthesiologist not involved in the study. The anesthesiologist performing the block and observing the patient was blinded to the treatment group. Data collection was done by the same anesthesiologist who was unaware of the group allocation.

The basal heart rate (HR); noninvasive arterial systolic blood pressure (SBP) and diastolic blood pressure (DBP); and peripheral oxygen saturation (SpO_2) were recorded. An 18 gauge (G) i.v. cannula was inserted in nonoperated arm and lactated Ringer's solution was started at 5 ml/kg/h.

The patients were administered brachial plexus block by supraclavicular route via the subclavian perivascular approach in supine position with arm adducted. Under all aseptic precautions, the injection site was identified to be 1 cm behind the midpoint of the clavicle, (where the pulsation of the subclavian artery was felt) and infiltrated with 1 ml of 2% lignocaine subcutaneously. A nerve stimulator (Neurostim LA II, Hugo Sachs Electronik, type 220/1 with 22G × 2" Pajunk needle) was used to locate the brachial plexus. The location endpoint was a distal motor response, that is, the movement of the fingers and the thumb with an output current of 0.5 mA. During injection of the drug solution, negative aspiration was done every 5 ml to avoid intravascular injection. Plexus block was considered successful when at least two out of the four nerve territories (ulnar, radial, median, and musculocutaneous) were effectively blocked for both sensory and motor block.

Sensory block (four nerve territories) was assessed by pin prick test using a 3-point scale: 0 = normal sensation, 1 = loss of sensation of pin prick (analgesia), and 2 = loss of sensation of touch (anesthesia). 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[18] on a 3-point scale:

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

Both sensory and motor blocks were assessed every 3 min till their onset and at 15, 30, 45, 60, 90, and 120 min; and then hourly (even after surgery) after the completion of injection, until they had resolved. Patients were asked to note the subjective recovery of sensation and movements which was then certified by an anesthesiologist or nurse.

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

HR, SBP, and DBP were also recorded at 0, 5, 10, 15, 30, 45, 60, 90, and 120 min. Sedation score was assessed according to the modified Ramsay Sedation Scale (RSS)[19] 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. Adverse effects comprised hypotension (i.e. 20% decrease relative to baseline), bradycardia (HR <50 beats/min), nausea, vomiting, and hypoxemia (SpO_2 <90%). Any need for additional medication was noted intraoperatively. Blood loss was calculated by the gravimetric method and

replaced if more than the allowable blood loss. Pain was assessed using visual analogue scale (VAS) 0-10. Nursing staff was directed to administer inj. diclofenac sodium 3 mg/kg intramuscular when VAS ≥ 3 (rescue analgesia). The time between the complete sensory block and the first analgesic request was recorded as duration of analgesia (DOA).

The data was compiled and subjected to statistical analysis using Statistical Package for Social Sciences (SPSS), version 15. Demographic and hemodynamic data were subjected to Student's *t*-test and for statistical analysis of onset time and duration of sensory and motor blocks, and DOA unpaired *t*-test was applied and reconfirmed with the Wilcoxon W and Mann-Whitney U tests. *P*-value < 0.05 was considered as statistically significant and $P < 0.001$ as highly significant. Any adverse effects were analyzed using the chi-square/ Fischer's exact test.

Results

The demographic data and surgical characteristics were comparable in both groups [Table 1]. Onset time was shorter while duration of sensory and motor blockade were longer in SD than S group and the difference was statistically significant ($P < 0.001$) [Table 2]. The mean onset time for sensory and motor blocks in group SD were 13.2 ± 1.8 and 16.2 ± 1.8 min, respectively and for group S were 19.0 ± 3.2 and 22.7 ± 2.8 min, respectively. The mean duration time for sensory and motor blocks for group SD were 755.6 ± 126.8 and 702.0 ± 112.6 min, respectively; but for the group S, the mean duration were 234.8 ± 47.9 and 208.0 ± 22.7 min, respectively. The mean duration of analgesia (DOA) for group SD was 776.4 ± 130.8 min, it was 241.4 ± 51.2 min for group S [Figure 2]. DOA was significantly longer in group SD than group S ($P < 0.001$). HR, SBP, and DBP in group SD at 15, 30, 45, 60, 90, and 120 min were significantly lower than in group S ($P < 0.001$) [Figures 1a and b]. In fact, when the percentage changes in the HR, SBP, and DBP were compared from 0-5 min up to 0-120 min, they were highly significant ($P < 0.001$) for group SD than group S. Bradycardia was observed in one patient in the group SD which responded to injection atropine. The modified RSS for group SD was either 2/6 (in 18 patients) or 3/6 (in 7 patients), while that for group S was 1/6. Other side effects like hypotension, nausea, vomiting, hypoxemia, pruritis, or urinary retention were not observed in either group.

Table 1: Demographic and Surgical characteristics

	Group S (*n* = 25)	Group SD (*n* = 25)
	Mean ± SD	Mean ± SD
Age (Years)	30.1±10.9	30.6±11.3
Height (Cm)	168.3±8.9	169.5±10.2
Weight (Kg)	57.9±7.8	64.0±9.4
Gender (M/F)	17/8	19/6
Type of Surgery (Bone/Soft Tissue)	14/11	12/13

S = Bupivacaine, SD = bupivacaine + dexmedetomidine, M = Male, F = Female. There was no significant difference between groups

Discussion

Dexmedetomidine, the pharmacologically active d-isomer of medetomidine is a highly specific and selective α2 adrenoceptor agonist with α2:α1 binding selectivity ratio of 1620:1 as compared to 220:1 for clonidine, thus decreasing the unwanted side effects of α1 receptors.[20,21] Presynaptic activation of α2 adrenoceptor in central nervous system (CNS) inhibits the release of norepinephrine, terminating the propagation of pain signals and their postsynaptic activation inhibits sympathetic activity, thereby decreasing HR and BP.[22,23] Transient hypertensive response with doses 1-4 μg/kg is attributed to initial stimulation of α- 2B subtype receptors in vascular smooth muscles. Bradycardia is a reflex response to this transient response and it persists subsequently due to central sympathetic inhibition. Baroreceptor reflex and HR response to a pressor agent is well preserved with the use of dexmedetomidine, thus hypotension and bradycardia are easily treatable conferring hemodynamic stability. High selectivity for α-2A receptors mediates analgesia, sedation, and anxiolysis. The research done so far shows encouraging results for its use in intravenous sedation (ICU and operative patients), spinal,[10,11] epidural,[12] caudal anesthesia,[13] and Bier's block.[5,6] By virtue of its effects on spinal α2 receptors, it prolongs analgesia when used with local anesthetics for neuraxial blocks.[24]

Table 2: Sensory and motor block onset, duration time and duration of analgesia in Groups S (bupivacaine) and SD (bupivacaine + dexmedetomidine)

	Group S (*n* = 25) (X ± SD)	Group SD (*n* = 25) (X ± SD)	*t*-value	*P*-value
Onset time sensory block (min)	19.04±3.195	13.20±1.848	–7.911	0.001
Onset time motor block (min)	22.7±2.8	16.3±1.7	–9.6	0.001
Duration time sensory block (min)	234.8±47.9	755.6±126.8	19.2	0.001
Duration time motor block (min)	208.0±22.7	702.0±111.6	21.7	0.001
Duration of analgesia (min)	241.4±51.2	776.4±130.8	19.0	0.001

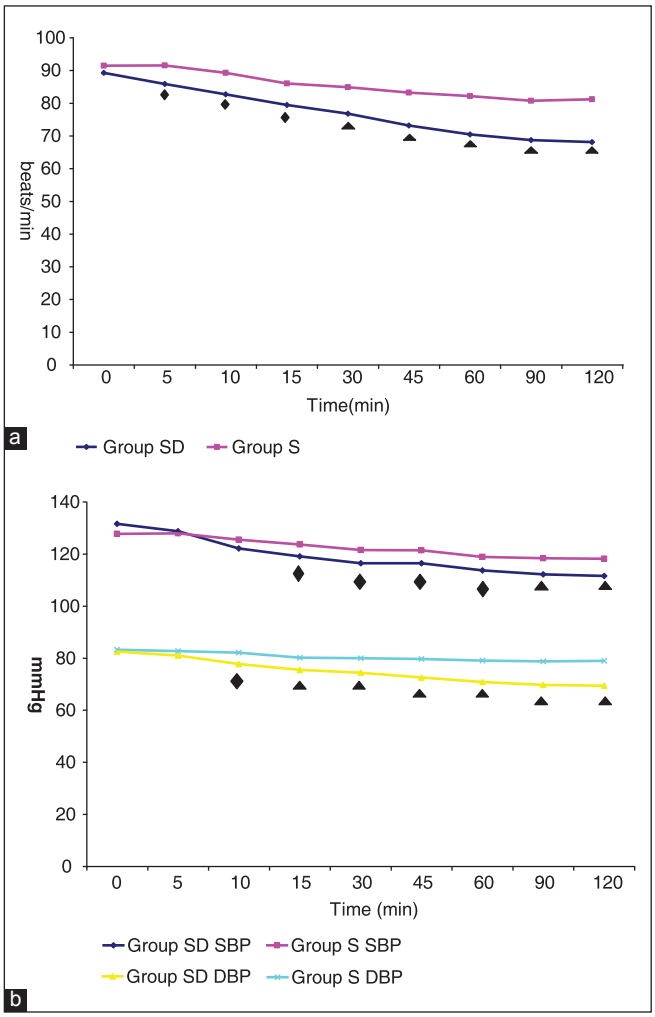

Figure 1: (a) Mean heart rate values in the groups S (bupivacaine) and SD (bupivacaine + dexmedetomidine). Diamonds indicate time points of a statistically significant difference ($P < 0.05$) when the groups were compared. Triangles indicate very significant difference ($P < 0.001$). (b) Mean systolic (SBP) and diastolic (DBP) arterial pressures for the groups S (bupivacaine) and SD (bupivacaine + dexmedetomidine). Diamonds indicate the time points of a statistically significant difference ($P < 0.05$). Triangles indicate very significant difference ($P < 0.001$)

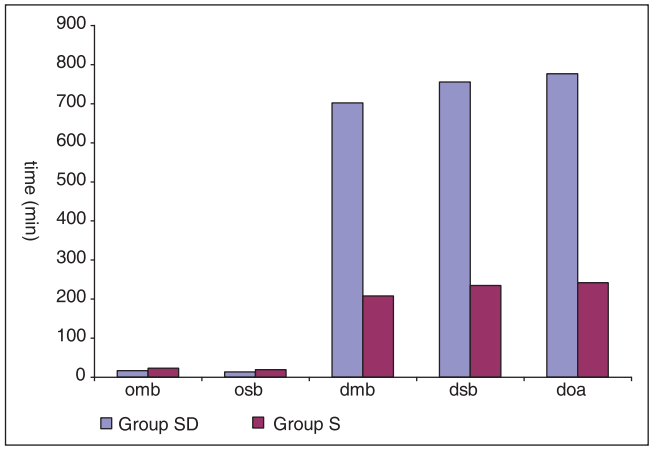

Figure 2: Comparison of mean onset time motor block (omb) and sensory block (osb); duration time motor block (dmb) and sensory block (dsb); and duration of analgesia (doa). The time difference between the two groups was statistically very significant ($P < 0.001$)

Studies by Brummett *et al.*, showed that dexmedetomidine enhances duration of bupivacaine anesthesia and analgesia of sciatic nerve block in rats without any evidence of histopathological damage to the nerve.[25,26] In another study, dexmedetomidine added to ropivacaine increased the duration of sciatic nerve blockade in rats, most likely due to the blockade of hyperpolarization-activated cation current (i.e., a direct effect on the peripheral nerve activity).[27] Kosugi *et al.*, examined the effects of various adrenoceptor agonists including dexmedetomidine, tetracaine, oxymetazoline and clonidine, and also an α2 adrenoceptor antagonist (atipamezole) on compound action potential (CAP) recorded from frog sciatic nerve, and found that CAPs were inhibited by α2 adrenoceptor agents so that they were able to block nerve conduction.[28] Yoshitomi *et al.*, demonstrated that dexmedetomidine as well as clonidine enhanced the local anesthetic action of lignocaine via peripheral α-2A adrenoceptors.[29] Studies have shown that clonidine when added to bupivacaine prolongs the duration of anesthesia and analgesia in brachial plexus block,[1,2] but was associated with bradycardia, hypotension, and respiratory depression as side effects. Masuki *et al.*, suggested that dexmedetomidine induces vasoconstriction via α2 adrenoceptors in the human forearm[30] possibly also causing vasoconstriction around the site of injection, delaying the absorption of local anesthetic and hence prolonging its effect. Esmaoglu *et al.*, reported prolongation of axillary brachial plexus block when dexmedetomidine was added to levobupivacaine.[14] This study was the basis for dose selection of dexmedetomidine (100 μg) for our study. They observed bradycardia in seven out of 30 patients in study group while we observed it in only one out of 25 patients. Dexmedetomidine also prolongs the effects of local anesthetic agents for posterior tibial nerve and greater palatine nerve sensory blockade.[15,16] Non availability of ultrasound at our center hindered usage of decreased dosages of local anesthetics. In our study, while the onset time of both sensory and motor blocks were shortened in the drug group, the duration of analgesia was significantly prolonged. To give us a better insight of its efficacy, safety profile, and cost effectiveness; its use needs to be explored in a larger study population and in different nerve blocks.

To conclude, in our study we found that dexmedetomidine when added to bupivacaine for supraclavicular brachial plexus block shortens the onset times for sensory and motor blocks and prolongs their duration. The significantly prolonged duration of analgesia obviates the need for any additional analgesics. The added advantage of conscious sedation, hemodynamic stability, and minimal side effects makes it a potential adjuvant for nerve blocks. Further studies with large sample sizes are warranted to validate these findings.

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