Recep Aksu, MD, Associate Professor
Cibangir Bicer, MD, Associate Professor

Department of Anesthesiology, Erciyes
University, Medical Faculty, Kayseri, Turkey

Addition of dexmedetomidine to bupivacaine in supraclavicular brachial plexus block

Abstract

Purpose: Research is ongoing to determine the lowest dose of local anesthetics in brachial plexus block that provides adequate anesthesia and postoperative analgesia and reduces complications related to local anesthetics.

Methods: Patients 18-65 years of age who underwent upper limb surgery and who received ultrasound-guided supraclavicular brachial plexus block at the Erciyes University Faculty of Medicine Hospital between February 2014 and January 2015 were included in the study (n=50). Supraclavicular brachial plexus blocks were performed on Group B cases by adding 30 ml 0.33% bupivacaine and on Group BD cases by adding 15 ml 0.33% bupivacaine and 1 µg / kg dexmedetomidine. Block success was evaluated by the onset and block duration of motor and sensory block and the duration of analgesia.

Results: The block success of Group B and Group BD was 92.6% and 89.3%, respectively ($P = 1.000$). Onset time of sensory block, degree of sensory block, duration of sensory block, onset time of motor block, degree of motor block and duration of motor block were similar in both groups in the intergroup comparison ($P > 0.05$). Duration of analgesia and the operative conditions of groups were similar ($P > 0.05$).

Conclusions: In the implementation of ultrasound-guided supraclavicular brachial plexus block, block success, sensory and motor block and analgesia duration were similar for patients anaesthetized with 30 ml of bupivacaine in comparison with dexmedetomidine+bupivacaine (when the bupivacaine dose was reduced by 50% by the addition of the adjuvant).

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Correspondence to:

Dr. Recep Aksu
Erciyes University, Medical Faculty,
Department of Anesthesiology and Reanimation, Kayseri, Turkey
E-mail: raksu@erciyes.edu.tr

Brachial plexus block is frequently used in upper extremity surgery anesthesia and in postoperative pain management in outpatients [1]. Many approaches have been described for brachial plexus block implementation, but the supraclavicular approach towards the brachial plexus, with ultrasound (US) guidance, is one of the preferred methods as it is straightforward and reduces the risk of pleural or arterial puncture in comparison with performing this block with landmark or nerve stimulation guidance [2,3]. A number of undesirable side effects can be observed with plexus block; from facial paresthesia to coma and cardiac arrest, depending on both the amount of local anesthetic used and the absorption rate from the tissues [4]. The long block and analgesic effects of bupivacaine are similar to those of other enantiomers, but the greater minimal local anesthetic potency required for motor block of bupivacaine compared with levobupivacaine and ropivacaine may make bupivacaine preferable [4,5]. Research is ongoing to determine the lowest dose of local anesthetic required that allows for adequate anesthesia and postoperative analgesia, while reducing complications, in brachial plexus block [4,6,7].

The duration and efficacy of peripheral nerve block can be increased by adding a number of adjuvants to local anesthetics [8-10]. Dexmedetomidine is a highly selective (eight times higher than clonidine) α_2 -adrenergic receptor agonist that is a highly effective sedative and analgesic [11]. It has been found that, in many experimental and clinical regional block practices, the addition of dexmedetomidine to a local anesthetic reduces tissue and nerve damage, increases duration of sensory and motor block and reduces postoperative pain [8,12-14].

We hypothesized that dexmedetomidine can be used to reduce the volume of bupivacaine in supraclavicular brachial plexus block while still achieve similar block success.

Materials and Methods

After obtaining approval from the Erciyes University Faculty of Medicine Ethics Committee (protocol number 2013/107), patients 18-65 years of age American Society of Anesthesiologists (ASA I and II) who underwent upper limb surgery and who received ultrasound-guided supraclavicular brachial plexus block, at the Erciyes University Faculty of Medicine Gevher Nesibe Hospital were included in this double blinded, prospective study (n=50). Written informed consent was obtained from each participant. Before the first patient was enrolled, the study was registered at ClinicalTrials.gov and the identifier number, NCT02049970,

was issued on 31 January 2014. This study was performed according to the principles of the Helsinki Declaration.

Those patients who had major psychiatric problems, neurological deficits, diabetes mellitus, pulmonary and cardiac disease or coagulopathy, or who were dependent on drugs, used analgesia for chronic pain, were unable to cooperate, were allergic to morphine, bupivacaine or dexmedetomidine or who were pregnant were excluded from the study.

All patients were randomly allocated to one of the two groups using sealed envelopes. Patients were taken into the operating room 45 minutes before surgery. Patients were monitored non-invasively with EKG, non-invasive arterial blood pressure and pulse oximetry. Skin cleaning with betadine was carried out on the location at which the block was to be performed. For the ultrasonography, the supraclavicular brachial plexus was view on short-axis using a 5-10 MHz linear probe (Mindray M7, China). The location was draped and a sterile probe sleeve was utilized. Local skin anesthesia was provided for the surgical area with 1 ml of 2% lidocaine (2% Aritmal, Osel İlaç San., Istanbul). A 50 mm, 22 G peripheral nerve block needle (Stimuplex® Ultra, B. Braun, Melsungen, Germany) was connected to the nerve stimulator (Stimuplex) and inserted using the in-plane method. The needle tip was directed from lateral to medial into the cluster of supraclavicular brachial plexus. Responses against electrical stimulation received in the hand muscles were lost below 1 Hz and 0.5 mA and it was noted that the patient did not bleed following aspiration. Then 15 ml (50 mg) or 30 ml (100 mg) pre-operatively prepared 0.33% bupivacaine was injected and the block was completed (Group BD received 10 ml 0.5% bupivacaine+4 ml 0.9 % NaCl+1 ml dexmedetomidine, 1 µg/kg; while Group B received 20 ml 0.5% bupivacaine+10 ml 0.9% NaCl) (0.5% Marcaine, AstraZeneca, Lüleburgaz, Turkey). The patient and the block assessor were blinded to the doses of local anesthetic.

Evaluation of the sensorial and motor block was carried out for 30 min and the findings were recorded. The level of sensorial block was evaluated with a pinprick test on the upper extremity using a 3-point scale (15) (0 = normal sensation, sharp to pinprick; 1 = loss of sensation of pin prick; 2 = no sensation, pinprick not felt).

Motor function was evaluated according to the modified Bromage scale (15) on a 3-point scale: (0 = normal motor function with full flexion and of elbow, wrist and fingers; 1 = decreased motor extension capacity, move the fingers only; 2 = full motor block, fingers cannot move).

Blocks, where sensory block still did not start within 30 min and where the motor block evaluation score was 1 or

above, were considered to be unsuccessful. These patients received supplemental block or general anesthesia.

Heart rate and blood pressure were measured for 120 min and recorded. Observed side-effects were checked in the first 24 hours postoperatively and recorded. Adverse events comprised hypotension (a 20% decrease in relation to the baseline value), bradycardia (HR < 50 beats per minute), dry mouth, nausea and vomiting. Observed bradycardia was treated with 0.5 mg atropine i.v., observed hypotension was treated with 10 mg ephedrine hydrochloride, and observed nausea and vomiting were treated with 10 mg metoclopramide (metpamid 5 mg/ml).

Evaluation of pain occurring when the arm was in the resting position was carried out with an 11-point (ranging from 0 = no pain to 10 = worst pain imaginable) Numerical Rating Scale (NRS) by an anesthetist who was blinded to the groups. The duration of analgesia was taken from the time of onset of block to the first complaint of pain. For additional analgesia, 50 mg of dexketoprofen trometamol (50 mg/2 ml, Arveles, Italy) was given i.v. to patients with NRS scores of 4 or higher.

Sensorial and motor block return time were checked in the postoperative period in hospital up to 24 hours and recorded.

Operative and postoperative patient satisfaction scores in the first 24 hours were evaluated using a 5-point scale (1 = very unsatisfactory, 2 = rather unsatisfactory, 3 = fair, 4 = rather satisfactory and 5 = very satisfactory).

The primary outcome of this study was the success (providing sufficient anesthesia for surgery) of supraclavicular brachial plexus block. The secondary outcome was the postoperative duration of sensorial block and analgesia time.

To calculate the sample size, with respect to 100% block success, expected difference among block success rates to be taken as 10%, and it was estimated that 15 patients should be in the groups with 90% power and a $\alpha = 0.05$ error margin.

Statistical Analysis

The normality of the parametric data was analyzed by the Shapiro - Wilk test. The comparison between groups for data with a normal distribution was performed using Student's *t* - test, and the comparison between groups for data that did not show a normal distribution was performed using the Mann-Whitney U test. The intergroup comparison of repeated measurements was evaluated by one-way repeated measures analysis of variance. Categorical variables were evaluated with the exact method of the Chi-squared test. All tests were two-sided, and *P* values < 0.05 were considered significant. All statistical analyses were performed using the R software

package, version 3.1.1 and MedCalc Software, Version 10.1.6© 1993 - 2009.

Results

Patients in the two groups were similar in terms of age, weight, height, BMI, gender, ASA categorization, tourniquet used, surgical time and surgical type (*P* > 0.05) (Table 1). Two cases in Group B and three cases in Group BD were not included in the study due to unsuccessful blocks; these operations were completed under general anesthesia. Block success was 92.6% in Group B and 89.3% in Group BD (*P* = 1.000).

Intergroup comparisons showed that the onset time of sensory block, degree of sensory block, and duration of sensory block, as well as the onset time of motor block, degree of motor block and duration of motor block were similar in both groups (*P* > 0.05) (Table 2). The duration of analgesia in the two groups, as well as operative and postoperative patient satisfaction scores, were similar (*P* > 0.05) (Table 2).

A statistically significant decrease within clinically normal limits was observed in heart rates after block between the two groups at 5, 15, 30, 45, 60 and 90 min (*P* < 0.05), but no statistically significant difference was observed in heart rates between the two groups at 120 min (*P* = 0.128) (Table 3). No statistically significant difference was observed in Group B at other times compared with the intra-group initial heart rates (*P* > 0.05). A statistically significant decrease (though clinically within normal limits) was observed in the heart rate of Group BD patients at 15, 30, 45, 60 and 90 min compared with the intra-group initial heart rates (*P* < 0.05) (Table 3).

A statistically significant decrease (within clinically normal limits) was observed in the intergroup comparison of mean arterial pressure after the block process in Group BD at 15 min compared with Group B (*P* < 0.05), but no statistically significant intergroup difference was observed at 5, 30, 45, 60, 90 and 120 min (*P* < 0.05) (Table 3). No statistically significant difference was observed in Group B in the post-block values compared with the initial mean arterial pressure values, although a statistically significant decrease within clinically normal limits was observed in Group BD at 15, 60 and 90 min compared to the initial mean arterial pressure (*P* < 0.05) (Table 3).

In terms of side effects, nausea and vomiting were seen in one (4%) case and dry mouth was seen in one (4%) case in Group B, while bradycardia was seen in three (12%) cases and dry mouth was seen in five (20%) cases in Group BD (*P* < 0.037). No neurologic abnormalities were observed in either group after block resolution.

TABLE 1. Patient demographic data and operation characteristics

	Group B (n = 25) Mean±SD or (n)	Group BD (n = 25) Mean±SD or (n)	P
Age (years)	44.4±15.2	47.2±15.2	0.531
Weight (kg)	73.6±12.8	76.4±10.8	0.407
Height (cm)	168.2±7.1	169.1±6.1	0.626
BMI (kg/m ²)	25.9±2.9	26.7±2.9	0.348
Gender (M/F) (n)	13/12	15/10	0.571
ASA (I/II) (n)	18/7	17/8	1.000
Duration of surgery (min)	77.8±42.1	62.1±31.3	0.142
Tourniquet used (yes/no) (n)	13/12	10/15	0.571
Operation type (n) humerus fracture/radial fracture / hand surgery (n)	13/5/7	11/6/8	0.931

$P < 0.05$ was considered statistically significant

BMI : body mass index

TABLE 2. Block degree, block and analgesia duration and patient satisfaction scores

	Group B (n = 25) Mean±SD or n (%)	Group BD (n = 25) Mean±SD or n (%)	P
Degree of sensory block (1 / 2)	4 (16) / 21 (84)	3 (12) / 22 (88)	1.000
Motor block degree (1 / 2) n (%)	12 (48) / 13 (52)	16 (64) / 9 (36)	0.393
Onset of sensory block (min)	7,5 ± 3.0	8.4 ± 2.3	0.062
Duration of sensory (min)	617.2 ± 216.7	649.0 ± 278.5	0.654
Onset of motor block (min)	9.6 ± 3.2	11.5 ± 4.2	0.105
Duration of motor block (min)	625.2 ± 191.7	728.4 ± 176.6	0.053
Analgesia duration (min)	627.4 ± 204.9	749.0 ± 290.9	0.094
PSS (3/4/5) n (%)	3 (12)/4 (16)/18 (72)	6 (24)/2 (8)/17 (68)	0.454

$P < 0.05$ was considered statistically significant

Sensorial block degree 0 = normal sensation, sharp pinprick; 1 = pinprick felt but not sharp; 2 = no sensation, pinprick not felt

PSS = patient satisfaction score 1 = very unsatisfactory, 2 = rather unsatisfactory, 3 = fair, 4 = rather satisfactory and 5 = very satisfactory.

Motor block degree 0 = normal motor function, elbow, wrist and fingers in full flexion and extension, 1 = motor extension capacity decreased, only fingers move; 2 = full motor block, fingers cannot move.

TABLE 3. Heart rate (HR) (beats / min) and mean blood pressure (MBP) (mmHg)

	Group B (n = 25) Mean±SD	Group BD (n = 25) Mean±SD	P
HR basal	81.6 ± 17.8	77.5 ± 14.5	0.403
HR 5 min	82.3 ± 18.0	69.5 ± 12.2†	0.009
HR 15 min	81.6 ± 17.4	68.2 ± 12.9*†	0.006
HR 30 min	81.6 ± 17.9	68.3 ± 10.4*†	0.005
HR 45 min	79.6 ± 16.9	66.6 ± 8.7*†	0.004
HR 60 min	80.8 ± 18.1	66.5 ± 8.9*†	0.003
HR 90 min	81.5 ± 17.9	70.2 ± 8.6*†	0.024
HR120 min	80.0 ± 20.4	71.3 ± 11.6	0.278
MBP basal	99.0 ± 15.8	104.1 ± 16.0	0.291
MBP 5 min	100.1 ± 16.3	97.4 ± 13.5	0.548
MBP 15 min	102.7 ± 14.6	92.0 ± 10.1*†	0.007
MBP 30 min	100.4 ± 18.4	94.4 ± 15.5	0.256
MBP 45 min	98.7 ± 15.7	95.3 ± 11.1	0.434
MBP 60 min	99.6 ± 14.8	92.1 ± 14.8*	0.124
MBP 90 min	94.8 ± 15.4	92.9 ± 17.1*	0.743
MBP120 min	96.3 ± 11.8	92.8 ± 19.8	0.639

*P < 0.05 statistically significant compared with the basal value.

†P < 0.05 statistically significant compared with Group B.

Discussion

An effective, reliable block has been shown to be provided by the application of ultrasound-guided supraclavicular brachial plexus during upper extremity surgery, leading to fewer complications [16-17]. In the present study, the block success in the group in which ultrasound-guided supraclavicular brachial plexus block was applied with 100 mg of 0.33% bupivacaine was found to be 92.6% and the block success in the group in which 50 mg of 0.33% bupivacaine+1 µg/kg dexmedetomidine was given was found to be 89.3%. Similarities were found between the groups in terms of the conduction of surgery and the degree of sensory and motor block.

Studies have been carried out to find the dose of local anesthetics that produces minimal effects for ultrasound-guided supraclavicular brachial plexus block

[4,6,7,18,19]. Duggan et al. (7) reported the 50% effective dose (ED₅₀) and 95% effective dose (ED₉₅) of a 50% mixture (2% lidocaine and 0.5% bupivacaine) of two different epinephrine doses added to anesthetics (23 ml and 42 ml, respectively). Kant et al. [4] reported that 27 ml is required for the ED₉₅ dose of 0.5% bupivacaine. Gupta et al. [18-19] reported that the average ED₅₀ volume of 0.5% bupivacaine is 10.8 ml according to the body mass index (BMI) and, as the BMI increases, the dosage decreased to 18.1 ml at the 0.375% bupivacaine concentration.

Many studies have reported that the addition of dexmedetomidine to a local anesthetic as an adjuvant in ultrasound-guided supraclavicular brachial plexus block application increases the duration of sensory and motor block [8,9,14,15,20]. Gandhi et al. [20] reported that the onset time of sensory and motor block was shorter in the groups for which 38 ml of 0.25% bupivacaine and 30 µg of dexmedetomidine were added than the groups for which dexmedetomidine was not added; however, the duration of analgesia, motor and sensory block was about 4-6 times longer in the groups for which dexmedetomidine was given. Agarwal et al. [15] reported that, with the use of 30 ml of 0.325% bupivacaine and 100 µg of dexmedetomidine, sensory and motor block onset time in the group for which dexmedetomidine was added was shorter, in contrast with the findings of Gandhi et al. [20], but that the duration of analgesia, sensory and motor block was similarly longer.

In this study, clinically insignificant decreases in the average heart rate between 15 and 90 min and in the mean arterial pressure at 15, 60 and 90 min were observed in the hemodynamic evaluation of the dexmedetomidine added group.

In terms of side effects, bradycardia was seen in three cases and dry mouth was seen in five cases in the group for which dexmedetomidine was given, and nausea and vomiting were seen in one case and dry mouth was seen in one case in the group for which dexmedetomidine was not given. Dexmedetomidine-associated bradycardia was temporary and was successfully treated with atropine, and bradycardia did not recur in the postoperative period.

The present work studied the evaluation of adding dexmedetomidine to bupivacaine in patients undergoing upper limb surgery under ultrasound-guided supraclavicular brachial plexus block anesthesia. Additional studies, including larger number of patients, should be performed to confirm our study findings about the usage of dexmedetomidine as a safe and effective adjuvant to bupivacaine.

The study established that the dose of bupivacaine used in ultrasound-guided supraclavicular brachial plexus block can be safely and significantly lowered by 50% with the addition of 1 µg/kg dexmedetomidine; providing an effective sensory and motor block and postoperative analgesia similar to that seen with high dose bupivacaine in patients undergoing upper limb surgery. In this way, nerve block may be performed using a low dose of local anesthetic, thereby reducing the undesired toxicity-related adverse effects of local anesthetic.

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