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Bupivacaine-dexmedetomidine versus bupivacaine-nalbuphine in ultrasound-guided supraclavicular brachial plexus block: a prospective, randomized, double-blind study

H. S. Mohamed[*] and G. S. Gad

Abstract

Background: Brachial plexus block is frequently performed for ambulatory upper limb surgery as an alternative to general anesthesia. It can significantly reduce pain, reduce post-operative nausea, and vomiting and allowing for faster discharge from hospital. Performing this block under ultrasound guidance has higher index of safety and can monitor the distribution of local anesthetic (LA) in real time.
The aim of this study is to compare the block characteristics among bupivacaine-dexmedetomidine (BD), bupivacaine–nalbuphine8 (BN), and bupivacaine-isotonic saline groups.

Results: The duration of both the sensory and motor blockade was statistically longer in both BD and BN groups with a longer duration of analgesia compared to the BS group. Also, the BD group showed statistically significant higher sedation scores at different times during the study compared with both the BN and BS groups.

Conclusion: Adding either dexmedetomidine or nalbuphine to isobaric bupivacaine in US-guided supraclavicular brachial plexus block prolongs both sensory and motor blockade. Dexmedetomidine produces significant sedation when added to bupivacaine.

Keywords: Brachial plexus, Dexmedetomidine, Nalbuphine, Supraclavicular

Background

Brachial plexus block is the practical alternative to general anesthesia for surgery on the upper limb as it provides superior quality of intra- and post-operative analgesia and rapid recovery and negates the common side-effects of general anesthesia such as postoperative nausea and vomiting. Also, it is useful in patients with profound co-morbidities such as severe cardiovascular and respiratory diseases and morbid obesity and those with difficult airways (Richman et al. 2006).

Ultrasound visualization of anatomical structures facilitates safe methods for regional blocks as the anesthesiologist secure an optimal needle position and can monitor the distribution of local anesthetic in real time (Griffin and Nicholls 2010; Russon and Pickworth 2010).

To prolong the duration of analgesia during the brachial plexus block, various drugs have been used as adjuvants to local anesthetics. Addition of adjuvants to local anesthetics improves the onset and duration of the blockade, gaining patient satisfaction and maintaining proper hemodynamics, together with reducing the need for postoperative analgesics (Kayser 2002).

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Dexmedetomidine is an α_2-receptor agonist that has been used as an adjuvant to local anesthetics (LA) as it has both analgesic and sedative properties (Swami et al. 2012a).

Nalbuphine, derived from 14-hydroxymorphine, is considered an agonist-antagonist analgesic having a mixture of k agonist and u antagonist properties. It has been used successfully and safely in epidural and intrathecal blocks (Gupta et al. 2016).

The present study aims at evaluating the block characteristics of dexmedetomidine and nalbuphine as L.A. adjuvants in US-guided supraclavicular brachial plexus block for patients undergoing upper arm surgeries.

Methods

This prospective, randomized, double-blind, controlled comparative clinical study was carried out in Qena University Hospitals. Written informed consent was taken from every patient participating in the study after getting approval from the Ethical Committee of Qena University Hospitals, Qena, Egypt.

Ninety patients were selected for this study, divided into three groups randomly using closed envelop method. The three groups were as follows: group BD (n = 30) received 24 ml of 0.5% isobaric bupivacaine + 1 ml (100 ug) dexmedetomidine, group BN (n = 30) received 24 ml of 0.5% isobaric bupivacaine + 1 ml (10 mg) nalbuphine, and group BS (n = 30) received 24 ml of 0.5% isobaric bupivacaine + 1 ml normal saline in the supraclavicular block under US-guidance. Patients of ASA physical statuses I and II, 21–60 years, both sexes, scheduled for mid humerus, elbow, forearm or hand surgery were included in the present study.

Exclusion criteria included patient refusal, bleeding disorders or patients on anticoagulants, pregnancy, cardiac or respiratory diseases, local infection at the site of injection, and neurological disorders including brachial plexus, patients receiving sedatives, and patients with known allergy to any of the studied drugs. All patients were kept safe according to the standard guidelines (6 h for solids and 2–4 h for clear fluids pre-operatively).

Upon arrival to the operating room, standard anesthetic monitoring (non-invasive blood pressure, pulse oximetry, ECG) was connected and recorded as pre-block values and an intravenous cannula (18–20 G) was applied on the upper limb on the contralateral side of the surgery and an infusion of lactated ringer solution was administered at a dose of 10–20 ml/kg.

Patients were positioned supine with the head turned away from the limb to be operated upon and the arm was placed by the side of the patient. The skin was sterilized and prepared. The skin at the point of the needle entry was locally anesthetized with a subcutaneous injection of 3 ml of 1% lidocaine. To identify the brachial plexus an ultrasound (M-turbo; sonosite, Bothell,

Washington, USA) was used. An adult linear ultrasound probe with a frequency range of 6–13 MHz was placed superior to the clavicle in the mid clavicular point. Sterile water-based gel was used between the probe and skin. The brachial plexus was identified in relation to the pulsating subclavian artery and the hyperechoic first rib. The brachial plexus was seen as a collection of hypoechoic oval structures lateral and superficial to the artery.

Under ultrasound guidance, a sterile 22-G spinal needle was then advanced using an in-plane technique from the lateral to the medial direction. Once the tip of the needle reached, the nerve sheath negative aspiration was performed, then 25 ml of the prepared study solution was injected incrementally (5 ml each) as per group assigned around the plexus under vision at the angle between the subclavian artery and first rib and also outside nerve sheath. Distension of the brachial plexus sheath was regarded as an indication of a successful block. All patients were given supplemental oxygen using the face mask. Neither the administrator nor the observer was aware about the drug solution used as it was prepared by a different investigator. The drug was to be revealed only on the occurrence of any adverse events.

The block was tested for both sensory, and motor block and was compared with the contralateral side. The sensory block was graded using a 3-point scale by the pin-prick method, where 0 = no pain, 1 = dull pain, and 2 = sharp pain (Koh et al. 2015). The sensory block was assessed in the dermatome areas corresponding to the median nerve, radial nerve, ulnar nerve, and musculocutaneous nerve (C_5–T_1) until the completion of sensory blockade. The supraclavicular block was considered successful when all dermatomes of brachial plexus (C_5–T_1) were blocked within 30 min. The onset of the sensory block was defined as the interval between the end of injection of LA mixture and complete loss of the pin-prick sensation in the median, radial, and ulnar dermatomes in the anesthetized upper limb. It was evaluated every 2 min for the first 30 min and every 60 min after completion of surgery till the complete resolution of the sensory block. Sensory block duration was defined as the time from injection of a local anesthetic solution to complete recovery for pain sensation in all dermatomes of the brachial plexus.

Assessment of the motor block was carried out according to the modified Bromage scale for upper extremities every 3 min till complete motor blockade (Swami et al. 2012b). (grade 0: normal motor function; grade 1: ability to move only fingers; grade 2: complete motor block with the inability to move the wrist and fingers). The onset of motor blockade was the time taken from the end of LA injection to the development of grade 3 motor block. The duration of the motor block was the time interval between the end of LA injection to

the recovery of the complete motor function of the hand and forearm.

The quality and duration of analgesia were assessed every hour postoperatively in the recovery room and in the surgical ward using visual analog scale (VAS) graded from 0 to 10 (where 0 = no pain and 10 = the worst possible pain) which were explained to all patients in their preoperative visit (Jensen et al. 2003).

At the score of 4, ketorolac amp. of 30 mg was administered intravenously as a rescue analgesic. The duration of analgesia was calculated from the time of LA injection to the time of the first analgesic requirement. The time of the first rescue analgesic requirement and the total amount of rescue analgesic medication given over the first 24 h (at VAS of 4 or more) were recorded.

Sedation was evaluated every 30 min (T_0 = sedation level by the end of injection of LA) for 2 h, then every 1 h for the next 6 h by a physician who is blind to the study protocol using a 4-point scale as per Filos et al. (Filos et al. 1994) where 1-awake and alert; 2-drowsy, responsive to verbal stimuli; 3-drowsy, arousable to physical stimuli; and 4-unarowsable.

Intra-operative heart rate (H.R.), mean arterial pressure (MAP), and oxygen saturation (SPO_2) were recorded at the following times: T_0 = basal readings before performing the block, T_1-T_3 = readings obtained every 5 min after LA injection for 15 min, and T_4-T_{10} = readings obtained every 15 min for 2 h after injection of LA. Hypotension was defined as a decrease in MAP more than 20% of baseline value and was planned to be treated with an infusion of isotonic saline and 5 mg bolus of ephedrine. Bradycardia was defined as a decrease of HR below 50 beat/min and was planned to be treated with atropine 0.5 mg. The patient was considered hypoxic if the oxygen saturation was less than 90% and was planned to be managed with supplemental oxygen through a nasal cannula or face mask.

All patients were observed for any possible side-effects such as hypotension (i.e., 20% decrease in the mean blood pressure relative to baseline), bradycardia (heart rate < 50 beats/min), nausea, vomiting, hypoxemia, pneumothorax, hematoma, and LA toxicity in the intra- and postoperative periods which were recorded and managed accordingly.

Sample size calculation

To calculate the sample size, the duration of the sensory block was considered as the primary outcome. Twenty-six patients were needed in each group to achieve an α error level of 0.05, with 80% power and 95% confidence level.

The enrollment of 30 patients in each group compensates for possible dropouts. The sample size was calculated using the G*Power 1.3.7.software.

Statistical analysis

Data analysis was performed using SPSS version 21 (SPSS Inc., Chicago, USA). Data were presented as mean ± SD, number (percentage), or median (range) as appropriate. To compare the mean values between the three groups, one-way analysis of variance (ANOVA) and Tukey's post hoc test were used. Variations within the same group were analyzed using the paired-samples t test. The X^2 test was used for the comparison of proportions and frequencies among groups. Kruskal-Wallis test was used to compare the groups. P value < 0.05 was considered statistically significant.

Results

A total of 99 patients were enrolled for this study; Of the 99 patients, 6 refused this regional technique and 3 did not meet the inclusion criteria and were excluded from the study as shown in Fig. 1. The demographic data of the patients (age, weight, height, gender, ASA grade) were comparable in the studied groups (Table 1).

The mean onset times of the sensory and motor blocks were not statistically significant in the three groups (Table 2). The mean duration of sensory and motor blocks was significantly more in groups BD and BN compared to the control group BS (P value < 0.001) (Table 2).

Regarding the duration of the sensory and motor blockade, the results obtained showed a highly statistically significant longer duration of the sensory and motor block in BD and BN groups when compared with the control group BS (P value < 0.001). There were no statistically significant differences in the duration of the sensory and motor block between the group BD and group BN (P value > 0.05) (Table 2).

The mean duration of analgesia was highly statistically significant longer in groups BD and BN when compared with the control group BS (P value < 0.001) (Table 2). The duration of the first rescue analgesic was statistically significant longer in both groups BD and BN than that in the group BS. Also, groups BD and BN showed a statistically significant decrease in the total amount of analgesic consumption during the first 24 h when compared with the control group (P value < 0.001) (Table 2).

The BD group patients showed statistically significant higher sedation scores at 30 min after completing the injection of the study drug and extended for 360 min compared to the control group (P value < 0.05) and were statistically significant higher than group

Fig. 1 Consort flow diagram showing the number of patients at each phase of the study
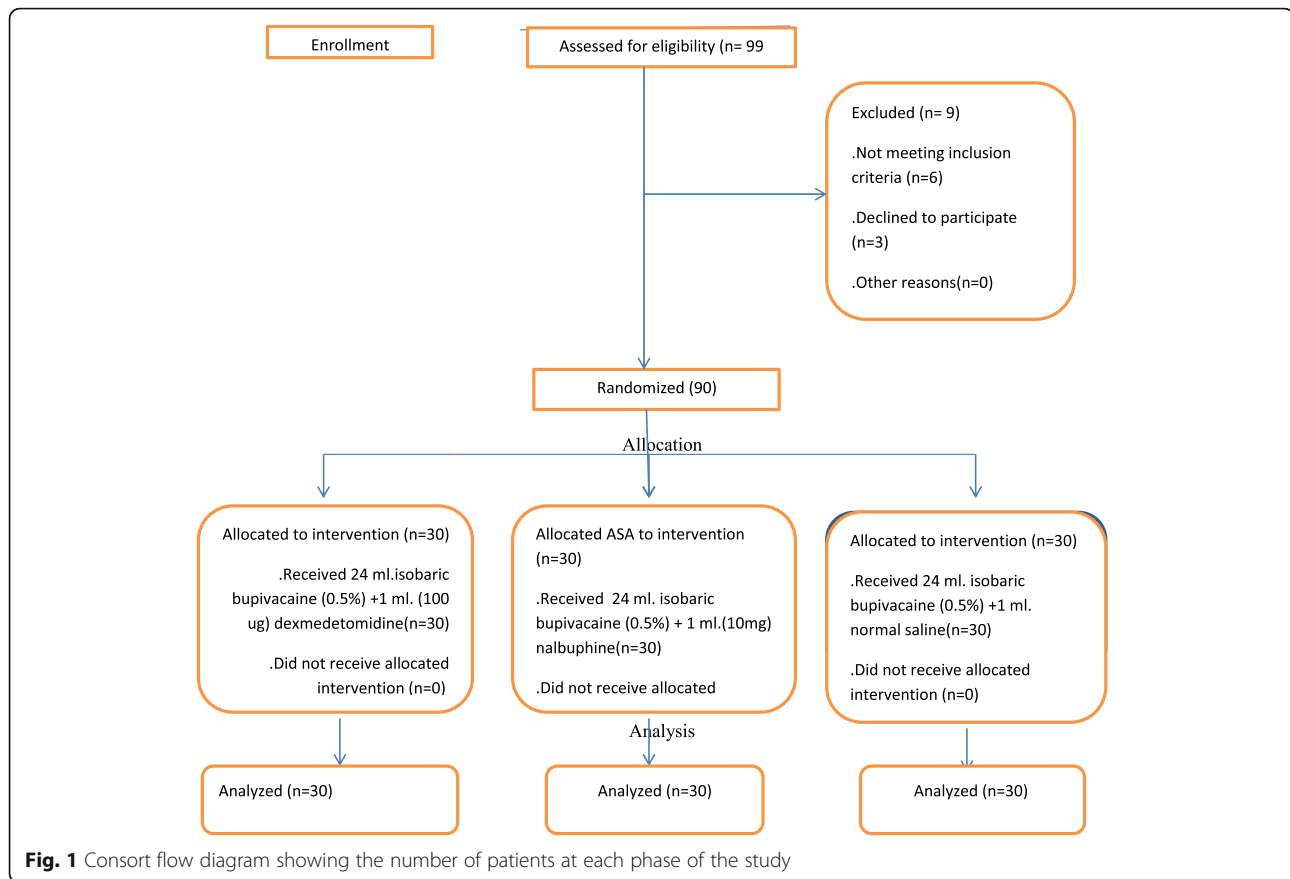
BN after 90 min and extended for 360 min (*P* value < 0.05). Also, the sedation level in the BN group was statistically significant higher when compared to group BS (control group) at 30 and 60 min as shown in Table 3 (*P* value < 0.05).

The BD group showed clinically lower HR and MAP values than the other two studied groups (groups BN and BS) but with no statistically significant differences compared with the other two studied groups (groups BN and BS) (Figs. 2 and 3). There were no reported adverse events in any of the studied groups.

Discussion

The present study showed that the addition of either dexmedetomidine or nalbuphine to bupivacaine in US-guided supraclavicular brachial plexus block prolongs the duration of both sensory and motor blockade and reduces postoperative analgesic requirements. Also, the addition of dexmedetomidine produces significant sedation during intraoperative and postoperative periods without significant hemodynamic effect.

Several studies had used dexmedetomidine as an adjuvant to LA in different regional and peripheral nerve

Table 1 Demographic data, ASA status, and duration of surgery

Parameter	Group DB	Group NB	Group SB	*P* value
Age (years)	37.4 ± 8.7	38.2 ± 9.1	38.6 ± 9.4	0.736
Weight (kg)	73.6 ± 5.3	74.3 ± 6.2	75.1 ± 6.3	0.852
Height (cm)	169.5 ± 11	173.2 ± 14	175.6 ± 16	0.865
Gender (M/F)	21/9	20/10	19/11	0.678
ASA (I/II)	22/8	21/9	20/10	0.723
Duration of surgery (min)	127.6 ± 14.8	131.2 ± 16.2	129.6 ± 15.6	0.428

Data are represented as either mean ± SD or by absolute numbers
M/F male to female ratio, *ASA* American Society of Anesthesiologists
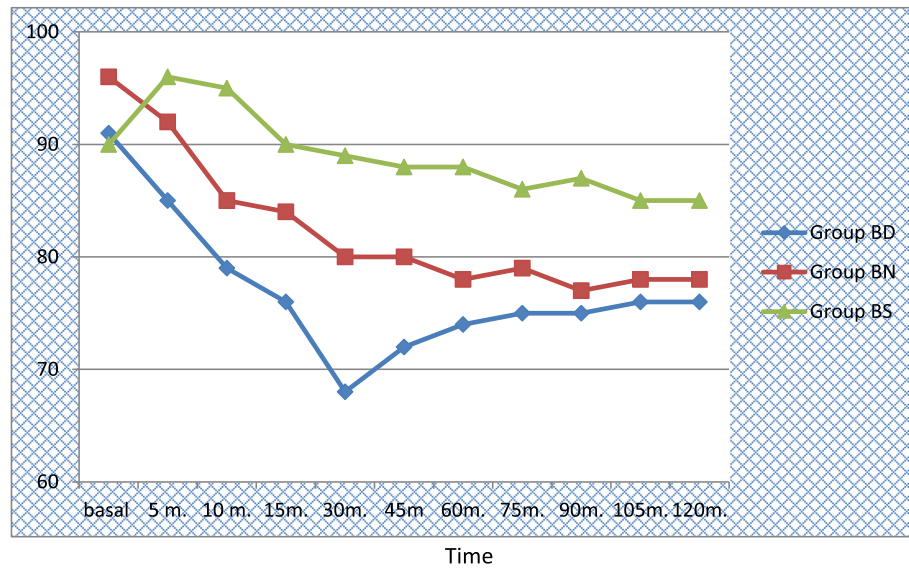
Group BD: Group Bupivacaine-Dexmedetomidine; Group BN :Group Bupivacaine-Nalbuphine; Group BS:Group Bupivacaine-Saline.

Values are in mean ± SD

Fig. 2 Heart rate changes in the studied three groups. Group BD group bupivacaine-dexmedetomidine, Group BN group bupivacaine-nalbuphine, Group BS group bupivacaine-saline. Values are in mean ± SD

blocks and found that it has a marvelous effect in potentiating the local anesthetic effect (Kanazi et al. 2006; Masuki et al. 2005; Yoshitomi et al. 2008; Marhofer et al. 2012; Brummett et al. 2008).

Possible mechanisms for dexmedetomidine-induced prolongation of both sensory and motor blockade include vasoconstriction through an action on α_2 adrenoceptors or it produces analgesia peripherally by reducing norepinephrine release and increasing the potassium conduction in C- and A-delta neurons responsible for the transmission of pain signals, whereas it produces analgesia and sedation centrally by inhibition of substance P release in the nociceptive pathway at the level of dorsal root ganglia and locus ceruleus (Masuki et al. 2005; Yoshitomi et al. 2008).

Marehofer et al. and Brummett et al. mentioned in their studies (Marhofer et al. 2012; Brummett et al. 2008) that the duration of analgesia achieved by dexmedetomidine may be due to block of the hyperpolarization-activated cation current (Ih current) which prevents the nerve from returning from a hyperpolarized state to resting membrane potential for subsequent firing and generation of a new action potential. This (Ih current) seems to be more obvious in the unmyelinated C fibers (pain) than in A α fibers (motor). So, blocking the (I_h) current may have

Table 2 Onset and duration of the sensory and motor blocks, duration of analgesia, time of the first rescue analgesic requirement, and total dose of rescue analgesia over 24 h in the studied three groups

Parameter	Group BD	Group BN	Group BS	P value
Sensory onset (min)	10.6 ± 2.9	11.3 ± 3.4	12.1 ± 3.6	0.263
Motor onset (min)	13.7 ± 4.1	14.2 ± 3.9	14.3 ± 4.1	0.352
Sensory duration (min)	625.7 ± 25.4***	598.4 ± 22.7***	263.7 ± 15.9	<0.001
Motor duration (min)	542.3 ± 13.7***	519.6 ± 12.8***	197.6 ± 14.3	<0.001
Duration of analgesia (min)	683.4 ± 31.7***	648.7 ± 23.5***	285.7 ± 16.4	<0.001
Time to the first analgesic request (min)	726.3 ± 32.5***	687.5 ± 28.4***	297.6 ± 17.3	<0.001
Total dose of rescue analgesia over 24 h (mg)	35.2 ± 7.4	38.4 ± 8.1	74.8 ± 11.3***	<0.001

***high statistical signicance
Values are in mean ± SD. *P* value < 0.05 is statistically significant

Table 3 Sedation level in the studied three groups

Variable	Group BD	Group BN	Group BS	P value
T_0 (basal)	1 (1–2)	1 (1–2)	1 (1–2)	0.987
T_1 (after 30 min)	2 (1–3)*	2 (1–3)*	1 (1–2)	0.029
T_2 (after 60 min)	2 (1–3)*	2 (1–3)*	1 (1–2)	0.032
T_3 (after 90 min)	2 (1–3)*	1 (1–2)	1 (1–2)	0.028
T_4 (after 2 h)	2 (1–3)*	1 (1–2)	1 (1–2)	0.031
T_5 (after 3 h)	2 (1–3)*	1 (1–2)	1 (1–2)	0.033
T_6 (after 4 h)	2 (1–3)*	1 (1–2)	1 (1–2)	0.035
T_7 (after 5 h)	2 (1–3)*	1 (1–2)	1 (1–2)	0.036
T_8 (after 6 h)	2 (1–3)*	1 (1–2)	1 (1–2)	0.038

*slight statistical significance

Data are represented as median (range). T_0: sedation level by the end of injection of local anesthetic. T_1–T_4: sedation level as evaluated every 30 min for 2 h. T_5–T_8: sedation level evaluated every 1 h for the next 4 h. Kruskal-Wallis test was used. P value < 0.05 is statistically significant

a more pronounced effect on pain than in motor response and this may explain the action of dexmedetomidine in prolongation of local anesthetics in the peripheral nerve block.

In our study, we found that the addition of 100 μg dexmedetomidine to 24 ml bupivacaine significantly prolonged the block and analgesia duration. These results met with Marhofer et al. and Masuki et al.

Several studies had used opioids as local anesthetic adjuvants, and it was found to improve the efficacy of peripheral nerve blocks through stimulation of opioid receptors but they were associated with significant adverse effects (Saryazdi et al. 2015).

It may augment the action of LA_s through central opioid-receptor-mediated analgesia by peripheral uptake of nalbuphine to the systemic circulation. However, studies regarding the effect of nalbuphine as an adjuvant to LA_s in peripheral nerve blocks are few (Gunion et al 2004, Abdelhaq and Elramely 2016).

Gupta et al. (Gupta et al. 2016) as well as Abdelhaq and Elramely (19) studied nalbuphine as an adjuvant to bupivacaine for supraclavicular brachial plexus block for upper arm procedures and found that nalbuphine had significantly increased the duration of both sensory and motor block in association with prolonged post-operative analgesia which come in accordance with the results obtained in this study.

Regarding the significant sedation observed with the addition of dexmedetomidine to bupivacaine, the results of this study were similar to those obtained by Mathew et al. (Mathew et al. 2018) and Agrawal et al. (Agrawal et al. 2014).

The clinically observed, but not statistically significant, bradycardia that occurred in the present study was in accordance with the study performed by Nazir and Jain (Nazir and Jain 2016).
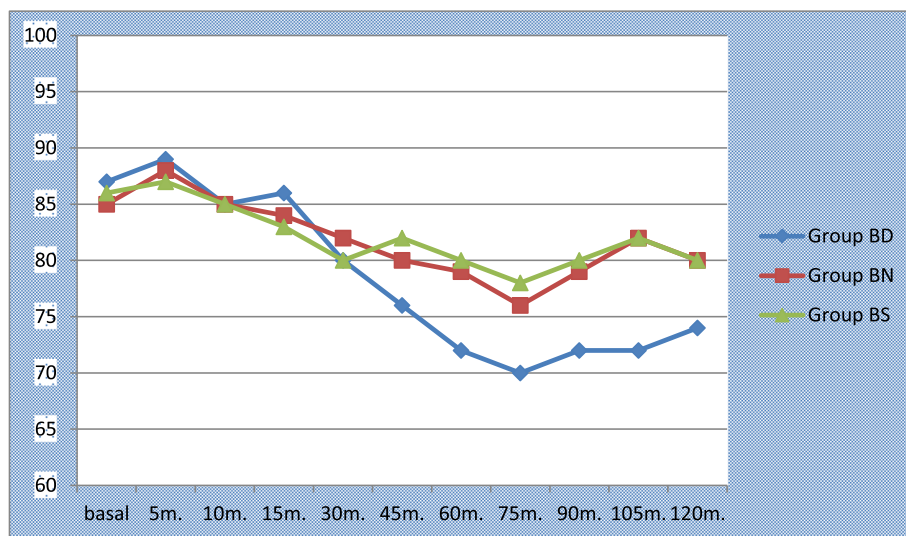
Group BD: Group Bupivacaine-Dexmedetomidine; Group BN: Group Bupivacaine-Nalbuphine; Group BS: Group Bupivacaine-Saline.

Values are in mean± SD.

Fig. 3 Mean blood pressure changes (MBP) in the studied three groups. Group BD group bupivacaine-dexmedetomidine, Group BN group bupivacaine-nalbuphine, Group BS group bupivacaine-saline. Values are in mean ± SD

Conclusion

To conclude, the addition of either dexmedetomidine or nalbuphine to bupivacaine in the US-guided supraclavicular brachial plexus block prolongs both the sensory and motor blockade with prolongation of the time of the first rescue analgesic requirement in the postoperative period. Moreover, the addition of dexmedetomidine produces notable sedation during the surgery and may extend to the postoperative period.

Abbreviations

ASA: American Society of Anesthesiologists; BD: Bupivacaine-dexmedetomidine group; BN: Bupivacaine-nalbuphine group; BS: Bupivacaine-saline group; ECG: Electrocardiography; HR: Heart rate; LA: Local anesthetic; MAP: Mean arterial pressure; SD: Standard deviation; US: Ultrasound

Authors' contributions

H.S. Mohamed analyzed and interpreted the patient data, performed data collection and tabulation, and shared writing and revision of the manuscript. G. S. Gad contributed to the writing and revision of the manuscript. The authors read and approved the final manuscript.

Availability of data and materials

The datasets used during the current study are available from the corresponding author.

Ethics approval and consent to participate

The study protocol was approved by the Ethics Committee of Qena University Hospitals on December 2, 2017, and written informed consent was given from participants before the study.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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