The effect of dexmedetomidine with bupivacaine combination and only bupivacaine on sensory and motor block time and pain score in supraclavicular block

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Research

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Abstract

Background: This study was designed to assess the effect of dexmedetomidine on the effect of dexmedetomidine with bupivacaine combination and only bupivacaine on sensory and motor block time, pain score, and hemodynamic variations in supraclavicular block in upper extremity orthopedic surgery.

Methods: This prospective double-blind study was performed on 60 patients aged 20-60 years who were candidates for upper extremity orthopedic surgeries. The sensory block was evaluated using the pinprick method and motor block by the modified Bromage scale method. The post-operative pain was assessed by a visual analog scale.

Results: The mean onset time of sensory and motor block in patients receiving bupivacaine alone was respectively 31.03± 9.65 min and 24.66 ± 9.2 min and in the dexmedetomidine receiving group was about 21.36±8.34 min and 15.93 ± 6.36 minutes. The changes in heart rate and mean arterial blood pressure was similar in both groups. The duration of sensory and motor block and the time of the first analgesia request in the intervention group were longer. Postoperative pain was lower in the intervention group for 24 hours (P = 0.001).

Conclusion: The use of dexmedetomidine plus bupivacaine, without side effects, reduced the onset time of sense and motor blocks and increased the duration of numbness and immobility. Also, dexmedetomidine reduced postoperative pain significantly in use with bupivacaine for supraclavicular blocks.

Trial registration: IRCT, IRCT20160430027677N15. Registered 05/28/2019, http:// https://www.irct.ir/trial/39463

Background:

The use of supraclavicular blocks of the brachial plexus is used extensively and effectively for the surgical operation of the distal upper extremity [1, 2]. This technique is used with general anesthesia or alone, as an anesthesia method for distal limb surgery with very low complication. However, about of effectiveness of this method in upper extremity surgery, various reports have been presented but so far selective drug combination for the supraclavicular block has not been considered [1]. To increase the duration of local anesthetic action in supraclavicular block, epinephrine, α2 agonist, corticosteroids, bicarbonate, and opioids have been used. In between, epinephrine is mostly utilized. Even though epinephrine reduces absorption of local anesthetics and also reduces their toxicity and prolongs anesthetic duration. But it can cause hypertension and tachycardia. Therefore its usage is limited when the patients have cardiovascular disease or hyperthyroidism [3–6]. The use of upper extremity blocks instead of general anesthesia has the potential to provide longer pain relief and less use of postoperative analgesia, fewer complications from these drugs, and ultimately early recovery and faster discharge from the hospital [7]. The rare complications of supraclavicular nerve block can be mentioned to pneumothorax, phrenic nerve block, Horner syndrome, and neuropathy and nerve damage [8].

In modern anesthesia, the use of safe, effective and newer drugs has been emphasized. Use the additive drugs in local anesthesia can be reduced the dosage of local anesthesia drugs for nerve block and reduced the probable side effects of these drugs and as well as the advantages of adjuvant drugs can be used. The new drugs have been used in this field such as Buprenorphine [10], Dexamethasone [11], Magnesium [12], and Midazolam [13] that the use of these drugs in order to reduce onset block time, increasing the duration of analgesia without incidence of unwanted systemic complications, motor block prolongation and finally reducing the total dose of local anesthetics drugs has been proposed and studied. Recently, alpha-2 receptor-stimulating drugs due to excellent sedative effects, analgesia, and anesthesia with hemodynamic stability have been considered [14].

Bupivacaine is a potent local anesthetic with unique characteristics from the amide group of local anesthetics which was first discovered in 1957 and widely used for prolonged local and regional anesthesia. [15]

The dexmedetomidine is a specific Alpha2 agonist with an α2:α1 ratio of 1620:1 and is metabolized in two ways via liver glucuronidation and cytochrome P450. [16–18] dexmedetomidine recently added to the drugs used in the nerve block, including bupivacaine. Singh AP et al in 2016 studied the effect of dexmedetomidine with levobupivacaine [19] and also Tripathi A et al in 2016 compared the effect of adjuvant dexmedetomidine and clonidine to bupivacaine in brachial plexus block for upper extremity surgery [20]. They concluded that using dexmedetomidine reduces the onset time of the sensory and motor block. And also it prolongs the duration of anesthesia and analgesia and increases quality in anesthesia in the block.

Limited studies have been conducted on the use of local anesthetics with additive agents [10–13, 21, 22]. However, a unit drug for adding local anesthetic to improve block quality is not recommended [9]. According to the above items, this study was designed to assess the effect of dexmedetomidine with bupivacaine combination and only bupivacaine on sensory and motor block time, pain score, and hemodynamic variations in supraclavicular block in upper extremity orthopedic surgery. We hypothesized that the addition of dexmedetomidine as an adjuvant to bupivacaine can be useful in improving the quality of the brachial plexus block. The primary endpoints of our study were sensory and motor block quality as assessed by the pinprick method and Bromage scale and post-operative pain was evaluated by the visual analog scale of pain (VAS) [23] and secondary outcomes included the effect of dexmedetomidine on hemodynamics, complication and time to the first analgesic request.

Methods:

Study design:

After being approved by the Research and Ethics Committee (**IR.UMSU.REC.1397.181**) of the Urmia University of Medical Sciences and Iranian Registry of Clinical Trials (**IRCTID: IRCT20160430027677N15)**, this randomized double-blind prospective study was conducted among 60 patients (30 patients in each group), aged 20 to 60 years old, by American Society of Anesthesiologists (ASA) class I and II who were

candidates for upper extremity orthopedic surgeries with supraclavicular block was performed. Based on the Tripathi A et al study in 2016 [20], considering the power (probability) test 80% and confidence interval 95% (α =0.05 β10% =), The sample size 30 patient in each group was determined. Patients were divided into two groups (intervention and control groups) according to the random number table, and the anesthesiologist did not know which patient belonged to which group. To data collection, the researcher used direct observation and preset self-made checklist that validity and reliability were already proven.

Subjects and setting:

All patients were visited by anesthesiologist the day before the surgery. Adequate explanation and training were given to patients about the Visual Analog Scale (VAS) (zero: no pain and, ten: the worst pain ever experienced). In this study Patients with history of central nervous system disease or neuromuscular disorders, psychiatric, renal dysfunction, respiratory, cardiovascular and hepatic disease, pregnant women, lactating mothers, history of allergy to any of the drugs used during the study, diabetics, and patients who performing a supraclavicular block in them is contraindication such as coagulopathy, local infection and patients' refusal was excluded from the study.

Intervention design:

Patients in the dexmedetomidine group (intervention) received 39 ml of 0.25% bupivacaine +0.75 μg/kg dexmedetomidine that the volume with normal saline was increased to 1 ml and in control group, patients received 39 ml of 0.25% bupivacaine + 1 ml normal saline for increased volume to 40 ml. patients were kept fasting for at least 8 hours before surgery. The patients, surgeons, and anesthesiologists were blinded to the division of the groups.

In the operating room, standard pulse oximetry monitor, noninvasive blood pressure (SBP and DBP) measurement system and an electrocardiogram were attached. And baseline of heart rate, respiratory rate, SPO2, and ECG were noted. After insertion of an 18-cm venous catheter on the non-operative arm before to performing supraclavicular block, All patients sedated by midazolam 0.04 mg/kg IV and received oxygen at 5 L/min and they were placed in the supine position and slightly turned their heads to the opposite side with the upper arm abducted at 90°. Before performing procedure all antiseptic and aseptic precautions were performed for block site. supraclavicular plexus site was determined by using a nerve stimulator (Stimuplex; B. Braun Melsungen, Melsungen, Germany) attached to 22-gauge, 55 mm long stimulating needle (Stimuplex D; B. Braun Melsungen, Melsungen, Germany) under ultrasonic apparatus was applied. The needle location was considered to be acceptable when an output current of 0.5 mA still evoked an appropriate motor response at the distal of the limb. The solution was injected under the guidance of the ultrasonic apparatus. Sensory and motor blocks were assessed every 3 min until the first 30 minutes after full injection of the drug and if the block was determined to be sufficient, surgery allowed. All Vital parameters including HR, NIBP, RR, and SPO2were measured and recorded in the checklist every 5 min for the first 30 min and afterward every 10 min till the end of surgery.

Variables:

Sensory and motor block and vital signs were measured instantly after surgery in the recovery room (where the block was done). sensory blockade of each nerve evaluated by pinprick method in sensory dermatomes related to the sensory areas and graded as score 0 = no sensation, score 1 = dull sensation, score 2 = sharp pain felt [23] and motor blockade was evaluated by using modified Bromage scale as 3 = elbow flexion against gravity force, 2 = wrist flexion against gravity force, 1 = finger movement and 0 = no motion [23]. The onset of sensory block was defined as the time between the local anesthetic administration till dull sensation to pinprick test and the onset time of motor block was considered as the time between injection till Bromage score 2. The duration of sensory block was determined as the time interval onset of sensory block till the first pain sensation in the Pinprick test, and the duration of the motor block was described as the time interval between the complete motor paralysis and full movement of the limb. Patients postoperative pain perception was assessed by Visual Analog Scale score (VAS) that was explained to the patients by scored pain severity between 0 and 10 (0, no pain and 10, worst pain imaginable) The severity of pain was measured and noted in recovery at 6, 12 and 24 hours after surgery. When the VAS was greater than 4, analgesia was administered. The time of local anesthetic injection and the first analgesic administration was considered as the duration of analgesia. Patients were monitored for All adverse effects such as hypotension (a 20% decrease from baseline value), bradycardia (HR <50), hypoxemia (SpO_2<90%), or nausea and vomiting and were recorded in the questionnaire.

Statistical analysis:

In providing descriptive features, tables and Frequency Charts and descriptive statistics including Mean and standard deviation were used. For normal data, the Repeated Measures test was used to compare the mean pain at 6, 12 and 24 hours after surgery And the Friedman test was used for non-normal data. In this study, to investigate qualitative variables such as gender, the Chi-square test was used, and for quantitative variables in two groups, an independent t-test was used for normal data and for non-normal data the Man-Whitney test was used. The normality of data was tested using the Kolmogorov-Smirnov test. The results were analyzed by SPSS software version 23 and p-value ≤ 0.05 was considered significant.

Result:

The patient's demographics data in the two groups were presented in table 1. According to the table 1 data and the chi-square test, there was no statistically significant difference between the two groups characterizes data including gender, weight, age, and kind of surgery (P>0.05).

Sensory and motor block onset time:

Onset time of upper extremity sensory block in the intervention group was lesser than the control group and this difference was significant (p =0.026). Also the upper extremity motor block onset time in the control group was more than intervention group and it was statistically significant (p =0.041).

Sensory and motor block score:

According to the non-normal distribution of data in the Mann-Whitney test, the mean score of sensory block in the control group was 31.25 with a total score of 937.5 and in the intervention group mean score and the total score was respectively 29.75 and 892.5. This difference was not significant (p = 0.809) but the score was less in the intervention group.

The mean score of the motor block (Bromage score) in the control group was 35.58 with a total score of 10.567 and in the intervention group, the mean score was 25.42 with a total score of 765.5. This difference was statistically significant (p = 0.012) and the mean score was lower in the intervention group.

Sensory and motor block duration:

In the bupivacaine group, the duration of sensory block in the upper extremity was 333.5 ±94.35 min and in the intervention group was 475 ±137.5 minutes. In the intervention group, the duration of anesthesia was longer than the control group and this difference was statistically significant (p = 0.022)

In the control group the duration of motor block was 317 ±10.52 minutes and in the intervention group was 488 ±157.5 minutes and this difference was significant (p = 0.03)

The first analgesia request in the control group was 308 ±109. 14 minutes and in the intervention group was 458 ±205/43 minutes. The time of the first analgesic request in the intervention group was more than the control group and this difference was significant (p = 0.001).

Heart rate variation:

The mean of heart rate variations in the outset and at the end of the surgical procedure was reduced in both groups, in the intervention group was 72.45±8.05 beats and in the control group was 76.3±14.4 beats. In conducted independent t-test it was not significant (P = 0.454).

Mean arterial pressure changes:

The mean changes in mean arterial pressure during surgery in the intervention group was 83.24 ±11.36 mm Hg and in the control group was 76.93 ±10.06 mm Hg that in conducted independent t-test it was not significant (P = 0.123).

Pain score after surgery:

Mean pain score based on VAS after surgery, recovery, 6 hours after surgery, 12 hours and 24 hours after surgery in the control group (receiving bupivacaine alone) were 0.633, 2.633, 3.313, 6.017 and 5.11 respectively and in the intervention group (bupivacaine + dexmedetomidine) were 0.47, 1.14, 3.23, 5.12 and 3.92, respectively. In Two Way Repeated Measure Anova test with P=0.001, this difference inpatient pain evaluation was significant and in all hours of study in the intervention group was lesser than the control group.

Complications:

Hypotension occurred in 3 patients in both intervention and control groups that it was not statically significant (p = 0.217). Nausea in 4 patients in the control group and 1 patient in the intervention group was observed that was not significant (p = 0.353). 4 patients in the control group and 2 patients in the intervention group had bradycardia it was not significant (p = 0.554).

Discussion:

Rapid onset and prolonged analgesia and motor block without adverse effects highlighted an ideal local block. Hence many various drugs have been added to topical anesthetic drugs as an adjuvant. In prior studies, clonidine has been used as an α2 agonist with ropivacaine in the axillary block [24]. In recent studies, Intravenous administration of dexmedetomidine has been described as an effective drug in increasing the time of spinal anesthesia [25, 26]

Dexmedetomidine is an active D-isomer of medetomidine and a specific agonist of the α2 adrenoceptor. Dexmedetomidine is similarly related to clonidine, but dexmedetomidine has an (α-2: α-1) selectivity 1620:1 compared with Clonidine that has a specificity of 220: 1 (α-2: α-1) [25, 27]. The activation of the presynaptic receptor in the central nervous system prevents the nor-epinephrine releases and pain signals. It also prevents sympathetic activity by postsynaptic effects and reduces heart rate and blood pressure. Dexmedetomidine produces a natural sleep for the patient with an effect on the Locus coeruleus [28, 29].

Dexmedetomidine has been used without nerve damage. In the Brummet et al. study that had been done on rats, After 24 hours and 14 months, axons and myelin have been reported as no damage [30].

In the Rachana G et al. study in 2012 that it was conducted on 70 patients, the onset time of sensory block was lower in the bupivacaine group compared to bupivacaine with dexmedetomidine and also in the control group the onset of motor block was less than dexmedetomidine group and duration of sensory and motor block was prolonged in dexmedetomidine group. Mean arterial pressure and heart rate variations were similar between the two groups and the duration of analgesia in the control group was less than the intervention group (dexmedetomidine) [31]. The results of this study are consistent with our finding.

In this study, the rapid onset of motor block compared to sensory block indicated the existence of motor fibers in the outer layers of the nerve versus central sensory fibers have been mentioned and in Winnie et al. study has been explained [32]. In the study that had done on 50 patients in 2014 by Saudlyer A et al. the onset time of sensory block and limb immobilization in the group that they had received dexmedetomidine with bupivacaine was less than of bupivacaine singly and it also the duration of sensory and motor block in group who had received dexmedetomidine was more. The duration of analgesia in the dexmedetomidine group was prolonged than the control group. The results of this study are consistent with our study, however; the dose of the drug used in the two studies is different.

In a study by Neerja Bharti et al was conducted on 60 patients in two groups were divided into control (Ropivacaine and lidocaine with adrenaline) and intervention (Dexmedetomidine 1 μg / kg plus other drugs) groups, the onset of sensory block was similar in the two groups. The onset of immobility was less in the receiving dexmedetomidine group and the duration of sensory block and immobility was higher in the dexmedetomidine group that had reduced postoperative pain and need for analgesia in patients in the intervention group. [33] In the present study, the onset of sensory block was less in the dexmedetomidine group and this difference was statistically significant. In other measured parameters, the results of the two studies were not different. It seems, no difference in the onset time of sensory block in two groups Due to used the low dose of dexmedetomidine combined with the high volume of other drugs that have reduced the effective dose of local dexmedetomidine.

In a recent meta-analysis that performed by Abdallah Brull, the adding of dexmedetomidine to other drugs has been reported to prolong the motor block of the brachial plexus and prolonged the postoperative analgesia [34]. The results of this study are consistent with our study findings.

In separate studies conducted by Saumya B and Suncet Katarina et al., Dexmedetomidine with ropivacaine had improved the onset of sensory and motor block and the duration of sensory block and motor block compared with ropivacaine[35].

In our study, dexmedetomidine reduced the onset time of sensory and motor block and had increased the duration of sensory and motor block. This was similar to previous studies. The decrease of the onset time of sensory and motor block in present study and the inconsistent results of previous studies, it’s due to the use of multiple drugs at the same time and there was a difference in definition of the onset of sensory and motor block however in Rachana Gandhi's study did not provide a precise definition of the onset time of sensory and motor block [31].

In explaining the mechanism of dexmedetomidine effect in previous studies that conducted on rat, Cationic hyperpolarization block and maintaining of nerve stimulus mode has been attributed to the prolonged sensory and motor blocks [36]. In a study that performed by Kosung et al. on α2 agonist, the intravenous dose required for nerve block have reported more than 1000 times of topical dose and they have reported the effect of dexmedetomidine with local anesthetic is through vasoconstriction and delayed in local anesthetic uptake and as well as nerve conduction direct block[37].

In another study conducted by Fritsch G et al. in 2014, they have reported the use of dexmedetomidine with ropivacaine in intrascalen block, decreases postoperative pain and prolonged block time [38]. Also in our study, postoperative pain reduction was more prominent in the dexmedetomidine group.

Postoperative pain score in all hours of the present study in the intervention group was lesser than the control group. In Bharti N et al study, pain score was comparable among groups except at 8 and 10 hours, and pain scores were lower in the dexmedetomidine group versus the control group [33]. The results of this study are consistent with our study findings. In Gyu Choi et al. in their study that used the MgSO4 with Bupivacaine they illustrated there were no differences in VAS scores between the two groups [12].

Hypotension and bradycardia are the most common side effect observed with α2 agonists. In a study that Esmaglu and his colleagues had done, adding 100 μg of dexmedetomidine to levobupivacaine had caused bradycardia in 7 of the 30 patients [39]. In Youngsuk Kwon et al. study heart rate and mean arterial pressure in the dexmedetomidine group had decreased significantly [40]. Whereas in our study, this decrease occurred in mean arterial pressure and mean heart rate, and it was not statistically significant.

In our study, bradycardia was observed in 4 of the 30 patients in the intervention group, which seems to be due to the low dose of dexmedetomidine. Hypotensions in 3 patients have occurred in both groups and this difference was not statistically significant. However, in previously conducted studies, the use of dexmedetomidine was not associated with hypotension and bradycardia [41, 42].

Finally, the use of dexmedetomidine with bupivacaine in the supraclavicular block was effective in reducing the onset time of sensory and motor blocks and increasing the duration of sensory and motor blocks without considerable side effects such as hypotension and bradycardia. Besides, dexmedetomidine significantly reduced postoperative pain in the dexmedetomidine with the bupivacaine group.

Limitations of our study included:

The limitations of our study were the no measurement of dexmedetomidine serum dose during surgery that would make unpredictable the evaluation of the systemic effect of this drug after local absorption and evaluation of another group of patients with receiving intravenous dexmedetomidine in future studies will be resolved this restriction.

Increased duration of surgery and the needs for general anesthesia were other limitations of the present study that led to the exclusion of these cases.

Declarations

Ethical approval:

Ethical approval was obtained from the Research and Ethics Committee (**IR.UMSU.REC.1397.181**) of the Urmia University of Medical Sciences, Urmia, Iran and The trial was registered in Iranian Registry of Clinical Trials (**IRCTID: IRCT20160430027677N15).** Before the trial was started all participated patients signed Informed consent form.

Availability of data and materials

All relevant data will be included in the article. Additional information is available from the corresponding author on reasonable request.

Competing interests

Authors have no competing interests

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Conflict of Interest:

The authors have no conflicts of interest.

Publication consent

Authors consent to the publication of this article.

Authors' contributions

The study concept was designed by Sh S, Sh Sh and B K H. Sh S, P G, M R and B K H participated in the study design. Sh Sh, P G, M R and B K H drafted the manuscript. Sh S, Sh Sh, P G and B K H performed the critical revision of the manuscript. All authors read and approved the final manuscript.

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Tables

Table 1. Studied patients demographic data and surgical characteristics

	Intervention group N= 30 patients		Control group N= 30 patients		P value
Gender (F/M)	Female	Male	Female	Male	0.133
	12	18	7	23	
Age (year)	39.5±14.9		34.7±10.8		0.165
Kind of Surgery	Soft tissue	Bone tissue	Soft tissue	Bone tissue	0.398
	14	16	16	14	
Weight (Kg)	76.72±18.9		73.75±24.9		0.9

Values are Mean ± SD or number of patients and kind of surgery. There are no significant differences between the two groups.

Intervention group=Dexmedtomidine + Bupivacaine and Control group= Bupivacaine alone

Table 2. Patients' supraclavicular block characteristics in two groups.

	Control group	Intervention group	P-Value
Onset time of motor block	24.66 ±9.2 min	15.93±6.36 min	p =0.041
Onset time of sensory block	31.03 ±9.65 min	21.36 ±8.34 min	p =0.026
Duration of motor block	317 ±10.52 min	488 ±157.5 min	p = 0.03
Duration of sensory block	333.5 ±94.35 min	475 ±137.5 min	p = 0.022
First analgesia request	308 ±109. 14 min	458 ±205/43 min	p = 0.001
score of sensory block	31.25	29.75	p = 0.809
score of motor block	35.58	25.42	p = 0.012

Values are Mean ± SD or mean of sensory and motor block score. Intervention group= Dexmedtomidine + Bupivacaine and Control group= Bupivacaine alone. P-value ≤0.05 is significant.

Figures

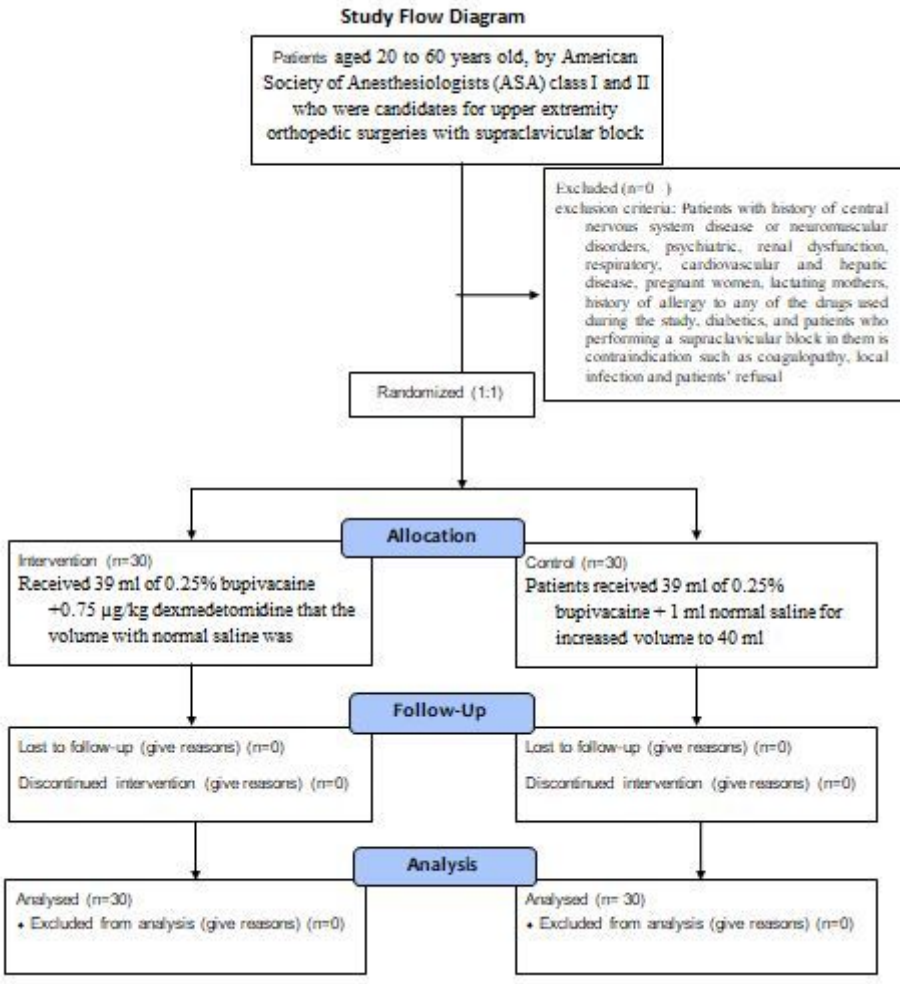

Figure 1

Study Flow Diagram

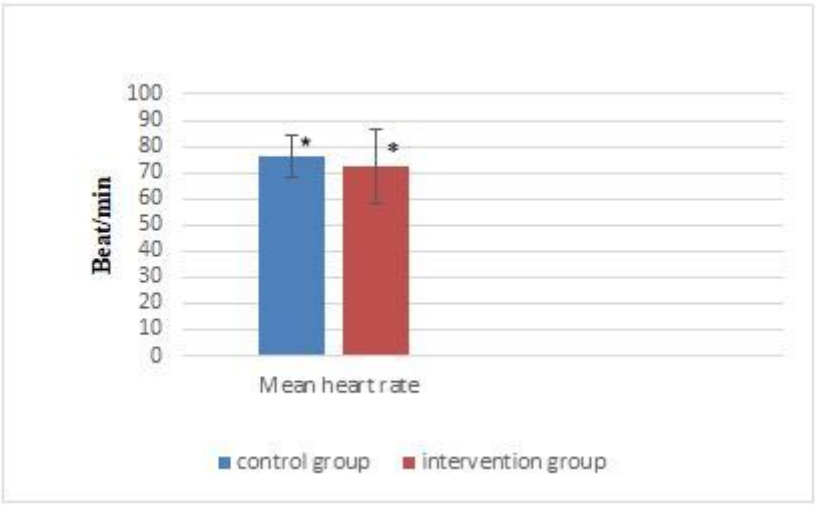

Figure 2

The mean of heart rate variations in both groups during the study period. * P = 0.454 and not significant.

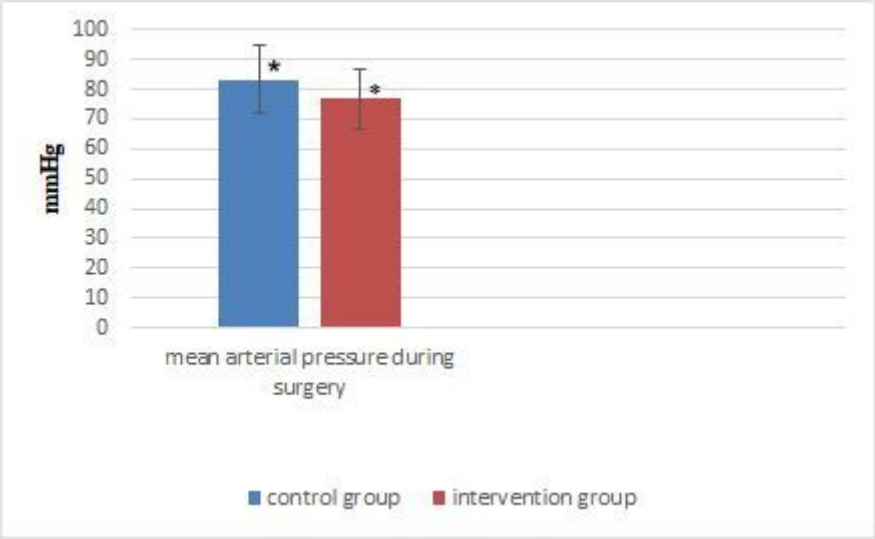

Figure 3

Mean arterial pressure during surgery in both groups during the study period. * P = 0.123 and not significant.

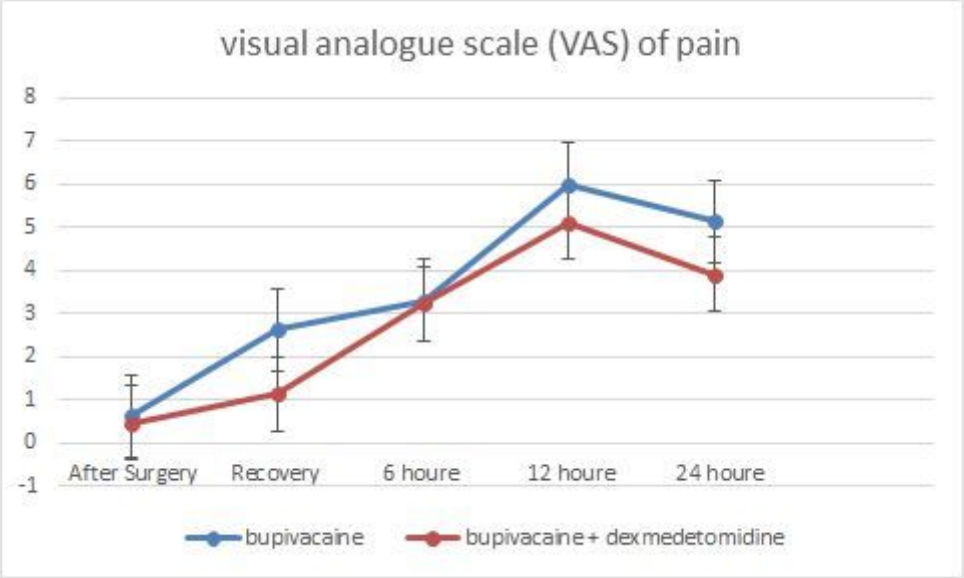

Figure 4

Comparison of visual analogue scale (VAS) of pain in patients' groups within 24 hours after surgery. The VAS score in all hours of study in the intervention group was lesser than the control group and it was significant P=0.001.

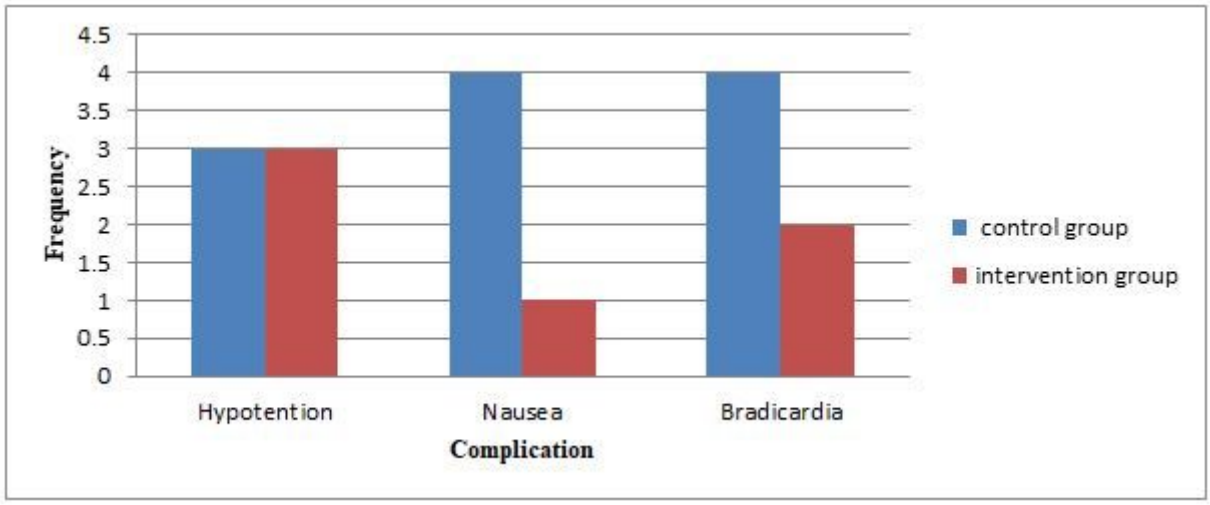

Figure 5

Frequency of complications in two groups. The difference in all of the side effects frequency was not significant (P>0.05)

Supplementary Files

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- CONSORT2010ChecklistMSWord.doc