Original Article

Effect of Axillary Perineural Dexmedetomidine on Hemodynamic Changes and Postoperative Pain in Patients Undergoing Upper Limb Surgery under General Anesthesia: A Randomized Double-Blind Study

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Abstract

Background and Objectives: Perineural dexmedetomidine as an adjuvant of local anesthetics has been used in regional anesthesia to prolong the duration of analgesia. This study aimed to assess the effects of perineural injection of dexmedetomidine alone on the duration of postoperative analgesia, narcotic consumption, and hemodynamic changes in the patients undergoing upper limb surgery under general anesthesia. **Methods:** Sixty patients undergoing upper limb surgery were randomly allocated into two equal groups. The intervention group received 100 μg dexmedetomidine/20 ml normal saline (NS) as perineural axillary brachial plexus injection, whereas the control group received 20 ml NS injection. Patients were compared for hemodynamic changes, postoperative pain through Visual Analog Scale, consumed narcotics and side effects. **Results:** The postoperative analgesia in the dexmedetomidine group was significantly longer than the control one. The amount of opioid administered in the control group was significantly more than that amount used in the intervention group. Mean arterial pressure (MAP) and heart rate (HR), in parallel, in the intervention group at 15, 30, 45, and 60 min after induction of anesthesia were significantly decreased in the intervention group than the control group. No dramatic drop in MAP and HR was observed. No significant complication also was reported. **Conclusions:** Perineural axillary brachial plexus injection of 100 μg dexmedetomidine/20 ml NS prolonged postoperative analgesia and reduced narcotic consumption in patients undergoing upper limb surgery under general anesthesia without noticeable side effects.

Keywords: Analgesia, brachial plexus, dexmedetomidine, upper extremity, Visual Analog Scale

Introduction

Orthopedic surgeries, especially on upper extremities, are one of the most common surgical procedures[1,2] that could be done under the peripheral nerve blocks.[3] One of the main concerns for surgical operations under local blocks along with other factors is the duration of postoperative analgesia and hemodynamic stability (changes in blood pressure and heart rate [HR]).[4] Several studies have been done on the use of supplements with local anesthetics to improve block quality and increase postoperative analgesic time[5-7] and hemodynamic stability.[8,9] One of the medications recently studied for this reason is dexmedetomidine.[8] Dexmedetomidine is an alpha

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2-specific agonist that has known sedative and analgesic effects.[10] Some studies have been reported improvement in the quality of spinal and epidural anesthesia by adding it to local anesthetic drugs.[11,12] The use of this drug in the peripheral nervous system and its effects on block quality and analgesia also have recently been considered.[13,14] On the other hand, some studies have been mentioned the positive effects of intravenous dexmedetomidine administration on hemodynamic stability in the course of general anesthesia.[15] Some studies also showed that adding it as a supplement to local anesthetics during brachial plexus block could significantly prolong the duration of analgesia.[13,16] However, one study has been demonstrated that adding dexmedetomidine to high volumes of local anesthetics may reduce its analgesic features since its analgesic effect is concentration dependent.[17] A remarkable point in the mentioned studies is that dexmedetomidine has always been used as an adjunct to local anesthetics. To the best of our knowledge, there is no any study, which addresses the effects of perineural injection of dexmedetomidine (not as an adjuvant to the local anesthetics) on hemodynamic and postoperative pain. Therefore, this study as a randomized double-blinded, was designed to determine the effect of perineural axillary injection of dexmedetomidine on hemodynamic stability and postoperative pain in patients underwent orthopedic surgeries on upper extremities under general anesthesia.

Methods

This clinical trial was conducted in Kashan Shahid Beheshti Hospital after obtaining approval of the Institutional Review Board of Kashan University of Medical Sciences and registration in the Iranian Registry of Clinical Trials (Ethical Code: IR.KAUMS.REC.1396.16 and IRCT ID: IRCT2017050833860N1) in 2016. Written consent was obtained from all participants. Sixty ASA physical status I and II patients, 18–60 years undergoing upper extremity surgery under general anesthesia were enrolled in a randomized, double-blind, placebo-controlled trial.

The exclusion criteria were patients with evidence of any contraindication to brachial block such as neurological, psychiatric, neuromuscular, bleeding problems, pneumothorax, diabetes, and pregnancy.

The sample size was calculated based on the study of Helal *et al*.,[18] which investigated the effect of perineural injection of dexmedetomidine and bupivacaine in the femoral-sciatic nerve block (mean duration of analgesia in the study group 807 ± 112.85 and in control group 462.52 ± 54.26 min). Assuming α error of 0.05 and the power of the study (1 − β) to be 95%, 60 patients were enrolled into two groups of 30 each, dexmedetomidine (D) and control (C). In both groups, routine monitoring, including electrocardiogram, pulse oximetry and noninvasive blood pressure measurement was performed. HR, systolic and diastolic blood pressure were recorded as the baseline values before induction. An intravenous line was also established for all patients. Study modalities were prepared in 20 ml coded syringes (100 μg dexmedetomidine/20 ml normal saline (NS) for Group D and 20-milliliter NS for Group C to ensure blinding of the anesthetist. All patients received midazolam 0.05 mg/kg and fentanyl 3 μg/kg as premedication. Perineural axillary brachial plexus injection was performed with 22G, 38-mm short bevel needle, under ultrasound and nerve stimulator guide. All patients (n = 60) were randomly allocated into two groups using a computer-generated schedule. Group D received 100 μg dexmedetomidine/20 ml NS and Group C received 20 ml NS. Trained senior resident provided all injections under supervision of skilled anesthesiologist. Then in all patients, general anesthesia with tracheal intubation was performed by the same anesthetist using sodium thiopental and atracurium and was maintained with isoflurane and a mixture of N_2o and oxygen at a ratio of 50%. Depth of anesthesia was monitored by bispectral index (BIS) and adjusted with isoflurane concentration to maintain a BIS value in the range of 40–60. The HR, systolic, diastolic, and mean arterial blood pressure (MAP) of the patients was recorded before the induction and every 15 min during the operation. Possible complications also were recorded in both groups of the study. The duration of surgery was recorded and at the end of the operation, the patient was transferred to the recovery room and then after returning complete consciousness, to the orthopedic ward. Postoperative pain was assessed by Visual Analog Scale (VAS) (0–10) in the recovery room and at 3, 6, 12, and 24 h after surgery. In the recovery room and in the ward, in the presence of pain or VAS score >3, both groups received up to a maximum of 1 mg/kg pethidine or 0.1 mg/kg morphine if needed. The amount of consuming opioid was recorded either in the recovery room or in the first 24 h after the operation at the ward. Nurses, who were responsible for collecting data, were blinded to the study drug administered. Patients were followed up for 1 week regarding any possible neuropathy by using follow-up call.

Statistical analysis

Normality of the data was evaluated using the Kolmogorov–Smirnov test. The independent t-test was used to compare the means of two independent quantitative variables. The Chi-square test and Fisher's exact test were used to compare the means of qualitative variables. A repeated-measure ANOVA was also used to analyze the data. Statistical analysis was performed using the SPSS software (version 16, SPSS, Inc., Chicago, IL, USA). $P < 0.05$ was considered statistically significant.

Results

A total of 77 participants were considered for eligibility and 17 were excluded based on patients' refusal despite previous written consent [Figure 1]. A total of 60 patients were randomized and 60 analyzed. Baseline characteristics were comparable between the study groups [Table 1]. The postoperative VAS in the study group was significantly lower than the control [Table 1]. There was no significant

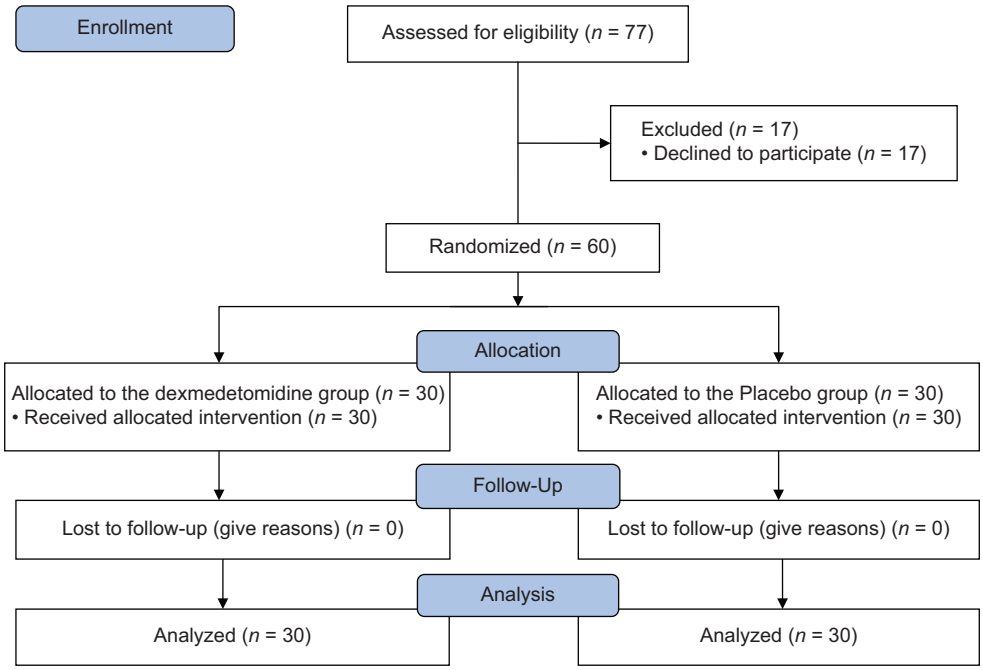

Figure 1: Consort flow diagram of the study

Table 1: Demographics and main outcomes of the study groups

	Group D	Group C	*P*
Gender			
Male	23 (76.7)	26 (86.7)	0.317*
Female	7 (23.3)	4 (13.3)	
Age	38.8±14.8	36.5±15.6	0.561**
Weight	76±13.4	76±9.4	0.991**
Height	170.6±9.8	172.4±5.9	0.410**
BMI	25.9±3.5	25.5±2.98	0.614**
ASA class			
I	29 (96.7)	30 (100)	NS***
II	1 (3.3)	0	
Operation duration (min)	75.3±21.3	83.2±30.3	0.225**
Postoperative VAS	4.36±0.85	5.83±1.51	<0.001
Hypotension events	26 (86.7)	29 (96.7)	0.161

*Chi-square test, **Independent *t*-test, ***Fisher's exact test. BMI: Body mass index, ASA: American Society of Anesthesiology, VAS: Visual Analogue Scale, NS: Not significant

difference between the two groups regarding hypotension events ($P = 0.161$) [Table 1]. The independent *t*-test did not show a significant difference ($P = 0.167$) between the two groups regarding preinduction and postinduction HRs while this difference was statistically significant at 15, 30, 45, and 60 min after induction of anesthesia ($P < 0.05$) [Figure 2]. The repeated measures analysis of variance showed the effect of time factor on HR changes ($P < 0.001$). Nevertheless, the time-group interaction was not significant on the HR variations that indicate no difference in the study groups regarding HR changes over the time ($P = 0.517$). The estimated effect size value was small (0.035) and this variable had no effect (data not shown). No significant differences were found between the study groups regarding preinduction and postinduction MAP ($P = 0.136$). In this case also, the estimated effect size value was small (0.059) and this variable had no effect. However, this difference was statistically significant at 15, 30, 45, and 60 min after induction ($P < 0.015$) [Figure 3]. Like HR, the repeated measures analysis of variance showed the effect of time factor on MAP changes ($P = 0.01$), but the time-group interaction was significant on the MAP variations that indicates the difference between groups regarding MAP changes over the time ($P = 0.034$). The amount of opioid administered in the control group was reported significantly more than in the intervention group in the recovery room ($P = 0.029$) and at 3 h after surgery ($P = 0.011$). There was also statistically significant difference between the two groups of the study regarding the number of patients received narcotics in the mentioned intervals ($P < 0.05$). At other time intervals, this difference was not statistically significant [Table 2].

Discussion

This study showed that VAS values after perineural axillary brachial plexus injection of 100 µg/20 ml dexmedetomidine were significantly lower in the dexmedetomidine group than the control group. Total analgesic consumption also was reduced in the dexmedetomidine group. MAP and HR in the intervention Group (D) at 15, 30, 45, and 60 min after surgery were significantly lower than the control group. Both groups were similar in terms of the incidence of hypotensive and bradycardia events during the surgical operation.

Dexmedetomidine combined with local anesthetics has been used widely for regional blocks.[13,19,20] This study produced results which corroborate the findings of a great deal of the previous work in this field. However, it should not be

Table 2: Frequency, mean and standard deviation of narcotic use at different hours after surgery

Time (h)	Number of cases			Consumed narcotics (mg)		
	Groups		*P*	Groups		*P*
	Dexmedetomidine	Control		Dexmedetomidine	Control	
During recovery	6 (20)	13 (43.3)	0.05	1.29±0.53	1.88±1.4	0.029
3	5 (16.7)	17 (56.7)	0.001*	1.58±0.65	4.8±3.1	0.011
6	10 (3.3)	10 (3.3)	NS	1.09±0.20	0.7±0.13	0.782
12	0	0	NS	0	0.36±0.6	0.321
24	0	0	-	0	0	-

*In cases where pethidine was used, it was adjusted to morphine (10 mg pethidine=1 mg morphine). Fisher's exact test

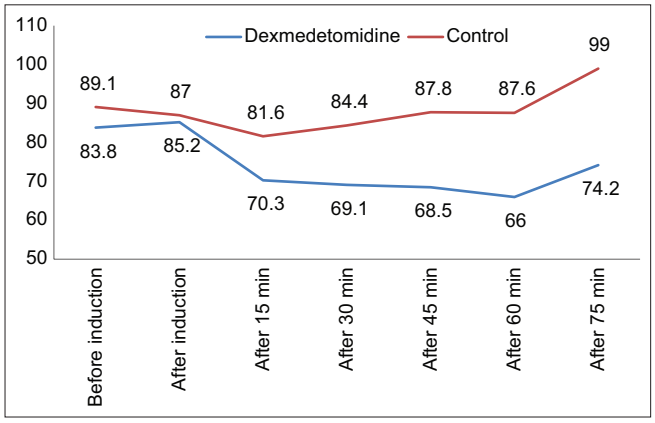

Figure 2: Mean of heart rates in the two groups of the study at different times

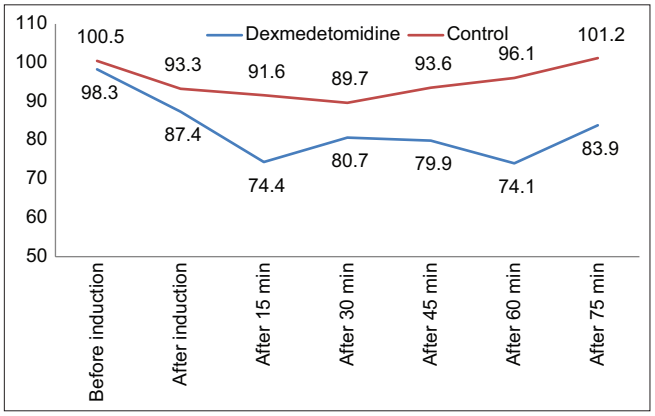

Figure 3: Mean arterial pressure in the two groups of the study at different times

overlooked that to the best of our knowledge, in studies in this field, dexmedetomidine has been used in combination with local anesthetics. In this study, however, in patients under general anesthesia, it was injected alone perineural in the brachial plexus. The findings of the current study are consistent with those of Bharti *et al*. who found in a randomized double-blind clinical trial study, that the addition of dexmedetomidine to ropivacaine-lidocaine prolonged the duration of supraclavicular brachial plexus block and improved postoperative analgesia without significant complication in patients undergoing upper extremity surgeries.[5] Sane *et al*. also have considered the effect of dexmedetomidine in combination with bupivacaine on sensory and motor block time and pain score in supraclavicular block. Based on their findings, bupivacaine in combination with dexmedetomidine reduced postoperative pain significantly after supraclavicular blocks.[21] The results of two above-mentioned studies are consistent with our study results. Our finding is also in agreement with Akhondzadeh et al. and Agarwal *et al*. which showed that dexmedetomidine added as an adjuvant to lidocaine and bupivacaine for supraclavicular brachial plexus block significantly prolongs the duration of sensory and motor blocks and duration of analgesia and reduced consumed analgesic.[20,22] Hussain et al. during a systematic review have concluded that perineural dexmedetomidine is associated with longer durations of neural blockade, a result that is corroborates with our findings.[8]

The most important side effect of α2-adrenergic receptor agonists is hypotension and bradycardia. Although in our study, the MAP and the HR decreased slightly at some measured intervals in the intervention group, these changes were not critical. In general, our study confirms that using perineural dexmedetomidine is associated with hemodynamic stability during the surgical operation, a result that has been confirmed by other studies.[20,23]

There are several possible explanations for the mechanism of peripherally effect of α2-adrenergic receptor agonists in producing analgesia. They produce analgesia by reducing the release of norepinephrine and causing α2-receptor–independent inhibitory effects on nerve fiber action potentials. They also exert a central effect by the inhibition of substance *P* release in the nociceptive pathway at the level of dorsal root neuron and the activation of α2-adrenoceptors in the locus coeruleus.[5] Considering the mechanism of action and the results in accordance with the similar findings of other studies, it can be expected that the present study will not cause controversy.

One of the strengths of this study is the perineural injection of the dexmedetomidine without combination with local anesthetics. In the literature review, it was found that almost all of the studies in the field of perineural injection of dexmedetomidine had performed with its combination with local anesthetics. From this point of view, this study

can be unique. However, a limitation of this study is that the numbers of patients and controls were relatively small. On the other hand, in this study, the axillary method was used for perineural injection of dexmedetomidine, while, in most studies, the supraclavicular method had been used. Therefore, in interpreting the results of this study, the mentioned issues should be considered.

Conclusions

This study has found that axillary perineural dexmedetomidine (100 μg in 20 ml) injection in patients undergoing upper limb surgery under general anesthesia prolonged the duration of analgesia and reduced narcotic consumption. Although a mild decrease in the patients' HR as well as hypotension was further observed in the dexmedetomidine group, but no significant side effects were detected.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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