Int J Med Invest 2022; Volume 11; Number 2; 125-135
http://intjmi.com

Original Research

Comparison Of Dexmedetomedine And Bupivacaine On Hemodynamic Stability And Analgesia In Patients Undergoing Lower Extremity Orthopedic Surgery Under Spinal Anesthesia

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Abstract:

Background: Adequate control of acute postoperative pain remains one of the major challenges after surgery. This study aimed to compare the effect of dexmedetomidine with and without bupivacaine on hemodynamic symptoms and pain in patients undergoing lower limb orthopedic surgery with spinal anesthesia.

Methods: This double-blind clinical trial study was conducted on 30 patients undergoing lower limb orthopedic surgery under spinal anesthesia in Peymaniyeh Jahrom Hospital in 2020. Patients were randomly divided into two equal groups, A (15 mg of bupivacaine) and group B (15 mg of bupivacaine plus 5 µg of dexmedetomidine). At 2, 6, 12, and 24 hours after surgery, patients' pain was evaluated using VAS. Patients' hemodynamic symptoms were recorded before anesthesia, immediately after anesthesia, 15, 30, 45, 60, 90, and 120 minutes during surgery and when entering and leaving recovery. Data analysis was done using SPSS version 21 software and using descriptive (mean, percentage and standard deviation) and inferential (ANOVA, t-test, ANOVA with repeated measures) tests.

Results: At 45, 30, 60, 90, 120 minutes after anesthesia and outside of recovery, the mean systolic blood pressure in group B was significantly lower than group A ($P<0.05$). The results of the Mann-Whitney test showed that the average pain in group B at 6 and 12 hours after the operation was significant ($P=.04$), so that at 6 hours after the operation, the average pain in group B was less than that of group A, but in 12 hours after the operation, the average pain in group B was higher than the bupivacaine group.

Conclusion: Dexmedetomidine drug is an effective drug in controlling hemodynamics in patients undergoing orthopedic surgery of the lower limb, but no statistically significant difference was seen in the amount of pain between the two groups. It is suggested to use dexmedetomidine in order to control and stabilize hemodynamics in patients undergoing orthopedic surgery.

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Key words: Dexmedetomidine, Bupivacaine, Hemodynamic Stability, Analgesia, Orthopedics.

Submitted: 4 April 2022, Revised: 16 May 2022, Accepted: 21 June 2022

Introduction

Lower extremity surgery can be performed under spinal, neuraxial, or general anesthesia. In fact, spinal anesthesia has several advantages, including rapid onset, deep block, less risk of infection, and lower cost (1). Adequate control of acute postoperative pain remains one of the major challenges after surgery (2-3). More than 70% of patients experience moderate to severe pain after surgery, and more than 25% of patients have had side effects after taking painkillers (4). Although opioids are widely used for postoperative pain control, they are associated with many side effects such as nausea and vomiting, respiratory depression, and hypotension. Non-steroidal anti-inflammatory drugs and acetaminophen and non-pharmacological techniques are also used in acute pain control (5). Dexmedetomidine is a specific agonist of the alpha two (α2) receptor, which has attracted the attention of anesthesiologists in recent years for sedation in various surgeries. Dexmedetomidine provides features such as analgesia, sedation and anti-anxiety effects without respiratory depression (6). Before surgery, α2 receptor agonists improve and stabilize hemodynamics by having multiple desirable effects, including analgesic effects, inhibition of sympathetic outputs, anti-anxiety properties, and reduction of norepinephrine levels. It also has positive effects on myocardial oxygen supply and cardiac demand for oxygen, thus protecting the myocardium (7-8). The use of dexmedetomidine before anesthesia has a positive effect on hemodynamic stability, which is associated with a decrease in postoperative mortality and a decrease in the incidence of postoperative problems (9). The use of painkillers along with local anesthesia is useful for increasing analgesia and reducing the complications of spinal anesthesia (10). In addition, it has been reported that dexmedetomidine as an effective adjunctive drug when added to the spinal anesthetic drug prolongs analgesia in abdominal surgeries; Lower limb and caesarean section (11-13). Bupivacaine is a long-acting amide anesthetic that is mainly used for spinal anesthesia (14). Rastegarian et al.(2020) investigated the effects of administering dexmedetomidine along with intrathecal bupivacaine in analgesia after orthopedic surgery of femur and tibia. The results of this study showed that the addition of dexmedetomidine to bupivacaine in the spinal anesthesia method prolongs the time of analgesia and reduces the pain intensity after the operation (15). Currently, due to the increase in the use of spinal anesthesia methods, but it is still noticeable in patients after the operation, it seems that by preventing the occurrence of pain after the operation, in addition to reducing the need to use narcotic drugs, management It is also possible for the patients to be more comfortable and complications that cause additional costs to the patient and the hospital are prevented. Therefore, the present study was conducted with the aim of comparing the effect of dexmedetomidine with and without bupivacaine on hemodynamic symptoms and pain in patients undergoing lower limb orthopedic surgery with spinal anesthesia.

Method:

The current study is a double-blind randomized clinical trial that was conducted during a three-month period from June 2020 to September 2020 in patients undergoing orthopedic surgery of

the lower limbs under spinal anesthesia in Peymaniyeh Hospital, Jahrom. Before entering the patients in this study, the research process was explained and written informed consent was obtained from them. In all stages of the study, researchers adhered to the principles of the Declaration of Helsinki and the confidentiality of patient information. All the costs of this project were covered by the researchers and no additional costs were created for the patients. This study was approved by the ethics committee of Jahrom University of Medical Sciences under the ethical code "IR.JUMS.REC.1399.011" and registered in the Iranian registry of clinical trial under the number IRCT20130926014779N6 (http://www. irct.ir).

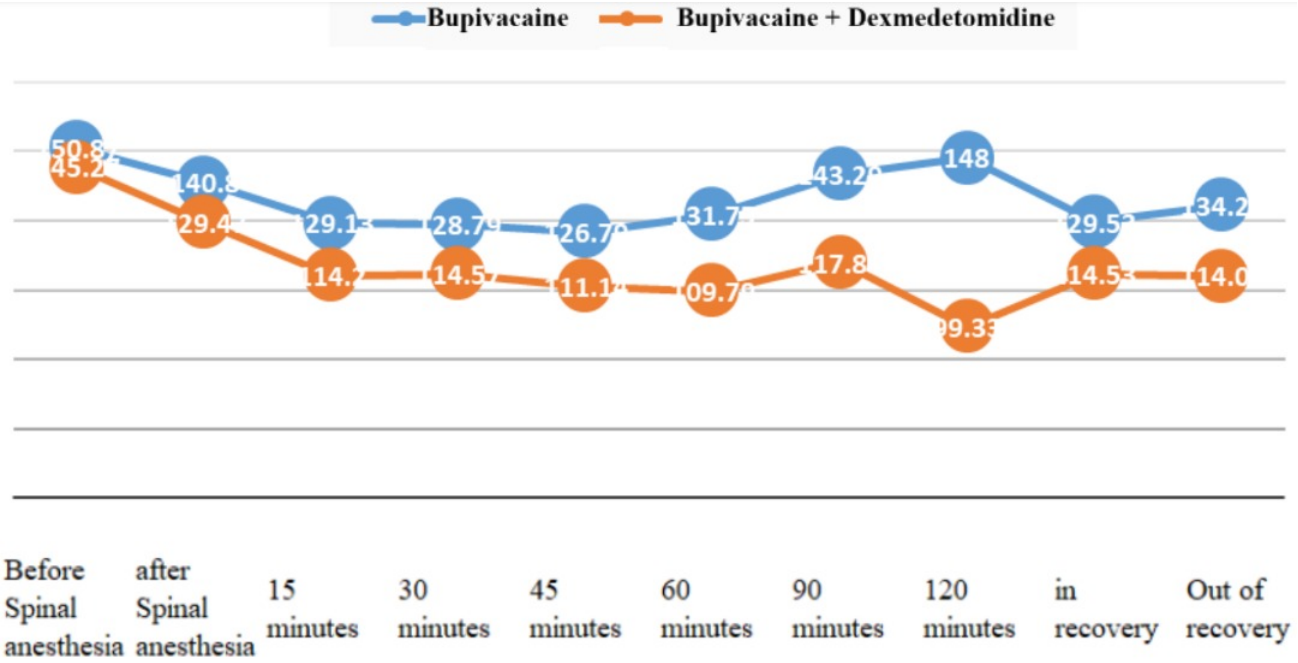

Figure 1: Distribution of changes in systolic blood pressure of patients undergoing lower limb orthopedic surgery under spinal anesthesia receiving dexmedetomidine with and without bupivacaine at different times

The population of the present study was patients undergoing orthopedic surgery of the lower limb. The sample size was determined by assuming standard difference = 0.85 and confidence limits of 95% and power = 80%, and assuming equal number of samples in each group using Altman normogram and including 15% attrition, 30 people (15). Then, in order to have an equal chance of being in the intervention group or the control group, the samples were randomly assigned to study groups (15 people in each group) using a table of random numbers (Figure 1).

Inclusion criteria include: II and I ASA (anesthesia class one and two), patients being NPO before surgery, having no history of severe cardiovascular disease, severe dyspnea, uncontrolled diabetes, severe kidney or liver disease, or any controlled systemic disease. No history of coagulation disorders, no history of allergy to drugs, history of taking antipsychotic and painkiller narcotics. Exclusion criteria

included prohibition of spinal anesthesia and non-cooperation of patients for spinal anesthesia.

All patients who met the inclusion criteria at the time of the study, after obtaining written informed consent and explaining the conditions of the study, were included in the study. 30 patients participating in the present study were divided into two intervention and control groups using a random number table.

The patients were transferred to the operating room for surgery and all underwent spinal anesthesia with the same method (needle number 25 and in L4-L5 space). In all cases, by placing the patients in a sitting position, the prepared solution was injected through a No. 25 spinal needle by an anesthesiologist. All patients received 5cc/kg/h fluid therapy before surgery. Patients were divided into two equal groups of bupivacaine and bupivacaine + dexmedetomidine. Group 1 (A) of the study received 15 mg of bupivacaine and group 2 (B) of the study received 15 mg of bupivacaine (2.5 ml) along with 5 micrograms of dexmedetomidine (manufactured by Elixir Pharmaceutical Company). At 2, 6, 12 and 24 hours after the operation, the pain level of the patients was evaluated using the VAS measuring scale. After the surgery, the information was recorded by the anesthesiologist who did not know about the medicine prescribed for the patients. Hemodynamic symptoms of patients before anesthesia, immediately after anesthesia, 15, 30, 45, 60, 90 and 120 minutes during surgery and when entering and exiting recovery using anesthesia machine monitoring became

Table 1. Distribution of patients undergoing lower limb orthopedic surgery under spinal anesthesia receiving dexmedetomidine with and without bupiocaine based on age and gender

		A	B	P-value
Age		**Mean±SD**	**Mean±SD**	
		55.07±20.55	51.33±20.26	0.62
Gender		**Frequency**	**Frequency**	
	Male	11(73.3)	12(80)	0.99
	Female	4(26.7)	3(20)	

Table 2: Distribution of patients undergoing lower limb orthopedic surgery under spinal anesthesia receiving dexmedetomidine with and without bupiocaine based on MAP and heart rate

Variable	Time	A		B		P-value
		Mean	**SD**	**Mean**	**SD**	
MAP	Before Spinal anesthesia	116.07	21.66	109.20	20.39	0.38
	after Spinal anesthesia	104.47	19.84	96.33	16.27	0.23
	15 minutes	95.73	23.10	3.0	17.60	0.12
	30 minutes	93.79	12.96	87.29	14.13	0.22
	45 minutes	92.43	15.39	83.93	16.05	0.16
	60 minutes	94.58	15.13	83.29	15.08	0.07
	90 minutes	103.86	26.52	89.11	15.47	0.18

	120 minutes	100.50	16.26	82.00	12.73	0.33
	in recovery	94.87	20.07	84.13	17.61	0.13
	Out of recovery	94.57	19.53	85.71	9.79	0.14
	P-value	0.89		<0.001		
HR	Before Spinal anesthesia	91.47	15.85	85.20	19.40	0.34
	after Spinal anesthesia	90.47	12.70	86.27	19.04	0.48
	15 minutes	89.27	17.45	77.93	17.67	0.09
	30 minutes	85.71	17.38	77.50	21.69	0.28
	45 minutes	83.29	18.09	77.43	23.63	0.47
	60 minutes	83.67	21.53	75.86	17.33	0.32
	90 minutes	82.43	30.63	75.22	17.18	0.56
	120 minutes	61.50	10.61	75.00	19.80	0.48
	in recovery	84.07	15.45	76.07	15.22	0.16
	Out of recovery	82.07	15.89	78.29	19.04	0.57
	P-value	0.25		0.28		

Data analysis was done by descriptive statistics indicators (mean, percentage and standard deviation) and inferential statistical tests (ANOVA, t-test, analysis of variance with repeated measures) using spss software version 21. A significance level of P<.05 was considered.

Results:

30 patients aged 18 to 85 years (in two groups of 15) with anesthesia class (ASA I, П) under orthopedic procedures of the lower limb (femur and tibia) were evaluated. The results in Table 1 showed that the study groups in terms of Age and gender variables are the same (p < 0.05) (Table 1).

At times 45, 30, 60, 90, 120 minutes after spinal anesthesia and outside of recovery, the mean systolic blood pressure in group B was significantly lower than that of bupivacaine group (P<0.05), but at other times the difference was No significance was observed in the mean systolic blood pressure between the two groups (P<0.05) (Table 2). Outside of recovery, the average diastolic blood pressure in group B was significantly lower than group A (P=0.037). However, at other times, there was no significant difference in mean diastolic blood pressure between the two groups (P<0.05) (Figure 1).

In group B, the average trend of systolic blood pressure from the time before spinal anesthesia to the time outside of recovery showed a significant difference (P < 0.001). (Figure 1). But in group A, the trend of the average diastolic blood pressure from the time before spinal anesthesia to outside of recovery showed a significant difference (P < 0.001), but the trend of the average systolic blood pressure was not significant (P < 0.05) (Figure 2).

In the times before and 45, 30, 60, 90, 120 minutes after spinal anesthesia and in recovery and out of recovery, there was no significant difference between the mean MAP and heart rate between group B and group A (P<0.05). Table 2). In group B, the average trend of MAP (mean arterial pressure) from the time before spinal anesthesia to outside of recovery showed a significant difference (P<0.001).

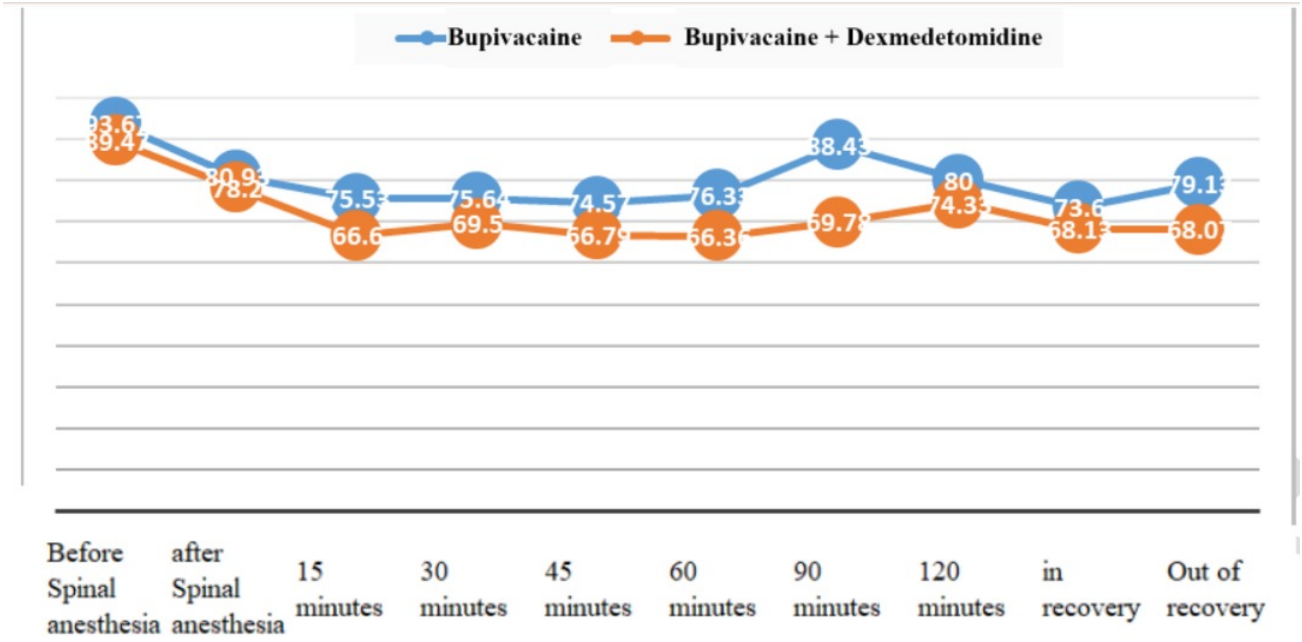

Figure 2: Distribution of diastolic blood pressure changes in patients undergoing lower limb orthopedic surgery under spinal anesthesia receiving dexmedetomidine with and without bupivacaine at different times

But the average heart rate trend was not significant (P<0.05). In group A, the trend of mean MAP and heart rate from the times before spinal anesthesia to outside of recovery showed no significant difference (P<0.05) (Table 2).

In the times before and 45, 30, 60, 90, 120 minutes after spinal anesthesia and in recovery and out of recovery, there was no significant difference between the mean MAP and heart rate between group B and group A (P<0.05). Table 2). In group B, the average trend of MAP (mean arterial pressure) from the time before spinal anesthesia to outside of recovery showed a significant difference (P<0.001). But the average heart rate trend was not significant (P<0.05). In group A, the trend of mean MAP and heart rate from the times before spinal anesthesia to outside of recovery showed no significant difference (P<0.05) (Table 2).

Before and 45, 30, 60, 90, 120 minutes after spinal anesthesia and in recovery and out of recovery, the average O2SAT (arterial blood oxygen saturation percentage) was not significantly different between groups A and B.

The results of the Mann-Whitney test showed that the average pain in group B at 6 and 12 hours after the operation was significant (P=0.04), so that at 6 hours after the operation, the average pain in group B was less than that of group A., but in 12 hours after the operation, the average pain in group B was more than group A. At other times, the average pain between the two groups B and A was not significantly different (P<0.05).The results of the Friedman test showed that in group B, the average pain increased until 12 hours after the operation, but then decreased (P<0.001). In group A, the average pain trend increased up to 6 hours after the operation, but then decreased (P<0.001). (Figure 3).

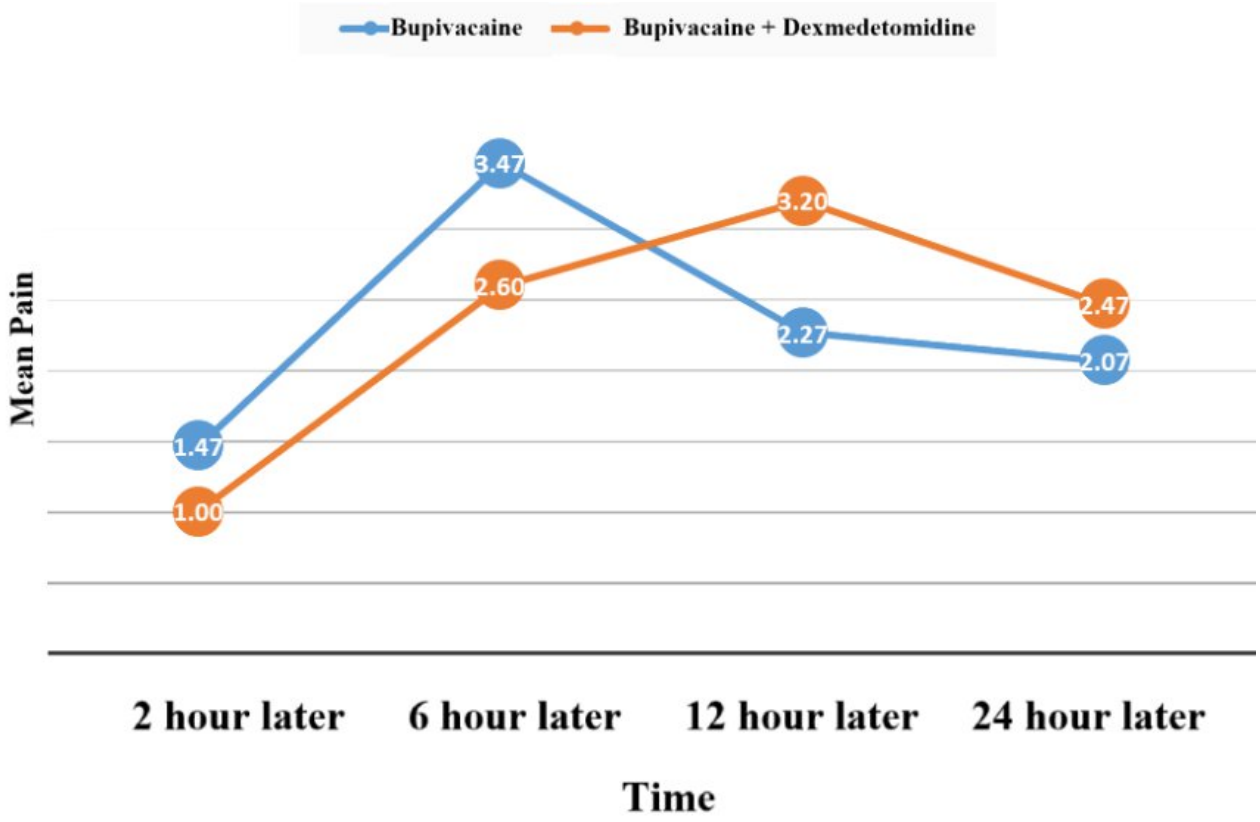

Figure 3: Distribution of average pain changes in patients undergoing lower limb orthopedic surgery under spinal anesthesia receiving dexmedetomidine with and without bupivacaine at different times

Discussion:

Pain control in orthopedic patients is particularly important because unfavorable pain control in them can be accompanied by movement delay and joint movement limitation (16-17). Several methods may be used to control pain during the operation period for orthopedic surgery patients, so that a combination of drugs with different multimodal techniques together precedes single drug treatment (18-19). The results of the present study showed that the average pain in 6 and 12 hours after the operation was significant in the bupivacaine + dexmedetomidine group. So that 6 hours after the operation, the average pain in the bupivacaine + dexmedetomidine group was lower than the bupivacaine group, but at 12 hours after the operation, the average pain in the bupivacaine + dexmedetomidine group was higher than the bupivacaine group. At other times, the average pain between the two bupivacaine + dexmedetomidine groups and the bupivacaine group was not significantly different (Figure 3).

In their study, Sarkar et al. (2018) investigated the comparison of two drugs, dexmedet-omidine and fentanyl, along with bupivacaine in lower limb orthopedic surgery. The results of this study showed that the combination of dexmedetomidine and bupivacaine causes analgesia after lower limb orthopedic surgery (20). In their study, Sane et al. (2021) investigated the effect of dexmedetomidine along with bupivacaine on pain in patients undergoing upper limb orthopedic surgery. The results of this study showed that the combination of dexmedetomidine and bupivacaine is more effective in reducing postoperative pain than bupivacaine alone (21). Gandhi

et al. (2012) investigated the use of dexmedetomidine and bupivacaine in brachial plexus block. The results of this study showed that the dexmedetomidine group has better hemodynamic stability and more analgesia after bupivacaine-based surgery (22). In their study, Elshahawy et al. (2022) investigated the comparison of dexmedetomidine, dexamethasone in combination with bupivacaine on the level of analgesia in lower limb orthopedics. The results of this study showed that intrathecal dexmedetomidine with bupivacaine is superior to dexamethasone and bupivacaine alone in terms of duration of analgesia and pain intensity (23). Rastegarian et al.(2020) investigated the effects of administering dexmedetomidine along with intrathecal bupivacaine in analgesia after orthopedic surgery of femur and tibia. The results of this study showed that adding 5 micrograms of dexmedetomidine to bupivacaine in the spinal anesthesia method prolongs the time of analgesia, reduces pain intensity and reduces the need for narcotics after surgery (15). In their study, Ghasemi et al. (2021) investigated the comparison of sufentanil and dexmedetomidine in combination with bupivacaine in patients with brachial plexus block in upper limb surgery. The results of this study showed that sufentanil in combination with bupivacaine had longer analgesia and less narcotic consumption in 24 hours after surgery (24). The results of the above studies are not consistent with the results of the present study. In the present study, the combination of dexmedetomidine + bupivacaine had less pain in the first 6 hours, and the bupivacaine group had less pain in the second 6 hours (12 hours after the operation). The analgesic effects of dexmedetomidine can be related to the antagonistic effects of the alpha-2 receptor in the posterior horn of the spinal cord. There have been various studies on the effectiveness of dexmedetomidine on hemodynamic stability. In some studies, dexmedetomidine has less hemodynamic side effects and better efficacy (26-25) and in some studies, no significant difference between dexmedetomidine and other compared drugs has been reported (27). In Alizadeh et al.'s study (2020), a comparison of the hemodynamic effects of dexmedetomidine and midazolam permedication was performed in patients undergoing upper limb surgery. The results showed that dexmedetomidine provided better hemodynamic control in anesthesia (28). Alimian et al.(2015) in their study compared the effects of dexmedetomidine and remifentanil on the rate of exit from recovery in patients undergoing posterior spinal fusion surgery. The results of this study showed that compared to remifentanil, dexmedetomidine stabilizes the hemodynamic status in patients undergoing posterior spinal fusion surgery (29). In their study, Masoudi Far et al. (2019) compared the effects of midazolam and dexmedetomidine on hemodynamics and complications in stereotaxic surgery. The results of this study showed that dexmedetomidine has better effects than midazolam and its use in sensitive surgeries where hemodynamic stability is important is preferable (30). In their study, Masoudi Far et al. (2022) compared the effects of fentanyl and dexmedetomidine on hemodynamic changes in patients undergoing stereotaxic surgery. The results of this study showed that there was no significant difference between the two groups based on systolic and diastolic blood pressure at different times (31). The

results of Rastegarian et al.'s study (2020) showed that the systolic and diastolic blood pressure in the bupivacaine-dexmedetomidine group was significantly lower at 15, 30, 45 and 60 minutes during surgery than the bupivacaine-normal saline group (15). The results of Sanat Kar et al.'s study (2020) showed that systolic and diastolic blood pressure and heart rate decrease after sedation with dexmedetomidine in patients undergoing cataract surgery (32). Dexmedetomidine is known as a selective α2 agonist, a central sympatholytic drug with hemodynamic stability, and it has been reported that it decreases heart rate and blood pressure in a dose-dependent manner (33). It seems that the main cause of heart rate drop and blood pressure drop indicates the pharmacological activity of dexmedetomidine on α2 receptors that are present in post-synaptic cells (34). Dexmedetomidine probably has an effect on postsynaptic vascular smooth muscle cells, which causes changes in vascular tone (35). One of the limitations of this study is the small sample size. It is suggested that future studies be conducted with a larger sample size.

Conclusion:

Dexmedetomidine drug is an effective drug in controlling hemodynamics in patients undergoing orthopedic surgery of the lower limb, but no statistically significant difference was seen in the amount of pain between the two groups. It is suggested to use dexmedetomidine in order to control and stabilize hemodynamics in patients undergoing orthopedic surgery.

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