

Original Research**Comparison Of Intrathecal Injection Of Dexmedetomidine And Bupivacaine With Bupivacaine Alone On Hemodynamic Changes In Pregnant Women Candidates For Caesarean Section Under Spinal Anesthesia: A Double Blind Randomized Clinical Trial Study**

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Abstract

Background: In choosing the anesthesia method, spinal anesthesia is more preferable for cesarean surgery. In cesarean surgery, it is very important to know the drug that has more hemodynamic stability, which can be useful in choosing the most suitable drug. Therefore, this study was conducted with the aim of comparing intrathecal injection of dexmedetomidine and bupivacaine with bupivacaine alone on hemodynamic changes in pregnant women candidates for caesarean section under spinal anesthesia.

Methods: This double-blind randomized clinical trial study was conducted on 82 pregnant women candidates for cesarean surgery. Patients were divided into two intervention (dexmedetomidine-bupivacaine) and control (bupivacaine) groups by random block method. Hemodynamic symptoms (systolic blood pressure, diastolic blood pressure and heart rate) were recorded and measured at 1, 3, 5, 30 and 60 minutes during surgery.

Results: The average age of 82 patients was 29.41 ± 4.75 years. The average duration of surgery was 158.78 ± 19.26 minutes in the intervention group and 127.31 ± 23.02 minutes in the control group. There was no statistically significant difference between the two groups of dexmedetomidine-bupivacaine and bupivacaine alone at times 1, 3, 5, 30 and 60 during surgery in terms of systolic and diastolic blood pressure. There was no statistically significant difference between the two groups in terms of heart rate at time 1, 3 and 60 during surgery, but at time 5 and 30 during surgery, there was a statistically significant difference between the two groups. In the dexmedetomidine-bupivacaine group, the heart rate was significantly lower than the bupivacaine group ($P=0.03$, $P=0.001$).

Conclusion: The results of this study showed that there is no difference between the two groups in terms of systolic and diastolic blood pressure, but the use of the combination of dexmedetomidine-bupivacaine had a certain effect on the heart rate at 5 and 30 minutes during cesarean surgery. At the same time, it is suggested to conduct more studies in this field.

Keywords: Dexmedetomidine, Bupivacaine, Hemodynamics, Caesarean Section, Spinal anesthesia.

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Introduction

In choosing the anesthesia method, spinal anesthesia is more preferable for cesarean surgery. This preference is due to the advantages of simplicity, greater reliability, less airway complications and aspiration, facilitation of postoperative analgesia, and less risk for the baby and mother (1). In cesarean surgery, spinal anesthesia is a common anesthesia method and since it facilitates the establishment of the mother-baby relationship and early feeding of the baby in the operating room, it seems to be a more appropriate choice than general anesthesia (2). Hyperbaric bupivacaine is the most common drug used for Intrathecal anesthesia, because in most cases, the duration of its effect corresponds well with the duration of cesarean section (3). Maintaining the patient's hemodynamic stability is important both in terms of the patient's own health during anesthesia and in terms of maintaining the blood flow of the fetus, especially in cases where there is a possibility of severe blood pressure changes or the fetus is sensitive to slight blood pressure changes. Therefore, knowing the drug that has more hemodynamic stability can be useful in choosing a more suitable drug (4). Dexmedetomidine has a small amount of opioid, anxiolytic, sympatholytic and respiratory protective properties and also maintains hemodynamic stability better than other sedative agents. Alpha-2 adrenergic agonists reduce Sympathoadrenal reactions to painful stimulation, improve hemodynamic stability during surgery and reduce the need for anesthesia for many surgical procedures (5-6). The use of alpha 2 agonists has reduced the need for anesthesia and hemodynamic stability of the patient, because these drugs have sympatholytic effects (7-8). Therefore, the present study aimed to compare intrathecal injection of dexmedetomidine and bupivacaine with bupivacaine alone on hemodynamic changes in pregnant women candidates for

caesarean section under spinal anesthesia as a double-blind randomized clinical trial study.

Methods

This double-blind, randomized clinical trial study was conducted on 82 patients aged 18 to 40 years with anesthesia class 1 and 2 candidates for elective cesarean surgery referring to Sayyad Shirazi Hospital, Gorgan in 2017. Inclusion criteria include; Anesthesia class I, II candidate for non-emergency cesarean surgery (elective), consent to participate in the study, age 40-18 years, having hemoglobin more than 10 mg/dL, normal clotting time and bleeding time, normal PT, PTT, INR, no history of airway problems and systemic diseases, no history of sensitivity to anesthetics or any other medicine, and no history of coagulation disease (such as hemophilia). Patients with anesthesia class 3 and 4, patients with uncontrolled diabetes or asthma, patients with a history of ischemic heart disease, IHD, patients with a history of stroke, patients with malignancies, patients with neurological and mental problems, patients with a history of drug abuse Substances or drugs, patients consuming alcohol, patients with a history of liver problems, the presence of fetal abnormalities, patients with a history of nausea and vomiting after previous surgery, the use of sedative and hypotonic drugs before entering the operating room, a third history of drug use, diabetes or High blood pressure during pregnancy, cardiovascular disease, pulmonary disease of the mother, psychosis or history of brain, nerve and mental diseases and stroke in the mother, blood disorders (such as thalassemia) of the mother, history of epilepsy and seizures, history of collagen diseases and Scoliosis or cancer under treatment, history of chronic gastrointestinal diseases, Oligopolyhydramnios, fetal IUGR, any defect or deformity of the fetus, use of anticoagulants such as heparin 48 hours before surgery, history of acute and chronic renal failure, deep

vein thrombosis, embolism Pulmonary and peripheral vascular diseases, preterm delivery of the mother were excluded from the study. 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. The patients participating in the study were allocated to two intervention (A) and control (B) groups using Block Randomization. In this way, using a dice that has 6 sides, the samples were assigned to their groups. A number is written on each face, and each number is assigned to one of the blocks in the table, which shows its special state. Group A (dexmedetomidine and bupivacaine) and B (bupivacaine). The patients were transferred to the operating room for surgery, and the surgical method and technique, the incision area was the same in all patients.

After establishing cardiovascular monitoring (ECG, Pulse Oximetry, NIBP), crystalloid solution was infused at the rate of 5 cc/kg and oxygen mask was placed for the patients. Patients were seated, with a 27G quincke spinal needle in the L3-L4 or L4-L5 space, induction of spinal anesthesia was performed, and the completion time of the injection was considered as zero time. Then the patients were placed in the supine position with 15 degrees of Trendelenburg. The selection of drugs was done in a double blind and random manner. The combination of drugs used in the form of 2.5 ml bupivacaine 5. % (12.5 mg of hyperbaric bupivacaine) plus 5ml was normal saline (total volume 3 ml) or 2.5 ml bupivacaine 0.5% (12.5 mg hyperbaric bupivacaine) plus 5 μ g dexmedetomidine (total volume 3 ml). After examining the level of spinal anesthesia and confirming the level of anesthesia, permission will be given to prepare and drape the patient. The data collection tool in this study includes a checklist. This checklist contains information such as; Age is the duration of surgery. Hemodynamic symptoms (systolic blood

pressure, diastolic blood pressure and heart rate) were recorded and measured at 1, 3, 5, 30 and 60 minutes during surgery. Data analysis was done using spss software version 21 and descriptive statistics (mean, standard deviation(SD), frequency and percentage) and inferential statistical tests (t-test and ANOVA) at a significance level of $P<0.05$.

Results

In general, in this study, 82 pregnant women who were candidates for caesarean section with spinal anesthesia and met the inclusion criteria were included in the study. The average age of these 82 participating patients was 29.41 ± 4.75 . The minimum and maximum ages of mothers participating in this study were 22 and 39 years. The average age of the intervention group (dexmedetomidine and bupivacaine) was 29.17 ± 3.90 and in the control group (bupivacaine) it was 29.65 ± 5.51 . The average duration of surgery was 158.78 ± 19.26 minutes in the intervention group and 127.31 ± 23.02 minutes in the control group (Table 1).

There is no statistically significant difference between the two groups of dexmedetomidine and bupivacaine and bupivacaine alone at times 1, 3, 5, 30 and 60 during surgery in terms of systolic and diastolic blood pressure. Also, no statistically significant difference was observed between these two groups in terms of heart rate at times 1, 3 and 60 during surgery. However, a statistically significant difference was seen between the two groups at 5 and 30 days of operation. In the dexmedetomidine-bupivacaine group, the heart rate was significantly lower than in the bupivacaine group. The use of the combination of dexmedetomidine and bupivacaine had an effect on heart rate 5 and 30 minutes after cesarean section (Table 2).

Discussion

Dexmedetomidine is also a selective alpha-2 adrenergic receptor agonist with sedative, anti-anxiety effects and causes hypotension, bradycardia and hemodynamic stability during surgery (9). The results of the present study

showed that there was no statistically significant difference between the two groups in terms of heart rate at times 1, 3 and 60 during surgery. However, a statistically significant difference was seen between the two groups at 5 and 30 days of operation. Based on that, the heart rate in the dexmedetomidine and bupivacaine group was significantly lower than the bupivacaine group.

The results of Jakob et al.'s study showed that the use of dexmedetomidine reduces the heart rate (10). The results of Alhashemi et al.'s study showed that the number of heartbeats in patients treated with dexmedetomidine was lower than in patients treated with midazolam (11). In their study, Sadeghi et al investigated the effect of dexmedetomidine along with bupivacaine after orthopedic surgery of femur and tibia. The results of this study showed that the heart rate immediately before and after spinal anesthesia and at 45 minutes during surgery was higher in the dexmedetomidine and bupivacaine group than in the bupivacaine group (), which is not consistent with the results of the present study (12). In their study, Ghazi et al compared the effect of bupivacaine with intrathecal ropivacaine on the hemodynamics of pregnant women candidates for elective cesarean section. Patients were divided into two groups of 38 people. Spinal anesthesia was performed in the first group with 12.5 mg bupivacaine and in the second group with 17.5 mg ropivacaine. The results of this study showed that the heart rate of patients in the bupivacaine group was significantly higher than the ropivacaine group, which is not consistent with the results of the present study (13).

In their study, Rastegarian et al investigated the effects of administering dexmedetomidine along with intrathecal bupivacaine after orthopedic surgery of the femur and tibia. The results of this study showed that there was a significant difference between the bupivacaine-normal saline and bupivacaine-

dexmedetomidine groups in terms of heart rate before and after anesthesia and 45 and 60 minutes during the procedure. The average heart rate in bupivacaine-dexmedetomidine group was higher than bupivacaine-normal saline. Between the two groups of bupivacaine-normal saline and bupivacaine-dexmedetomidine in terms of heart rate, no significant statistical difference was observed before and after anesthesia (14), which is not consistent with the results of the present study. It seems that the reason for the discrepancy between the results of the mentioned studies and the present study can be due to the different type of surgery and the length of the surgery in different studies. In recent studies, it has been confirmed that dexmedetomidine is better compared to common drugs such as midazolam in terms of reducing the prevalence of some side effects such as nausea and vomiting, and compared to propofol, it has better hemodynamic stability and faster recovery (15-16). The use of alpha 2-adrenergic agonist drugs as a pre-medication causes sleepiness and relieves the patient's anxiety, and also results in a decrease in heart rate and blood pressure during anesthesia (17-18).

One of the main disadvantages of spinal anesthesia is the high rate of blood pressure drop. The incidence of hypotension in pregnant women candidates for caesarean section who undergo spinal anesthesia is reported to be 50-65% (19). The results of the present study showed that there is no statistically significant difference between the two groups in terms of systolic blood pressure and diastolic blood pressure.

In their study, Khosravi et al. compared fentanyl and dexmedetomidine with intrathecal bupivacaine in caesarean section surgery. The results of this study showed that there is no statistically significant relationship between the two groups of fentanyl-bupivacaine and dexmedetomidine-bupivacaine in terms of systolic and diastolic blood pressure (20). In

their study, Amini et al investigated the comparison of dexmedetomidine and sufentanil added to spinal anesthesia with bupivacaine for hemodynamic stability and postoperative analgesia in elective cesarean section. The results of this study showed that there was no significant difference between the two groups in terms of changes in systolic and diastolic blood pressure in the first 60 minutes (21). In their study, Zirak et al investigated the effect of common dose of bupivacaine versus low dose of bupivacaine plus fentanyl in spinal anesthesia for caesarean section. In this study, patients were randomly divided into two groups of 50 people. To the people of the first group, Bupivacaine with a usual dose of 12 mg and to the people of the second group 8 mg of Bupivacaine along with 25 micrograms of fentanyl were injected into the spinal cord. The results of this study showed that there was no significant difference between the two groups in terms of average blood pressure (22). The results of the study by Rahimzadeh et al showed that there was no significant relationship between the bupivacaine-dexmedetomidine groups and the bupivacaine group in terms of systolic and diastolic blood pressure (23). In the study of Harsoor et al. in India, low dose marcaine combined with fentanyl was investigated in caesarean section. The amount of hemodynamic changes (systolic and diastolic blood pressure) was similar in the two groups (24). The results of studies by Khosravi, Amini, Zirak, Rahimzadeh and Harsoor are consistent with the results of the present study. The results of Rastegarian et al.'s study showed that there was a significant difference between the two groups of bupivacaine-normal saline and bupivacaine-dexmedetomidine in terms of systolic and diastolic blood pressure at 15, 30, 45 and 60 minutes during surgery (14). The results of this study indicated that the mean systolic blood pressure in the bupivacaine-dexmedetomidine group was lower than bupivacaine-normal

saline, which is not consistent with the results of the present study. It seems that the main cause of blood pressure drop indicates the pharmacological activity of dexmedetomidine on α_2 receptors that exist in post-synaptic cells (25). Dexmedetomidine probably has an effect on the smooth muscle cells of the post-synaptic vessels, which causes changes in the vascular tone (26).

Conclusion

Examining the hemodynamic parameters of the patients during the surgery did not show any significant difference between the two groups, and during the study, no case of severe hemodynamic disorder that led to medical intervention or patient withdrawal from the study was observed, but the use of the combination of dexmedetomidine and bupivacaine on the rate The heart rate was affected 5 and 30 minutes after cesarean section. Therefore, it seems that the combination of two drugs, dexmedetomidine and bupivacaine, is a safe and harmless combination in cesarean surgery.

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MD, AJ, SRM, and MJ conceptualized the study objectives and design. AJ, MD are infectious disease specialists who contributed to data collection from patients along with MD. MD, AJ and SRM drafted the study design protocols to be submitted to research centers. Data were was analyzed by MD and AJ. Manuscript was drafted by MD, AJ, and SRM. All authors contributed in revisions.

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Tables:**Table 1: Age and duration of surgery of patients participating in the study**

Variables	Bupivacaine	Dexmedetomidine - Bupivacaine
Age (Mean±SD)	29.65±5.51	29.17±3.90
Duration of surgery (minutes) (Mean±SD)	127.31±23.02	158.78±19.26

Table 2: Mean and standard deviation of hemodynamic indices (systolic, diastolic and heart rate) 1, 3, 5, 30 and 60 minutes during surgery

Hemodynamic indicators	Groups	N	Mean	SD	P
Systolic (1min)	intervention	41	122.21	10.28	0.73
	control	41	121.26	14.49	
systolic(3 min)	intervention	41	113.56	9.68	0.71
	control	41	112.46	16.23	
Systolic (5 min)	intervention	41	98.73	10.19	0.24
	control	41	102.56	18.11	
Systolic (30 min)	intervention	41	112.29	5.78	0.27
	control	41	114.43	10.93	
Systolic (60 min)	intervention	41	116.65	5.15	0.44
	control	41	114.68	15.80	
Diastolic (1min)	intervention	41	73.39	5.61	0.84
	control	41	73.09	7.89	
Diastolic (3 min)	intervention	41	65.36	5.74	0.13
	control	41	68.41	11.38	
diastolic(5 min)	intervention	41	56.92	7.45	0.86
	control	41	57.31	12.33	
diastolic (30 min)	intervention	41	69.92	4.52	0.92
	control	41	70.04	7.31	
Diastolic (60 min)	intervention	41	71.82	3.99	0.54
	control	41	72.68	7.92	
HR (1min)	intervention	41	94.43	9.61	0.69
	control	41	95.56	15.28	
HR (3 min)	intervention	41	88.31	11.30	0.69
	control	41	89.56	16.76	
HR (5 min)	intervention	41	76.41	9.96	0.03*
	control	41	83.73	19.72	
HR (30 min)	intervention	41	82.17	3.95	0.001*
	control	41	89.19	11.91	
HR (60min)	intervention	41	81.26	2.94	0.55
	control	41	80.51	7.70	

* P.value less than 5 percent = statistically significant difference