Original Article

The Effect of Two Different Dexmedetomidine Doses on the Prevention of Nausea and Vomiting in Discectomy Surgery under Spinal Anesthesia

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Abstract

Background: Considering the preventative effect of various medications on such complications after surgery, the present study evaluated the effect of two different dexmedetomidine doses on the prevention of nausea and vomiting in discectomy surgery.

Materials and Methods: The present controlled, double-blind clinical trial was performed on 135 patients that were candidates for discectomy surgery under spinal anesthesia, which were randomly allocated into three groups. Two different dexmedetomidine doses of 0.2 and 0.5 mcg/kg/h were intravenously administered using an infusion pump for 10 min in the first (DEX-0.2 group) and second (DEX-0.5 group) groups, respectively, with the third placebo group being used as a control group. Hemodynamic parameters, the severity of nausea and vomiting, and the incidence of complications were evaluated and recorded up to 24 h after surgery.

Results: The results of the present study revealed that, 20 min after the intervention, the severity of nausea and vomiting in the control group (with the mean of 1.95 ± 1.58) was significantly higher than that of the DEX-0.2 and DEX-0.5 groups with the means of 1.52 ± 1.11 and 1.27 ± 0.99, respectively ($P = 0.010$). In addition, no significant difference was found between the two dexmedetomidine doses in terms of the severity of nausea and vomiting ($P > 0.05$).

Conclusion: According to the results of the present study, a low dose of dexmedetomidine may be a more preferable choice as a preventive drug in the incidence of nausea and vomiting in discectomy surgery due to its lower complications, further reduction of nausea and vomiting, and more desirable hemodynamic stability.

Keywords: Dexmedetomidine, discectomy, nausea, spinal anesthesia, vomiting

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Introduction

Lumbar disc herniation (LDH) is one of the most common causes of low back pain which is characterized by an intervertebral disc herniation in the spinal canal. Its incidence is reported to be 1%–2% and 4.86 per 1000 persons per year in the general and young population, respectively. LDH is the most common cause for spinal surgery.[1,2] The goal of discectomy surgery is to relieve the symptoms of inflammation and pressure on the nerve roots by removing parts of or the entire disc.[3]

Moreover, general anesthesia is commonly used for spinal surgery; however, regional anesthesia is an option for one or two-level lumbar laminectomy or disc surgery. Although

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epidural anesthesia is used occasionally, spinal anesthesia is usually an acceptable alternative for selected patients that do not have any contraindications.[4]

In this regard, many previous studies have reported reductions in blood pressure, tachycardia, lower postoperative pain, and less nausea and vomiting after lumbar spinal surgery with spinal anesthesia.[5-7]

Although general, spinal, and epidural anesthesia are all suitable for discectomy, regional anesthesia is preferred by many physicians because of the possibility of performing motor and sensory tests and receiving immediate patient feedback during surgery. Moreover, patients under regional or local anesthesia can also benefit from the ability to change their position to prevent damage to the brachial nerve plexus and decrease pressure on the face and chest.[8]

Hemodynamic changes such as blood pressure and heart rate (HR) are typically common after spinal anesthesia.[9] Moreover, the incidence of postoperative nausea and vomiting (PONV) is approximately 18%–40%.[10] Female gender, postoperative opioid treatment, a history of motion sickness, and nonsmoking are significant risk factors for PONV.[11,12]

It can be stated that nausea and vomiting creates stress for the patient, surgeon, and anesthesiologist, causes the patient to feel anxious and confused, increases patient anxiety, delays discharge from recovery, and increases the cost of treatment. In addition, in case of its continuation, instability in hemodynamic parameters such as hypotension and decreased HR may occur.[4,12] Therefore, paying due attention to the management and implementation of prevention strategies with respect to this complication is of special importance.

As a result, the preventive use of antiemetic drugs such as dexmedetomidine has been studied in the present research.[11] Dexmedetomidine as a potent and highly selective agonist for the a2-adrenoceptor binds to the G protein-binding receptor membranes located in the brain and spinal cord. This action affects the function of the central nervous system (CNS) and blood circulation and has sedative, analgesic, and sympatholytic properties.[11]

Complications of dexmedetomidine with an approximate prevalence of 10% usually include cardiovascular complications, CNS complications, and gastrointestinal complications, the occurrence of which depends on the dose, duration, and indications for its administration.[13]

According to the results of previous studies, the effect of prescribing different dexmedetomidine doses as compared to other drugs such as ondansetron, fentanyl, and propofol in many other surgeries has been associated with fewer complications and lower incidence of PONV, although contradictory results have also been reported in some journals.[14-17]

Therefore, the present study aimed to evaluate the effect of two different dexmedetomidine doses on the prevention of nausea and vomiting during and after surgery with the least hemodynamic changes in discectomy under spinal anesthesia since few studies have been performed in order to compare the different dexmedetomidine doses administered using a continuous infusion pump to prevent PONV in discectomy under spinal anesthesia and also taking into account that one of the concerns of both surgeons and anesthesiologists is to choose the optimal dose of this drug that would be associated with the lowest risk of complications, the best stability of hemodynamic parameters, and the lowest incidence of nausea and vomiting.

Materials and Methods

The present study was a controlled, double-blind clinical trial. The study population included all patients that were candidates for discectomy under spinal anesthesia and referred to Al-Zahra Medical Education Center, in Isfahan during 2018–2019.

The sample size of 135 patients (45 patients in each group) was selected by simple random sampling technique from the mentioned population according to the sample size formula for between-group comparisons at 95% confidence interval, 80% test power, and considering the incidence of nausea and vomiting in previous studies[11] in the two groups receiving dexmedetomidine and placebo to be equal to 32% and 7%, respectively, and the error level of 0.27.

Inclusion criteria included patients that were candidates for discectomy surgery under spinal anesthesia with the age range of 18–60 years, the American Society of Anesthesiologists score of one or two, nonallergic to dexmedetomidine, not having used drugs with interactions with dexmedetomidine, and consent to participate in the study. In addition, patients were not included in the study in case of having a history of cardiovascular, respiratory, neurological, endocrine, thyroid diseases, dysautonomia, neuromuscular disorders, fever, pregnancy, obesity (body mass index >27), history of using vasoactive drugs, monoamine oxidase inhibitors, and tricyclic antidepressants, a history of drug abuse, and hypersensitivity to pethidine, ketamine, and magnesium sulfate. Moreover, patients were excluded from the study and substituted with another sample in case of the incidence of severe intra-operative hemodynamic disorders, severe intra-operative bleeding, allergic symptoms, or noncooperation in participation in the study.

After obtaining the code of ethics from the Ethics Committee of Isfahan University of Medical Sciences (IR.MUI.MED.REC.1398.173), and obtaining the code of Iranian Register of Clinical Trial (IRCT20160307026950N35), and obtaining informed written consent from eligible patients, 135 patients were selected by the nonprobability convenience technique. Then, the patients were divided into three groups of 45 using the random allocation software [Figure 1]. The demographic information of the patients including age, sex, and weight was recorded.

For all patients, 500 cc of Ringer's lactate solution was administered intravenously from the time of entering the operating room to the time before spinal anesthesia. After

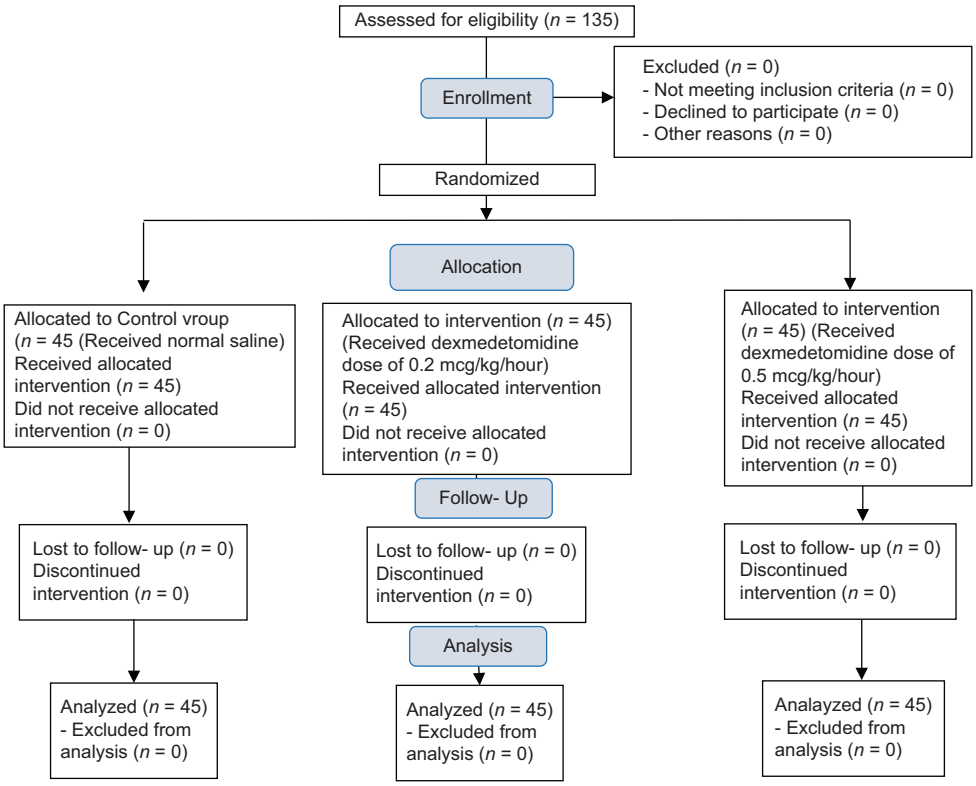

Figure 1: Consort flowchart of patients

entering the operating room and before performing the spinal anesthesia and administering intravenous dexmedetomidine, patients' hemodynamic parameters such as systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), HR, and oxygen saturation percentage (SpO2) were recorded. Moreover, the area of the intervertebral disc under surgery and the level of spinal needle entry point was determined and recorded. It should be noted that all surgeries are performed by a skilled surgeon in a single center.

In the first group, a dexmedetomidine dose of 0.2 mcg/kg/hour, which was increased to 10 cc volume using normal saline, was intravenously administered with an infusion pump in the course of 10 min after spinal anesthesia and providing proper patient positioning (DEX-0.2 group).[11]

In the second group, the dexmedetomidine dose of 0.5 mcg/kg/hour, which was increased to 10 cc volume with normal saline, was intravenously administered using an infusion pump in the course of 10 min after spinal anesthesia and providing desired patient positioning (DEX-0.5 group).[11]

It should be noted that the total dose of dexmedetomidine was recorded in the first and second groups.

In the third group, 10 cc of normal saline was intravenously administered using an infusion pump during a 10 min timeframe after spinal anesthesia and placing the patient in the desired position.

In order to fulfill the blindness condition in the present study, the two dexmedetomidine vials and normal saline were previously prepared, increased to the volume of 10 cc by the operating room nurse, and given daily to the anesthesiologist, who administered them without any knowledge of the type of each medication. Moreover, the person recording the clinical and basic information of the patients as well as the statistical analyst were not aware of the type of intervention.

The severity of nausea and vomiting according to the visual analog scale (VAS) scored from zero (no nausea) to 10 (severe nausea) were recorded for the three groups every 10 min in the 1st h of surgery, then every 30 min until the end of surgery; subsequently, every 30 min in the recovery room up to 1 h, and finally every 6 h in the ward for 24 h. If the severity of nausea based on VAS was >4, the minimum of 0.1 mg/kg and the maximum of 4 mg ondansetron were injected intravenously.

In addition, the length of stay in recovery, SBP, DBP, MAP, HR, and SpO2 were determined and recorded every 15 min until the end of surgery, then every 30 min at the recovery room up to 1 h, and subsequently every 6 h in the ward up to 24 h.

It should be mentioned that 0.01 mg/kg atropine was injected intravenously in case of bradycardia (HR <60 bpm). Moreover, 5 mg of ephedrine was injected intravenously if the SBP was <90 mmHg or the MAP was <20% of the baseline value.

The frequency of complications including hypertension (HTN) (SBP/DBP ≥140/90 mmHg), hypotension (SBP ≤90 mmHg), bradycardia (HR <60 bpm), apnea, and respiratory depression was recorded during surgery in the recovery room, and in the ward up to 24 h.

Finally, the collected information was entered into SPSS software (Ver. 25, IBM, USA). Data were presented as means ± standard deviation or frequency (percentage). At the level of inferential statistics, according to the result of Kolmogorov–Smirnov test indicating the normal distribution of data, tests such as repeated measures ANOVA, Chi-squared test, and Univariate analysis by adjusting the dose of ondansetron, ephedrine, and atropine were used. The significance level of < 0.05 was considered statistically significant in all analyses.

Results

In the present study, the group receiving dexmedetomidine 0.2 mcg/kg/h (DEX-0.2 group) included 37 (82.2%) male and 8 (17.8%) female patients with the mean age of 47.44 ± 9.75 years, the group receiving dexmedetomidine 0.5 mcg/kg/h (DEX-0.5 group) consisted of 36 (80%) male and 9 (20%) female patients with the mean age of 47.73 ± 10.77 years, and the control group comprised 39 (86.7%) male and 6 (13.3%) female patients with the mean age of 48.07 ± 10.18 years old. The three groups did not differ significantly in terms of age, sex, level of the needle spinal entry point, length of stay in recovery, the maximum level of sensory block, and the area of the intervertebral disc under surgery ($P > 0.05$) [Table 1].

In addition, the prescribed dose of ephedrine and ondansetron was not significantly different between the three groups ($P > 0.05$). Moreover, the prescribed dexmedetomidine dose in the DEX-0.5 and DEX-0.2 groups had the mean of 52.96 ± 2.09 mcg and 22.14 ± 8.45 mcg, respectively [Table 1].

In addition, the blood pressure parameters in the patients including SBP, DBP, and MAP were not significantly different between the three groups before the intervention and at 15 and 30 min after the intervention (during surgery) ($P > 0.05$). In contrast, the means of SBP, DBP, and MAP 45 min after the intervention in the control group with the means of 112.42 ± 12.47 mmHg, 75.11 ± 13.51 mmHg, and 87.37 ± 13.77 mmHg, respectively, exceeded those of DEX-0.2 group with the means of 117.60 ± 15.36 mmHg, 69.55 ± 11.84 mmHg, and 82.17 ± 12.04 mmHg, respectively, and those of DEX-0.5 group with the means of 109.27 ± 10.13 mmHg, 67.69 ± 9.40 mmHg, and 80.28 ± 9.29 mmHg, respectively ($P < 0.05$). It should be mentioned that the two intervention groups did not differ significantly in these parameters ($P > 0.05$). In addition, it is worth noting that the means of blood pressure in patients including SBP, DBP, and MAP in DEX-0.5 group were significantly less than those of DEX-0.2 and control groups with the control group having the highest mean of blood pressure till the end of the surgery ($P < 0.05$). Moreover, during recovery, the mean blood pressure in DEX-0.5 group was significantly lower than that of DEX-0.2 and control groups ($P < 0.05$); however, DEX-0.2 group was not significantly different from

Table 1: Basic and clinical characteristics of patients in the three groups

Variables	DEX-0.2 group	DEX-0.5 group	Control group	*P*
Sex, *n* (%)				
Male	37 (82.2)	36 (80.0)	39 (86.7)	0.693
Female	8 (17.8)	9 (20.0)	6 (13.3)	
Age (years)	47.44±9.75	47.73±10.77	48.07±10.18	0.960
Weight (kg)	68.15±7.60	66.62±11.35	66.31±8.11	0.595
Level of the needle spinal entry point	3.46±0.47	3.13±0.42	3.45±0.62	0.300
Length of stay in recovery	66.25±9.41	64.30±5.41	65.67±8.89	0.520
Maximum level of sensory block, *n* (%)				
T7	3 (6.7)	1 (2.2)	0	0.171
T8	8 (17.7)	9 (20)	11 (24.4)	
T9	13 (28.9)	11 (24.5)	12 (26.7)	
T10	12 (26.7)	17 (37.8)	20 (44.4)	
T11	3 (6.7)	2 (4.4)	2 (4.4)	
T12	6 (13.3)	5 (11.1)	0	
Area of the intervertebral disc under surgery, *n* (%)				
L2-L3	11 (24.4)	13 (29)	11 (24.4)	0.093
L3-L4	19 (42.3)	11 (24.4)	15 (33.4)	
L4-L5	5 (11.1)	10 (22.2)	16 (35.6)	
L1-L2	5 (11.1)	5 (11.1)	1 (2.2)	
T11-T12	3 (6.7)	1 (2.2)	1 (2.2)	
T12-L1	1 (2.2)	1 (2.2)	0	
T10-T11	1 (2.2)	3 (6.7)	0	
T5-S1	0	1 (2.2)	1 (2.2)	
Prescribed dose of ephedrine	0.50±0.15	0.62±0.25	0.50±0.15	0.680
Prescribed dose of ondansetron	6.67±2.89	8.33±2.89	6.00±2.24	0.493
Prescribed dose of dexmedetomidine	22.14±8.45	52.96±2.09	-	<0.001

Data is shown as, *n* (%) or means±SD. SD: Standard deviation, DEX: Dexmedetomidine

the control group in this respect ($P > 0.05$). After transferring the patients to the ward, no significant difference was found between the three groups in terms of the mean blood pressure at any of the evaluated times ($P > 0.05$). In addition, changes in the blood pressure from before the intervention to 24 h after the intervention (in the ward) were found to be significant in each of the three groups ($P < 0.001$) [Table 2].

Furthermore, the findings revealed that the HR before the intervention and 15 and 30 min after the intervention (during surgery) was not significantly different between the three groups ($P > 0.05$). In contrast, 45 min after the intervention, HR of the control group with the mean of 71.62 ± 11.04 was significantly higher than that of DEX-0.2 group and DEX-0.5 group with the means of 63.40 ± 10.52 and 60.82 ± 11.15, respectively ($P < 0.05$); however, the two intervention groups did not differ significantly in this regard ($P > 0.05$). Moreover, the mean of HR in the DEX-0.5 group was significantly lower than that of the DEX-0.2 and control groups till the end of surgery ($P < 0.05$). During recovery, the mean of HR in the DEX-0.5 group was significantly lower than that of DEX-0.2 and control groups ($P < 0.05$). However, there was no significant difference in the mean of HR between the three groups ($P > 0.05$). In addition, changes in HR from before the intervention to 24 h after the intervention (in the ward) were known to be significant in each of the three groups ($P < 0.001$). Besides, the mean of SpO2 from 30 min after the intervention during surgery to the end of surgery and also at 60 min in recovery was significantly lower in the control group as compared with the DEX-0.2 and DEX-0.5 groups ($P < 0.05$). However, the mean of SpO2 was not significantly different between the three groups at other follow-up times ($P > 0.05$) [Table 3].

The severity of nausea and vomiting was not significantly different between the three groups 10 min after the intervention ($P > 0.05$). However, the severity of nausea and vomiting 20 min after the intervention was significantly higher in the control group with the mean of 1.95 ± 1.58 as compared with the DEX-0.2 and DEX-0.5 groups with the means of 1.52 ± 1.11 and 1.27 ± 0.99, respectively ($P = 0.010$). In addition, the severity of nausea and vomiting in the control group was higher than that of the two intervention groups at other evaluated times up to 24 h after surgery ($P < 0.05$). It should be noted that the two intervention groups did not have any significant differences in terms of the severity of nausea and vomiting ($P > 0.05$). Each of the three groups had a significant decrease in the severity of nausea and vomiting over time within 24 h after the surgery ($P < 0.001$) [Table 4 and Figure 2].

Finally, the evaluation of the incidence of complications revealed that the percentage of HTN occurring during surgery and in the ward with 31.1% and 33.3%, respectively, was higher in the control group as compared with the DEX-0.5 group with 20% and 13.3%, and DEX-0.2 group with 6.7% and 13.3%, respectively ($P < 0.05$). In fact, it can be stated that this complication was significant in the control and DEX-0.5

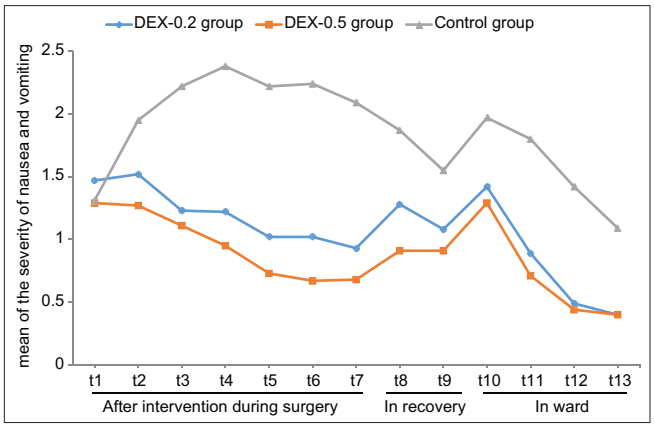

Figure 2: The mean of the severity of nausea and vomiting in the three groups

groups during surgery, while it was significantly lower at low DEX doses. Moreover, hypotension occurred only during surgery and was not significantly different between the three groups ($P > 0.05$); while the incidence of bradycardia during surgery in DEX-0.5 group with 31.1% was more than its incidence in the control and DEX-0.2 groups with 11.1% and 8.9%, respectively. In addition, the presence of apnea, and respiratory depression during surgery in the DEX-0.5 group with 8.9% and 31.1%, respectively, were far greater than those of the control and DEX-0.2 groups ($P < 0.05$) [Table 5].

Discussion

The results of the present study evaluating the intravenous administration of 0.2 and 0.5 mcg/kg/h dexmedetomidine using an infusion pump in discectomy surgery under spinal anesthesia revealed that hemodynamic parameters in the patients were not significantly different between the three groups up to 45 min after the intervention during surgery; however, the mean blood pressure parameters including SBP, DBP, and MAP as well as the mean HR in the control group as compared with the intervention groups were much higher, while the mean SPO_2 in the control group was less than that of the two intervention groups from 45 min after the injection during surgery. In addition, at the time of entering the recovery, the difference between the control and intervention groups was not significant, and this difference was only significant at the high prescribed dose of dexmedetomidine. In fact, the 0.5 mcg/kg/hour dexmedetomidine dose was associated with greater instability in hemodynamic parameters in recovery than the 0.2 mcg/kg/hour dexmedetomidine dose. In contrast, the 0.2 mcg/kg/hour dose was not significantly different from the control group in this regard. In other words, although low-dose dexmedetomidine may be associated with hemodynamic changes during surgery, the patient's condition stabilized and there was no difference between the control and DEX-0.2 groups over time during the transition to the recovery room or the ward. It should be noted that there was no significant difference between the three groups in terms of the changes in hemodynamic parameters in the ward. The mentioned finding

Table 2: Comparison of the patients' mean of blood pressure among the three groups

Variables	DEX-0.2 group	DEX-0.5 group	Control group	P_1	P_2	P_3
SBP						
After intervention during surgery						
t_0	129.78±11.55	130.62±11.56	129.35±13.42	0.744	0.870	0.623
t_1	121.28±12.48	119.97±12.39	117.24±15.88	0.650	0.163	0.345
t_2	114.11±11.71	113.53±13.78	111.93±16.04	0.845	0.460	0.587
t_3	117.60±15.36	109.27±10.13	112.42±12.47	0.246	0.048	0.003
t_4	111.91±12.48	104.97±10.52	121.44±11.73	0.005	<0.001	<0.001
t_5	111.80±10.78	104.95±10.95	123.35±13.61	0.007	<0.001	<0.001
t_6	112.74±9.64	105.18±9.49	123.42±10.74	0.001	<0.001	<0.001
In recovery						
t_7	125.84±10.13	119.68±11.03	127.95±11.27	0.009	0.359	<0.001
t_8	128.73±10.23	123.32±10.33	129.07±9.98	0.014	0.875	0.009
In ward						
t_9	129.37±12.06	124.28±12.44	127.33±12.44	0.052	0.432	0.243
t_{10}	127.71±11.16	125.67±12.12	129.00±13.23	0.428	0.617	0.197
t_{11}	126.69±10.65	125.26±13.28	127.64±13.72	0.594	0.720	0.373
t_{12}	124.78±11.64	124.18±12.36	128.31±12.53	0.816	0.171	0.110
P_4	<0.001	<0.001	<0.001			
DBP						
After intervention during surgery						
t_0	84.46±9.85	85.71±8.58	84.46±11.15	0.553	0.999	0.553
t_1	77.68±11.55	78.11±11.10	75.13±14.61	0.873	0.335	0.261
t_2	70.80±11.09	71.07±11.40	70.02±14.36	0.919	0.766	0.690
t_3	69.55±11.84	67.69±9.40	75.11±13.51	0.451	0.026	0.003
t_4	68.47±12.16	64.24±10.11	78.78±10.51	0.040	<0.001	<0.001
t_5	68.40±11.08	62.89±10.07	80.07±10.98	0.016	<0.001	<0.001
t_6	69.95±9.09	63.49±9.75	80.07±9.48	0.002	<0.001	<0.001
In recovery						
t_7	83.47±8.68	77.23±8.28	83.42±10.39	0.002	0.977	0.002
t_8	85.02±8.67	81.36±9.31	86.38±7.82	0.048	0.460	0.007
In ward						
t_9	84.71±9.77	81.47±12.01	85.02±10.96	0.162	0.893	0.126
t_{10}	83.87±10.00	84.18±11.04	86.40±11.14	0.891	0.265	0.328
t_{11}	83.57±9.30	83.02±12.42	84.02±11.71	0.815	0.851	0.673
t_{12}	81.69±10.92	82.68±12.15	85.06±10.36	0.672	0.154	0.314
P_4	<0.001	<0.001	<0.001			
MAP						
After intervention during surgery						
t_0	97.75±10.28	100.51±10.85	98.08±12.06	0.241	0.887	0.302
t_1	90.66±12.06	91.73±12.43	88.20±15.26	0.705	0.382	0.211
t_2	81.97±15.72	84.73±12.66	82.42±17.78	0.367	0.884	0.449
t_3	82.17±12.04	80.28±9.29	87.37±13.77	0.451	0.039	0.005
t_4	81.20±12.57	77.04±10.21	91.60±10.57	0.041	<0.001	<0.001
t_5	81.02±11.14	75.78±10.30	92.95±11.60	0.026	<0.001	<0.001
t_6	82.66±9.32	76.13±9.93	93.55±10.32	0.003	<0.001	<0.001
In recovery						
t_7	96.25±8.96	90.54±9.30	97.08±9.96	0.005	0.679	0.001
t_8	118.67±7.01	94.27±9.41	99.22±8.55	0.150	0.248	0.767
In ward						
t_9	97.91±10.17	95.35±13.05	97.91±11.41	0.298	0.999	0.298
t_{10}	97.22±10.02	97.31±11.95	99.22±11.55	0.970	0.430	0.399
t_{11}	96.73±9.34	96.29±12.88	96.62±12.37	0.857	0.964	0.892
t_{12}	94.82±11.21	96.42±13.04	97.89±10.73	0.518	0.216	0.553

Contd...

Table 2: Contd...

Variables	DEX-0.2 group	DEX-0.5 group	Control group	P_1	P_2	P_3
P_4	<0.001	<0.001	<0.001			

P_1: Significance level obtained from comparing the mean of DEX-0.2 and DEX-0.5 groups by adjusting the prescribed dose of ephedrine, P_2: Significance level obtained from comparing the mean of DEX-0.2 and control groups by adjusting the prescribed dose of ephedrine, P_3: Significance level obtained from comparing the mean of DEX-0.5 and control groups by adjusting the prescribed dose of ephedrine, P_4: Significance level obtained from comparing the mean of the variable over time up to 24 h after surgery in the ward in each of the three groups, t_0: Before intervention, t_1: 15 min after injection during surgery, t_2: 30 min after injection during surgery, t_3: 45 min after injection during surgery, t_4: 75 min after injection during surgery, t_5: 90 min after injection during surgery, t_6: 105 min after injection during surgery, t_7: The first 30 min in recovery, t_8: The second 30 min in recovery, t_9: The first 6 h in ward, t_{10}: The second 6 h in the ward, t_{11}: The third 6 h in the ward, t_{12}: The fourth 6 h in the ward. SBP: Systolic blood pressure, DBP: Diastolic blood pressure, MAP: Mean arterial pressure, DEX: Dexmedetomidine

Table 3: Comparison of the patients' mean of HR and SpO2 among the three groups

Variables	DEX-0.2 group	DEX-0.5 group	Control group	P_1	P_2	P_3
HR						
After intervention during surgery						
t_0	72.84±11.63	76.20±12.39	75.91±11.12	0.177	0.217	0.907
t_1	67.96±11.49	67.82±12.85	68.28±11.01	0.957	0.814	0.852
t_2	65.75±11.49	63.02±11.47	67.33±13.11	0.284	0.536	0.092
t_3	63.40±10.52	60.82±11.15	71.62±11.04	0.264	<0.001	<0.001
t_4	64.08±12.75	58.71±9.21	72.20±10.09	0.020	<0.001	0.001
t_5	68.44±9.49	58.82±8.18	73.04±8.57	<0.001	0.014	<0.001
t_6	68.53±9.07	59.37±10.49	74.60±9.72	<0.001	0.004	<0.001
In recovery						
t_7	71.62±8.52	67.72±8.97	75.91±8.15	0.035	0.020	<0.001
t_8	71.88±9.77	71.22±8.08	76.42±7.97	0.724	0.015	0.005
In ward						
t_9	72.69±11.15	72.91±10.25	72.14±10.84	0.922	0.809	0.735
t_{10}	72.33±10.29	73.33±8.65	73.27±9.41	0.617	0.641	0.976
t_{11}	72.04±9.50	74.64±8.70	73.39±9.78	0.189	0.499	0.526
t_{12}	73.09±9.68	75.09±9.30	74.09±8.63	0.305	0.609	0.611
P_4	<0.001	<0.001	<0.001			
SPO_2						
After intervention during surgery						
t_0	94.93±1.36	95.11±1.22	94.98±0.89	0.468	0.061	0.072
t_1	96.97±1.36	95.68±1.27	94.57±1.30	0.229	0.185	0.905
t_2	95.37±1.73	95.45±1.67	94.44±1.45	0.813	0.008	0.004
t_3	95.58±1.57	95.61±1.79	94.68±1.20	0.922	0.008	0.005
t_4	95.58±1.49	95.56±1.67	94.95±1.04	0.966	0.042	0.045
t_5	95.83±1.41	95.77±1.52	95.08±1.36	0.834	0.016	0.026
t_6	95.70±1.54	95.54±1.52	94.97±1.19	0.619	0.021	0.042
In recovery						
t_7	95.70±1.34	95.88±1.36	95.31±1.34	0.559	0.187	0.056
t_8	95.65±1.15	95.94±1.05	95.06±1.30	0.125	0.023	0.010
In ward						
t_9	95.52±3.67	95.81±1.59	94.97±1.12	0.104	0.382	0.110
t_{10}	95.02±1.70	95.83±1.57	95.02±1.26	0.104	0.999	0.155
t_{11}	95.98±1.77	95.79±1.54	95.02±1.44	0.219	0.893	0.217
t_{12}	95.86±1.62	95.58±1.45	95.02±1.20	0.220	0.606	0.074
P_4	0.433	0.345	<0.001			

P_1: Significance level obtained from comparing the mean of DEX-0.2 and DEX-0.5 groups by adjusting the prescribed dose of atropine, P_2: Significance level obtained from comparing the mean of DEX-0.2 and control groups by adjusting the prescribed dose of atropine, P_3: Significance level obtained from comparing the mean of DEX-0.5 and control groups by adjusting the prescribed dose of atropine, P_4: Significance level obtained from comparing the mean of the variable over time up to 24 h after surgery in the ward in each of the three groups, t_0: Before intervention, t_1: 15 min after injection during surgery, t_2: 30 min after injection during surgery, t_3: 45 min after injection during surgery, t_4: 75 min after injection during surgery, t_5: 90 min after injection during surgery, t_6: 105 min after injection during surgery, t_7: The first 30 min in recovery, t_8: The second 30 min in recovery, t_9: The first 6 h in ward, t_{10}: The second 6 h in the ward, t_{11}: The third 6 h in the ward, t_{12}: The fourth 6 h in the ward. HR: Hear rate, SpO_2: Oxygen saturation percentage, DEX: Dexmedetomidine

Table 4: Comparison of the mean of the severity of nausea and vomiting in the three groups

Nausea and vomiting	DEX-0.2 group	DEX-0.5 group	Control group	P_1	P_2	P_3
After intervention during surgery						
t_1	1.47±0.75	1.29±0.81	1.31±1.08	0.349	0.412	0.907
t_2	1.52±1.11	1.27±0.99	1.95±1.58	0.337	0.106	0.010
t_3	1.23±1.05	1.11±0.96	2.22±1.56	0.655	<0.001	<0.001
t_4	1.22±0.99	0.95±0.88	2.38±1.32	0.244	<0.001	<0.001
t_5	1.02±0.84	0.73±0.75	2.22±1.22	0.156	<0.001	<0.001
t_6	1.02±0.81	0.67±0.79	2.24±1.26	0.088	<0.001	<0.001
t_7	0.93±0.96	0.68±0.71	2.09±1.09	0.205	<0.001	<0.001
In recovery						
t_8	1.28±0.61	0.91±0.65	1.87±0.81	0.061	<0.001	<0.001
t_9	1.08±0.84	0.91±0.87	1.55±0.89	0.371	0.017	0.001
In ward						
t_{10}	1.42±0.75	1.29±0.79	1.97±1.16	0.492	0.005	0.001
t_{11}	0.89±0.86	0.71±0.69	1.80±1.14	0.359	<0.001	<0.001
t_{12}	0.49±0.59	0.44±0.62	1.42±0.86	0.765	<0.001	<0.001
t_{13}	0.40±0.58	0.40±0.62	1.09±1.02	0.999	<0.001	<0.001
P_4	<0.001	<0.001	<0.001			

P_1: Significance level obtained from comparing the mean of DEX-0.2 and DEX-0.5 groups by adjusting the prescribed dose of ondansetron, P_2: Significance level obtained from comparing the mean of DEX-0.2 and control groups by adjusting the prescribed dose of ondansetron, P_3: Significance level obtained from comparing the mean of DEX-0.5 and control groups by adjusting the prescribed dose of ondansetron, P_4: Significance level obtained from comparing the mean of the variable over time up to 24 h after surgery in the ward in each of the three groups, t_1: 10 min after injection during surgery, t_2: 20 min after injection during surgery, t_3: 30 min after injection during surgery, t_4: 40 min after injection during surgery, t_5: 50 min after injection during surgery, t_6: 60 min after injection during surgery, t_7: 60-90 min after injection during surgery, t_8: The first 30 min in recovery, t_9: The second 30 min in recovery, t_{10}: The first 6 h in the ward, t_{11}: The second 6 h in the ward, t_{12}: The third 6 h in the ward, t_{13}: The fourth 6 h in the ward. DEX: DEX: Dexmedetomidine

Table 5: Comparison of the frequency distribution of complications in the three groups

Complication	Variables	DEX-0.2 group, *n* (%)	DEX-0.5 group, *n* (%)	Control group, *n* (%)	*P*
HTN	After intervention during surgery	3 (6.7)	9 (20.0)	14 (31.1)	0.013
	In recovery	0	1 (2.2)	4 (8.9)	0.067
	In ward	6 (13.3)	6 (13.3)	15 (33.3)	0.024
Hypotension	After intervention during surgery	5 (11.1)	6 (13.3)	6 (13.3)	0.935
	In recovery	0	0	0	-
	In ward	0	0	0	-
Bradycardia	After intervention during surgery	4 (8.9)	14 (31.1)	5 (11.1)	0.008
	In recovery	0	0	0	-
	In ward	0	0	0	-
Apnea	After intervention during surgery	0	4 (8.9)	0	0.016
	In recovery	0	0	0	-
	In ward	0	0	0	-
Depression	After intervention during surgery	2 (4.4)	14 (31.1)	8 (17.8)	0.004
	In recovery	0	0	0	-
	In ward	2 (4.4)	1 (2.2)	0	0.360

P: Significance level obtained from comparing the frequency distribution of complications among the three groups studied. HTN: Hypertension, DEX: Dexmedetomidine

means that regardless of the dose of dexmedetomidine, the hemodynamic parameters stabilized and had minimal changes after at least 6 h of surgery.

Consistent with the findings of the present study, a meta-analysis indicated that dexmedetomidine increased hypotension at loading dose or at loading dose with continuous infusion.[11]

In fact, dexmedetomidine had an onset of an action of about 15 min, and its maximum effect was 1 h after continuous infusion. In addition, the distribution half-life (t½a) of dexmedetomidine in the dose range of 0.2–0.7 mcg/kg/h was 6 min in adults while its terminal elimination half-life (t½b) was between 2 and 2.5 h. Moreover, its clearance was 39 L/h. A similar rate of infusion can be used in children and adults to establish a stable level of plasma concentration.[11]

In addition, a number of studies have reported that dexmedetomidine causes less hemodynamic changes and improved quality before the end of surgery.[18] In another study, dexmedetomidine infusion was reported to reduce

hemodynamic stress, decrease the pain-free period after surgery and reduce the need for analgesia.[19]

It should be mentioned that according to the hemodynamic goals, vasopressors can be administered prophylactically to maintain the blood pressure in the normal range, or atropine, glycopyrrolate, ephedrine, and, if necessary, epinephrine can be used to prevent bradycardia and maintain HR in the normal range.[9] In the current study, atropine and ephedrine were used for some patients. To eliminate the intervening role of the mentioned drugs, these therapeutic interventions were adjusted as confounding factors in order not to affect the results of the study.

In the present study, the severity of nausea and vomiting was not significantly different between the three groups 10 min after the intervention. However, 20 min after the intervention (during surgery) up to 24 h after surgery, the severity of nausea and vomiting in the control group was more than that of DEX-0.2 and DEX-0.5 groups. Moreover, the severity of nausea and vomiting was not significantly different between the two prescribed doses of dexmedetomidine. It should be taken into consideration that the administration of ondansetron for preventing the severity of nausea and vomiting was adjusted in the analyses of this study. Therefore, the potential role of this confounder was also controlled.

In line with the findings of the present study, another study revealed that dexmedetomidine infusion during elective spinal surgery could better reduce the PONV and also reduce the risk of respiratory depression and opioid-dependent hypoxia.[20]

In addition, in accordance with the findings of the present study, Jin *et al*. indicated that dexmedetomidine significantly decreased the incidence of PONV in children or adults regardless of the method of administration (loading dose alone, with continuous infusion, or infusion only). Furthermore, dexmedetomidine as compared with placebo appears to reduce the need for fentanyl use during surgery. However, as dexmedetomidine increases complications such as bradycardia at loading dose or loading dose with continuous infusion, the continuous administration of dexmedetomidine using continuous infusion alone seems to be a preferable method to prevent PONV.[11]

After assessing the severity of nausea and vomiting and changes in hemodynamic parameters, the incidence of complications is of particular importance. According to the results of the present study, HTN complication during surgery was significant in the control and DEX-0.5 groups; however, this value was significantly lower at the low dose DEX (0.2 mcg/kg/h). Furthermore, the incidence of bradycardia, apnea, and respiratory depression during surgery in the DEX-0.5 group was far higher than that of the control and DEX-0.2 groups. In fact, it can be stated that the incidence of complications during surgery was more likely to occur in the control and DEX-0.5 groups as compared with the DEX-0.2 group.

In concurrence with the findings of the present study, other studies have also reported that this drug can cause hypotension and bradycardia, especially in patients with hypovolemia or atrioventricular block. In fact, since alpha 2 presynaptic receptors are stimulated by dexmedetomidine, it can lead to hypotension and bradycardia by reducing the secretion of norepinephrine.[21,22] Although other studies have not reported a difference in the dose of this drug in the incidence of complications, it seems that the possibility of the incidence of complications is more likely at higher doses.

Overall, the objective of the present study was the evaluation of the effect of two varying dexmedetomidine doses on hemodynamic changes as well as the severity of nausea and vomiting during and after surgery (in recovery and up to 24 h after surgery) in discectomy surgery. The present study, in addition to evaluating hemodynamic changes, has also paid due attention to evaluating the other most likely complications after surgery in long term. However, the administration of an extra dose of analgesia may be one of the limitations of the present study that is suggested to be addressed in future studies.

Conclusion

According to the results of the present study, the severity of nausea and vomiting during and after surgery in the two dexmedetomidine groups was much lower than that of the control group while there was no significant difference between the two doses of this drug. Finally, the incidence of complications such as HTN, bradycardia, apnea, and respiratory depression in the high dexmedetomidine dose was much higher than its lower dose. Therefore, generally it can be stated that the lower dose of dexmedetomidine may be a preferable choice as a preventive drug in the incidence of nausea and vomiting in discectomy surgery due to lower complications, further reduction of nausea and vomiting, and superior hemodynamic stability.

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Conflicts of interest

There are no conflicts of interest.

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