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Comparison of the Effect of Dexmedetomidine and Remifentanil on Pain Control After Spinal Surgery: A Double-Blind, Randomized Clinical Trial

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Abstract

Background: A variety of spinal surgery procedures are performed on patients with different cardiac, vascular, and respiratory comorbidities. Postoperative pain management is a major determinant of hemodynamic and respiratory status in these patients and promotes clinical results, prevents complications, saves health services, and improves the quality of life of patients.
Objectives: We compared the effects of dexmedetomidine and remifentanil on pain control after spinal surgery.
Methods: Sixty patients aged 18 - 65 years undergoing spinal surgery were randomized into the two groups of dexmedetomidine and remifentanil. The dexmedetomidine group (group D, n = 30) received dexmedetomidine infusion (0.6 mcg/kg/h), and the remifentanil group (group R, n = 30) received remifentanil infusion (0.1 mcg/kg/min) from induction of anesthesia until extubation. Propofol (1.5 mg/kg) and fentanyl (2mcg/kg) were used to initiate anesthesia, and propofol (100 - 150 mcg/kg/min) was infused to maintain anesthesia. Postoperative pain, hemodynamic parameters, and recovery characteristics were evaluated after surgery.
Results: The mean pain intensity in the dexmedetomidine group was significantly lower than in the remifentanil group (2.98 $\pm$ 1.29 vs. 3.80 $\pm$ 1.1; $P < 0.001$). Hemodynamic changes in the dexmedetomidine group (MAP: 92.60 $\pm$ 5.56, HR: 73.07 $\pm$ 7) were less, and their condition was significantly more stable than in the remifentanil group (MAP: 93.85 $\pm$ 4.78, HR: 79.15 $\pm$ 7.03; $P < 0.05$). The mean arterial oxygen saturation (O_2 sat) in the dexmedetomidine group was significantly higher and more stable than in the remifentanil group (98.87 $\pm$ 0.51 vs. 97.92 $\pm$ 0.46; $P < 0.05$). The incidence of nausea and vomiting was significantly lower in the dexmedetomidine group compared to the remifentanil group ($P < 0.05$). The administration of analgesics in the post-anesthetic care unit (PACU) was significantly higher in the remifentanil group than the dexmedetomidine group ($P = 0.016$).
Conclusions: Anesthetic maintenance with either dexmedetomidine or remifentanil infusion until extubation provided more smooth and hemodynamically stable conditions, without complications. However, dexmedetomidine provides better analgesia, causes a more stable hemodynamic state, and reduces postoperative nausea-vomiting, shivering, and the need for analgesics.

Keywords: Dexmedetomidine, Pain, Remifentanil, Spinal Surgery

1. Background

Today, a variety of spinal surgery procedures are performed, which has posed a variety of challenges for anesthesiologists. Most of these patients have different comorbidities such as severe heart failure and vascular and respiratory diseases. Managing the hemodynamic status of these patients is one of the major challenges for anesthesiologists. Surgery causes additional stress to the patient, especially on the cardiovascular system, due to blood loss, prolonged anesthesia, and perioperative pain (1).

Postoperative analgesia with various methods promotes clinical results, prevents complications, saves health services, and improves patients' quality of life. Proper control of postoperative pain improves postoperative rehabilitation, which can lead to improved short- and long-term recovery and quality of postoperative life (2-5). Short-acting opioids such as fentanyl can meet this goal (6). One of the most common drugs used for pain control is narcotics, such as the use of remifentanil, which is a safe drug in the induction and maintenance of anesthesia. Remifentanil binds to opioid μ receptors in many areas of the central nervous system (CNS), increasing pain thresholds, altering pain perception, and inhibiting the ascending pain pathway (7). Remifentanil is fast-acting

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and has a fast metabolism, and even after a long period of infusion, the patient will definitely wake up immediately after stopping the infusion (8, 9). However, complications such as nausea, vomiting, itching, opioid tolerance, and urinary retention have caused doubts about the use of narcotics.

In addition to narcotics, various drugs such as ketamine, chlorpromazine, promethazine, and clonidine have been studied for improving anesthesia, recovery, and controlling pain thereafter (10, 11). The use of α_2-receptor agonists such as dexmedetomidine, alone or in combination with other drugs, improves hemodynamic stability by having several favorable effects, including analgesic effects, inhibition of sympathetic outputs, anti-anxiety properties, reduction of norepinephrine levels and stress response, and improving the quality of recovery (12, 13). It also has positive effects on myocardial oxygen supply and cardiac oxygen demand, and thus, myocardial protection (1, 14). The maintenance of anesthesia with remifentanil or dexmedetomidine until extubation provides stable hemodynamics without complications (15). In elderly patients, dexmedetomidine reduces respiratory depression, mean arterial pressure (MAP), and heart rate (HR), but has a less analgesic effect than remifentanil (16). The addition of dexmedetomidine to other analgesics provides better postoperative analgesia and improves patient satisfaction (17).

2. Objectives

To compare dexmedetomidine and remifentanil in the pain management of patients during and after spinal surgery, we decided to conduct this study to find a safe drug with low complications to control postoperative pain and reduce opioids use.

3. Methods

Patients: In this clinical trial, after obtaining permission from the Ethics Committee of Ahvaz Jundishapur University of Medical Sciences (IR.AJUMS.REC.1398.593) and completing the informed consent forms, 60 patients who were candidates for spinal column surgery (lumbar discectomy) from February 2019 to June 2020 were enrolled. The patients aged 18 to 65 years and ha ASA class I or II (inclusion criteria). The included patients were allocated to either the Dexmedetomidine group or the Remifentanil group by the use of the random digits table method for receiving dexmedetomidine or remifentanil as an infusion during surgery. Patients requiring emergency surgery, previous spinal surgery, drug addiction, history of neurological, neuromuscular, or psychiatric diseases, history of pulmonary or cardiovascular diseases, an patients with unpredictable events during the operation (such as massive bleeding) were excluded from the study.

Interventions: The monitoring and anesthesia protocol of all the patients was similar. In detail, when the patient entered the operating room, noninvasive blood pressure monitoring (systolic and diastolic), heart rate, electrocardiography, arterial oxygen saturation (pulse oximetry), and capnography were performed. All the patients received 5 mL/kg body weight crystalloid fluid (from lactated Ringer's solution), and 2 μg/kg fentanyl and 0.02 mg/kg midazolam were prescribed to the patients intravenously as premedication. Intravenous propofol at a dose of 1.5 mg/kg and 0.5 mg/kg atracurium was used to induce anesthesia. Patients in the dexmedetomidine group received 1 μg/kg dexmedetomidine (Exir pharmaceutical company, Borujerd, Iran) for 10 minutes at the beginning of anesthesia. Anesthetic drugs included infusion of 100 - 150 μg/kg/min propofol and infusion of 0.01 μg/kg/min dexmedetomidine. Patients in the remifentanil group received 1 μg/kg remifentanil (Abureihan pharmaceutical company, Tehran, Iran) as a bolus at the start of anesthesia. Anesthetic maintenance drugs included infusion of 150-100 μg/kg/min propofol and remifentanil infusion of 0.1 μg/kg/min.

Dexmedetomidine or remifentanil was prepared in 50-mL syringes mixed with normal saline coded A or B so that the patients and researchers were blinded to the drug used for each patient (double-blinded).

Study measurements: At the end of the surgery in the stages of extubation, immediately after entering the post-anesthesia care unit (PACU), 30, 60, and 120 minutes after entering the PACU, and 24 hours after the surgery, the pain level of the patients was assessed using the visual analog scale (VAS) and registered. In case of pain score of more than 6, 25 mg intravenous meperidine was administered. Also, changes in systolic and diastolic blood pressure, heart rate (HR), arterial oxygen saturation, nausea and vomiting (based on simplified postoperative nausea and vomiting impact scale 2 or more), and shivering (based on bedside shivering assessment scale [BSAS] grade 1 or more) were assessed at the same time as pain.

Statistical analysis: According to the significance level of 0.05 and the measurement accuracy of 0.05, a sample size of 58 patients was calculated based on the following Formula:

$$n = \frac{Z_1 - \frac{\alpha}{22} P\ (1 - P)}{d^2}$$

However, to increase the measurement accuracy, 60 patients were selected as samples. The collected data was analyzed using SPSS version 22 (SPSS Inc., Chicago, IL, USA) and presented the results as mean ± standard deviation. Post hoc analysis was performed using the Mann-Whitney U, chi-square, and Kruskal tests. A P-value of less than 0.05 was considered significant.

4. Results

There was no significant difference between the two groups with respect to demographic data, including age, male-to-female ratio, and ASA class, as shown in Table 1 (Remifentanil group: 45.2 ± 6.72 years, Dexmedetomidine group: 46.7 ± 6.83 years).

The mean pain intensity after extubation, immediately after entering the PACU, at 30, 60, and 120 minutes after entering the PACU, and 24 hours after surgery in the two groups were compared and recorded. The mean intensity of pain in the dexmedetomidine group was significantly lower than the remifentanil group (Remifentanil: 3.80 ± 1.1, Dexmedetomidine: 2.98 ± 1.29, P < 0.001; Table 1). The results showed the greater effect of dexmedetomidine in controlling postoperative pain.

Preoperative assessment revealed no significant difference between the two groups with respect to HR, MAP, and SPO_2 (HR: 74.2 ± 5.6, MAP: 97.6 ± 4.5, SPO2: 98.4 ± 0.5 in the remifentanil group and HR: 74.4 ± 6.3, MAP: 96.8 ± 6.6, SPO2: 98.3 ± 0.5 in the dexmedetomidine group; Table 2). Mean HR, MAP, and SPO_2 were significantly lower in the dexmedetomidine group than in the remifentanil group both during and after surgery in the extubation time, immediately after entering the PACU, 30, 60,120 minutes after entering the PACU, and 24 hours after surgery (HR: 79.15 ± 7.03, MAP: 93.85 ± 4.78, SPO_2: 97.92 ± 0.46 in the remifentanil group vs. HR: 73.07 ± 7, MAP: 92.60 ± 5.56, SPO2:98.87 ± 0.51 in the dexmedetomidine group, P < 0.05; Table 2). The frequency of nausea and vomiting in the two groups was compared (Table 3). In the dexmedetomidine group, immediately after entering the PACU and 30 and 120 minutes after entering the PACU, the frequency of nausea and vomiting was significantly lower than in the remifentanil group (P < 0.05). At the other times (immediately after extubation, 60 minutes after entering the PACU, and 24 hours after surgery), no significant difference was found between the two groups in this regard (P > 0.05).

The frequency of shivering was compared between the two groups (Table 3). According to the results, immediately after entering the PACU and 30 minutes after entering the PACU in the dexmedetomidine group, the mean was significantly lower than in the remifentanil group, (P < 0.05). While at other times recorded (immediately after extubation, 60 and 120 minutes after entering the PACU, and 24 hours after surgery), no significant difference was found between the two groups in this regard (P > 0.05).

5. Discussion

The present study was a double-blind clinical trial that compared the effect of dexmedetomidine and remifentanil infusion on pain and hemodynamic changes in patients after spinal surgery. In the present study, there was a significant difference in the variables of pain intensity, HR, systolic and diastolic blood pressure, arterial oxygen saturation, nausea, vomiting, and shivering between the dexmedetomidine and remifentanil groups. The statistical data showed a significant difference in the hemodynamic conditions, respiratory depression, pain score, and the need for the postoperative analgesia between the two groups. The results showed that dexmedetomidine infusion causes more analgesia, reduces the need for opioids, and creates more stable hemodynamic conditions in patients. This drug has strong anesthetic and analgesic effects that reduces the need for opioids and their side effects, lowers stress response, and improves the quality of recovery. Dexmedetomidine is a central sympatholytic and, in a dose-dependent manner, stabilizes hemodynamic conditions and reduces HR and blood pressure (18, 19). In a study, infusion of dexmedetomidine at a rate of 0.4 mcg/kg/h stabilized HR and blood pressure compared to placebo. Reduce HR and blood pressure has also been exhibited in another study, where dexmedetomidine and fentanyl were compared in surgery of obesity (20, 21). The findings of both of the above studies were consistent with the results of our study.

In 2018, a study compared the effects of dexmedetomidine and remifentanil on hemodynamic changes and pain intensity in 30 candidates for hysterectomy. Vital signs and pain intensity of patients in both groups were evaluated and recorded at 5, 10, 20, and 30 minutes after surgery. The results showed that the rate of hemodynamic changes and pain intensity at 5, 10, and 30 minutes after the surgery were lower than those in the remifentanil group. They concluded that dexmedetomidine was effective in reducing patients' postoperative pain (P < 0.05) (22), which was in line with our findings.

Table 1. Comparison of Demographic Characteristics and Pain Data Between the Two Groups

Patient's Data	Group		P-Value
	Remifentanil	Dexmedetomidine	
Age	45.2 ± 6.72	46.7 ± 6.83	0.14
Sex			0.39
Male	17	16	
Female	13	14	
Pain			
After extubation	6.1 ± 1.16	4.87 ± 1.1	< 0.001
At entering the PACU	2.47 ± 1.11	2 ± 1.23	< 0.05
30 minutes after PACU	2.38 ± 1.02	1.43 ± 1.11	< 0.05
60 minutes after PACU	3.6 ± 1.14	2.5 ± 1.06	< 0.001
120 minutes after PACU	3.73 ± 1.03	3.23 ± 1.12	< 0.05
24 hours after PACU	4.53 ± 1.16	4.27 ± 1.14	< 0.05

Abbreviation: PACU: Post anesthesia care unit

In South Korea (2016), a study compared the intravenous injections of dexmedetomidine, fentanyl, and remifentanil on postoperative hemodynamics, sedative quality, and postoperative pain control. Pain scores did not differ significantly between groups. Blood pressure and HR in the dexmedetomidine group were significantly lower than the other groups in the PACU ($P < 0.05$). The dexmedetomidine group had better postoperative hemodynamic stability than the remifentanil or fentanyl group ($P < 0.05$) (23). The results of the above study were consistent with our findings. In a study in 2015, the effects of dexmedetomidine versus remifentanil on pain control after spinal cord surgery were examined in a clinical trial. The results showed that pain intensity in the remifentanil group was significantly higher than in the dexmedetomidine group immediately after surgery ($P < 0.05$). Patients in the remifentanil group showed higher PONV up to 24 hours after surgery. They concluded that dexmedetomidine is extremely effective in reducing pain and controlling postoperative pain up to 48 hours after surgery. Therefore, dexmedetomidine may be used instead of remifentanil alongside propofol, which confirms the results of the present study (24).

In a clinical trial study on the effects of dexmedetomidine and remifentanil injection on pain after rhinoplasty in 2015, the results obtained were similar to those of the present study. According to the results, the dose of analgesics in the PACU and the rate of nausea and vomiting in the dexmedetomidine group were significantly lower than in the remifentanil group ($P < 0.05$). The results of that study showed that maintenance of anesthesia with remifentanil injection or dexmedetomidine injection until extubation provided stable hemodynamics without complications after rhinoplasty. While remifentanil was better than dexmedetomidine due to its avoidance of anxiety and agitation in patients after surgery, dexmedetomidine was more effective than remifentanil in lowering vomiting and pain (15).

The effect of remifentanil and dexmedetomidine on hemodynamic changes in patients under general anesthesia was examined in a study in 2015. The results showed that the hemodynamic changes in both groups were similar, but in the remifentanil group, patients were more likely to have hypoxia. However, in our study, hemodynamic changes were significantly different between the two groups and were more stable in patients receiving dexmedetomidine (25). The results of comparing arterial blood oxygen levels in patients in the above two studies were consistent.

In a study of the effect of dexmedetomidine on spinal surgery in 2013, the results showed that dexmedetomidine was effective in controlling hemodynamic response and reducing blood loss in spinal surgery (26). The results of the above studies were consistent with our findings. In 2016, a clinical trial study compared the effects of the remifentanil and dexmedetomidine on supervised anesthesia care in 57 elderly patients during vertebroplasty and kyphoplasty. Postoperative anxiety and agitation were assessed in both groups. The results showed no significant difference between the remifentanil and dexmedetomidine groups. In

Table 2. Comparison of Preoperative Heart Rate, Mean Arterial Pressure, and O_2 Saturation Between the Two Groups

Variable & Time	Group		P-Value
	Remifentanil	Dexmedetomidine	
Preoperation			
HR	74.2 ± 5.6	74.4 ± 6.3	0.63
MAP	97.6 ± 4.5	96.8 ± 6.6	0.45
O_2 Sat.	98.4 ± 0.5	98.3 ± 0.5	0.37
After extubation			
HR	100.1 ± 4.2	85.16 ± 5.4	< 0.001
MAP	112 ± 3.5	105.69 ± 6.3	< 0.05
O_2 Sat.	97.76 ± 0.4	98.47 ± 0.5	0.43
At entering PACU			
HR	79.06 ± 5.1	72.23 ± 4.9	< 0.05
MAP	95.33 ± 5.2	90.58 ± 4.7	< 0.05
O_2 Sat.	98.43 ± 0.5	99.00 ± 0.5	0.52
30 min after PACU			
HR	74.83±9.1	70.63±7.4	< 0.05
MAP	93.52 ± 4.8	90.30 ± 6.3	< 0.05
O2 Sat.	98.76 ± 0.7	99.53 ± 0.5	0.45
60 min after PACU			
HR	74.90 ± 6.4	70.26 ± 8.3	< 0.05
MAP	94.48 ± 4.7	88.20 ± 3.3	< 0.001
O_2 Sat.	97.33 ± 0.5	98.70 ± 0.6	0.23
120 min after PACU			
HR	73.20 ± 11.3	69.66 ± 8.7	< 0.05
MAP	94.95 ± 4.1	91.37 ± 5.6	< 0.05
O2 Sat.	97.66 ± 0.3	98.73 ± 0.5	0.37
24 h after surgery			
HR	72.83 ± 6.1	70.50 ± 7.3	0.66
MAP	92.78 ± 6.4	89.49 ± 7.2	< 0.05
O_2 Sat.	97.63 ± 0.4	98.80 ± 0.5	0.29

Abbreviation: PACU: Post-anesthesia care unit; HR: Heart rate; MAP: Mean arterial pressure; O_2 Sat.: O_2 saturation

the dexmedetomidine group, patients showed higher MAP, HR, and SPO_2 levels than patients in the remifentanil group (16). According to the results, remifentanil reduces the need for drugs after surgery compared to dexmedetomidine. They concluded from their study that during postoperative anesthesia care, dexmedetomidine reduced respiratory depression, MAP, and HR, but it had less analgesic effects than remifentanil in the elderly undergoing vertebroplasty or kyphoplasty. The results of the above study were in line with our results. The reason for this difference can be attributed to differences in sample size, types of surgery, or measurement times.

The findings of this study led to the evaluation of the benefits of both dexmedetomidine and remifentanil in controlling pain in patients after spinal surgery. According to the results of this study, dexmedetomidine is helpful in controlling postoperative pain. The results showed a greater effect of dexmedetomidine infusion in preparing analgesia, reducing the need for opioids, and achieving more stable hemodynamic conditions after spinal surgery. Dexmedetomidine also reduces nausea, vomiting, and shivering in patients.

Table 3. Comparison of Frequency of Nausea and Vomiting and Shivering Between the Two Groups

Variable & Time	Group		P-Value
	Remifentanil	Dexmedetomidine	
After extubation			
PONV	0	0	0.93
Shivering	0	0	0.132
At entering PACU			
PONV	2	0	< 0.05
Shivering	3	0	< 0.05
30 min after PACU			
PONV	5	1	< 0.001
Shivering	8	0	< 0.001
60 min after PACU			
PONV	1	1	0.071
Shivering	1	1	0.163
120 min after PACU			
PONV	1	0	< 0.05
Shivering	0	0	0.118
24 h after surgery			
PONV	0	0	0.117
Shivering	0	0	0.136

Abbreviation:PACU: post-anesthesia care unit

Footnotes

Authors' Contribution: F.J. developed the original idea and the protocol, participated in designing the evaluation, abstracted and analyzed the data. M.Z. contributed to the development of the protocol, abstracted the data, prepared and wrote the manuscript. All the authors read and approved the final manuscript.

Clinical Trial Registration Code: IRCT20191023045206N1.

Conflict of Interests: The authors declare no conflicts of interest.

Ethical Approval: The Ethics Committee of Jundishapur University of Medical Sciences approved this study. (IR.AJUMS.REC.1398.593).

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References

1. Blaudszun G, Lysakowski C, Elia N, Tramer MR. Effect of perioperative systemic alpha2 agonists on postoperative morphine consumption and pain intensity: systematic review and meta-analysis of randomized controlled trials. *Anesthesiology*. 2012;**116**(6):1312–22. doi: 10.1097/ALN.0b013e31825681cb. [PubMed: 22546966].
2. Miller RD, Pardo M. *Basics of anesthesia e-book:*. Elsevier Health Sciences; 2020.
3. Mentes O, Harlak A, Yigit T, Balkan A, Balkan M, Cosar A, et al. Effect of intraoperative magnesium sulphate infusion on pain relief after laparoscopic cholecystectomy. *Acta Anaesthesiol Scand*. 2008;**52**(10):1353–9. doi: 10.1111/j.1399-6576.2008.01816.x. [PubMed: 19025527].
4. Bailey PL, Pace NL, Ashburn MA, Moll JW, East KA, Stanley TH. Frequent hypoxemia and apnea after sedation with midazolam and fentanyl. *Anesthesiology*. 1990;**73**(5):826–30. doi: 10.1097/00000542-199011000-00005. [PubMed: 2122773].
5. Javaherforooshzadeh F, Amirpour I, Janatmakan F, Soltanzadeh M. Comparison of effects of melatonin and gabapentin on post operative anxiety and pain in lumbar spine surgery: A randomized clinical trial. *Anesth Pain Med*. 2018;**8**(3):e68763. doi: 10.5812/aapm.68763.
6. Rupniewska-Ladyko A, Malec-Milewska M. A high dose of fentanyl may accelerate the onset of acute postoperative pain. *Anesth Pain Med*. 2019;**9**(5). e94498. doi: 10.5812/aapm.94498. [PubMed: 31903331]. [PubMed Central: PMC6935250].
7. Lee JH, Kim H, Kim HT, Kim MH, Cho K, Lim SH, et al. Comparison of dexmedetomidine and remifentanil for attenuation of hemodynamic responses to laryngoscopy and tracheal intubation. *Korean J Anesthesiol*. 2012;**63**(2):124–9. doi: 10.4097/kjae.2012.63.2.124. [PubMed: 22949979]. [PubMed Central: PMC3427804].
8. Selim MF, Elnabtity AM, Hasan AM. Comparative evaluation of epidural bupivacaine - dexmedetomidine and bupivacaine -fentanyl on Doppler velocimetry of uterine and umbilical arteries during labor. *J Prenat Med*. 2012;**6**(3):47–54. [PubMed: 23181173]. [PubMed Central: PMC3503522].
9. Javaherforooshzadeh F, Monajemzadeh SA, Soltanzadeh M, Janatmakan F, Salari A, Saeed H. A comparative study of the amount of bleeding and hemodynamic changes between dexmedetomidine infusion and remifentanil infusion for controlled hypotensive anesthesia in lumbar discopathy surgery: A double-blind, randomized, clinical trial. *Anesth Pain Med*. 2018;**8**(2):e66959. doi: 10.5812/aapm.66959.
10. Imani F, Varrassi G. Ketamine as adjuvant for acute pain management. *Anesth Pain Med*. 2019;**9**(6):e100178. doi: 10.5812/aapm.100178.
11. Imani F, Rahimzadeh P, Faiz SHR. Comparison of the efficacy of adding clonidine, chlorpromazine, promethazine, and midazolam to morphine pumps in postoperative pain control of addicted patients. *Anesth Pain Med*. 2011;**1**(1):10–4. doi: 10.5812/kowsar.22287523.1336. [PubMed: 25729649]. [PubMed Central: PMC4335752].
12. Patel CR, Engineer SR, Shah BJ, Madhu S. Effect of intravenous infusion of dexmedetomidine on perioperative haemodynamic changes and postoperative recovery: A study with entropy analysis. *Indian J Anaesth*. 2012;**56**(6):542–6. doi: 10.4103/0019-5049.104571. [PubMed: 23325938]. [PubMed Central: PMC3546240].
13. Imani F, Zaman B, De Negri P. Postoperative pain management: Role of dexmedetomidine as an adjuvant. *Anesth Pain Med*. 2020;**10**(6):e112176. doi: 10.5812/aapm.112176.
14. Bekker A, Haile M, Kline R, Didehvar S, Babu R, Martiniuk F, et al. The effect of intraoperative infusion of dexmedetomidine on the quality of recovery after major spinal surgery. *J Neurosurg Anesthesiol*. 2013;**25**(1):16–24. doi: 10.1097/ANA.0b013e31826318af. [PubMed: 22824921]. [PubMed Central: PMC3557800].

15. Polat R, Peker K, Baran I, Bumin Aydin G, Topcu Guloksuz C, Donmez A. Comparison between dexmedetomidine and remifentanil infusion in emergence agitation during recovery after nasal surgery: A randomized double-blind trial. *Anaesthesist*. 2015;**64**(10):740–6. doi: 10.1007/s00101-015-0077-8. [PubMed: 26329913].
16. Lee JM, Lee SK, Lee SJ, Hwang WS, Jang SW, Park EY. Comparison of remifentanil with dexmedetomidine for monitored anaesthesia care in elderly patients during vertebroplasty and kyphoplasty. *J Int Med Res*. 2016;**44**(2):307–16. doi: 10.1177/0300060515607385. [PubMed: 26912506]. [PubMed Central: PMC5580066].
17. Imani F, Rahimzadeh P, Faiz HR, Nowruzina S, Shakeri A, Ghahremani M. Comparison of the post-caesarean analgesic effect of adding dexmedetomidine to paracetamol and ketorolac: A randomized clinical trial. *Anesth Pain Med*. 2018;**8**(5). e85311. doi: 10.5812/aapm.85311. [PubMed: 30538943]. [PubMed Central: PMC6252045].
18. Talke PO, Lobo EP, Brown R, Richardson CA. Clonidine-induced vasoconstriction in awake volunteers. *Anesth Analg*. 2001;**93**(2):271–6. doi: 10.1213/00000539-200108000-00006.
19. Ayoglu H, Yapakci O, Ugur MB, Uzun L, Altunkaya H, Ozer Y, et al. Effectiveness of dexmedetomidine in reducing bleeding during septoplasty and tympanoplasty operations. *J Clin Anesth*. 2008;**20**(6):437–41. doi: 10.1016/j.jclinane.2008.04.008. [PubMed: 18929284].
20. Feld JM, Hoffman WE, Stechert MM, Hoffman IW, Ananda RC. Fentanyl or dexmedetomidine combined with desflurane for bariatric surgery. *J Clin Anesth*. 2006;**18**(1):24–8. doi: 10.1016/j.jclinane.2005.05.009. [PubMed: 16517328].
21. Tanskanen PE, Kytta JV, Randell TT, Aantaa RE. Dexmedetomidine as an anaesthetic adjuvant in patients undergoing intracranial tumour surgery: a double-blind, randomized and placebo-controlled study. *Br J Anaesth*. 2006;**97**(5):658–65. doi: 10.1093/bja/ael220. [PubMed: 16914460].
22. Gazi M, Abitagaoglu S, Turan G, Koksal C, Akgun FN, Ari DE. Evaluation of the effects of dexmedetomidine and remifentanil on pain with the analgesia nociception index in the perioperative period in hysteroscopies under general anesthesia. A randomized prospective study. *Saudi Med J*. 2018;**39**(10):1017–22. doi: 10.15537/smj.2018.10.23098. [PubMed: 30284585]. [PubMed Central: PMC6201036].
23. Choi JW, Joo JD, Kim DW, In JH, Kwon SY, Seo K, et al. Comparison of an intraoperative infusion of dexmedetomidine, fentanyl, and remifentanil on perioperative hemodynamics, sedation quality, and postoperative pain control. *J Korean Med Sci*. 2016;**31**(9):1485–90. doi: 10.3346/jkms.2016.31.9.1485. [PubMed: 27510395]. [PubMed Central: PMC4974193].
24. Hwang W, Lee J, Park J, Joo J. Dexmedetomidine versus remifentanil in postoperative pain control after spinal surgery: a randomized controlled study. *BMC Anesthesiol*. 2015;**15**:21. doi: 10.1186/s12871-015-0004-1. [PubMed: 25750586]. [PubMed Central: PMC4352285].
25. Xu T, Li M, Ni C, Guo XY. Dexmedetomidine versus remifentanil for sedation during awake intubation using a Shikani optical stylet: a randomized, double-blinded, controlled trial. *BMC Anesthesiol*. 2016;**16**(1):52. doi: 10.1186/s12871-016-0219-9. [PubMed: 27484783]. [PubMed Central: PMC4970200].
26. Ibraheim OA, Abdulmonem A, Baaj J, Zahrani TA, Arlet V. Esmolol versus dexmedetomidine in scoliosis surgery: study on intraoperative blood loss and hemodynamic changes. *Middle East J Anaesthesiol*. 2013;**22**(1):27–33. [PubMed: 23833847].