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*Original Article*

# The effect of intranasal dexmedetomidine on hemodynamic disturbances caused by laryngoscopy and endotracheal intubation

Seyed Mohammad Reza Safavi[1], Azim Honarmand[2], Behzad Nazemroaya[2], Amir Mohammad Ataie[3], Zahra Kamran[4]

*[1]Department of Anesthesiology and Critical Care, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran; [2]Anesthesiology and Critical Care Research Center, Isfahan University of Medical Sciences, Isfahan, Iran; [3]Urology & Nephrology Research Center, Hamadan University of Medical Sciences, Hamadan, Iran; [4]School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran*

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**Abstract:** Background: Induced stimulation while endotracheal intubating affects hemodynamic status. The present study compares the hemodynamic changes caused by endotracheal intubating after administering two doses of intranasal Dexmedetomidine. Methods: In an experimental (before-after) trial, 88 patients undergoing general anesthesia enrolled in the study. The Iranian Register of Clinical Trial (IRCT) code of the study was IRCT20160307026950N15 (https://en.irct.ir/trial/39269). Patients were allocated to two intervention groups and one control group by random. Intranasal Dexmedetomidine and Normal saline 0.9% were administrated 30 minutes before induction of anesthesia. (1 μg/kg Dexmedetomidine in group 1, 2 μg/kg Dexmedetomidine in group 2 and 1 mg Normal saline 0.9% in group 3). Vital signs and hemodynamic parameters were measured and recorded in minutes 1, 3, 5, and 10th after induction. Data analysis was done by ANOVA and Chi-square tests. Results: Heart rate, systolic and diastolic blood pressure, and mean arterial pressure were reduced in patients receiving dexmedetomidine ($P<0.05$), but there were no significant changes in the control group. In arterial oxygenation ($P>0.05$), there was no significant difference between the three groups in the arterial blood oxygen amount. Conclusion: Premedication of intranasal dexmedetomidine influences the hemodynamic changes due to anesthesia induction. The dose of 2 μg/kg is better than one μg/kg in improving the hemodynamic state following intubation.

**Keywords:** Intranasal administration, hemodynamic responses, laryngoscopy, dexmedetomidine

## Introduction

Painful pressure stimuli following laryngoscopic maneuvers and endotracheal intubation can lead to hemodynamic changes. Following these stimuli, patients may have increased blood pressure and pulse rate; these reactions are especially threatening for patients with high blood pressure or those with coronary artery disease and valvular disease [1]. For artificial ventilation, endotracheal intubation is performed. In addition to endotracheal intubation, a mask on the face or inside the larynx is also effective. New technologies, such as fiberoptic laryngoscopy have reduced the rate of complications. The most crucial cause of laryngoscopic injury is the lack of skillfulness in performing this procedure [2, 3]. To reduce hemodynamic changes after intubation, opioids, anesthetics, and muscle relaxants can be used at appropriate doses before laryngoscopy [4].

Dexmedetomidine is a short-acting alpha-2 agonist, which can have sedative and analgesic effects with minimal breathing disruption, making it an excellent anesthetic adjunct and an ideal option for relieving anxiety and stress before anesthesia [5]. However, reports of side effects, such as cardiac arrest, have prevented its widespread use. Lower doses of this sedative or methods other than rapid intravenous injection seems to be effective in reducing its

hemodynamic side effects [6, 7]. The intranasal route is a convenient and effective method of administering many drugs; accordingly, intranasal dexmedetomidine has been highly accepted by patients [8, 9].

No scientific studies have specifically reported an association between dexmedetomidine as a sedative prodrug and delay in recovery from anesthesia. In this regard, a recent study compared intramuscular dexmedetomidine with intranasal ketamine and placebo in children undergoing anesthesia for a procedure. The results showed that the time-out period of anesthesia duration was shorter in dexmedetomidine groups than in the control group [10]. Recent studies have also demonstrated that intranasal dexmedetomidine is well tolerated [11]. According to a previous study, 1 μg/kg of intranasal dexmedetomidine as a prodrug did not delay recovery after anesthesia [12]. This drug has several benefits, such as reduced preoperative anxiety, a stable hemodynamic status, and improved patient satisfaction [13].

To the best of our knowledge, no study has yet compared two different intranasal doses of dexmedetomidine to prevent changes in increased HR and BP made by laryngoscopy stimulation and endotracheal intubation. In the present study, we aimed to investigate the effects of two intranasal doses of dexmedetomidine on changes in heart rate and blood pressure following laryngoscopy and endotracheal intubation and to compare the results with a placebo group.

## Methods and material

### *Study design*

This double-blind, randomized clinical trial was performed after obtaining approval from the Medical Ethics Committee (code: IR.MUI.REC.1396.3.794). The Iranian Register of Clinical Trial (IRCT) code of the study was IRCT20160307026950N15.

### *Inclusion and exclusion criteria*

The inclusion criteria were age between 18-65 years, candidates of general anesthesia, requiring endotracheal intubation for anesthesia, and signing the written informed consent to participate in this study. The exclusion criteria were previous history of surgical interventions and anesthesia, history of smoking and substance abuse, pregnancy, chronic medical diseases including diabetes mellitus, hypertension and respiratory diseases, history of intubations, allergies to the study medications, previously known medical conditions that interfere with anesthesia, and patient's will to exit the study.

### *Sampling and data collection*

Consecutive sampling continued until reaching the target sample size. The patients were randomly assigned to three groups using a computer program (random allocation).

After entering the operating room, the patient's complete history was taken, and they were transferred to the operating room bed. Complete monitoring, including electrocardiography (EKG), pulse oximetry, and non-invasive blood pressure measurement, was performed for the patients.

### *Interventions*

All eligible patients were divided into three groups randomly. Group 1 was administered one mcg/kg of dexmedetomidine, while group 2 was administered two mcg/kg of dexmedetomidine. Group 3 received similar amounts of normal saline as the control. Next, hemodynamic changes, including hypertension (blood pressure >140/90), hypotension (systolic blood pressure <90), tachycardia (pulse rate >100), and bradycardia (pulse rate <60), were recorded. Intravenous nitroglycerin was used for cases of atropine bradycardia, labetalol tachycardia, and hypertension without increased heart rate. The person who prescribed the medications differed from the person who recorded the symptoms.

### *Evaluated indicators*

In this study, we evaluated the following data before and during the study:

- Heart rate: by cardiac monitor (beats/min).
- Systolic blood pressure: by pressure monitoring devices (mmHg).
- Diastolic blood pressure: by pressure monitoring devices (mmHg).

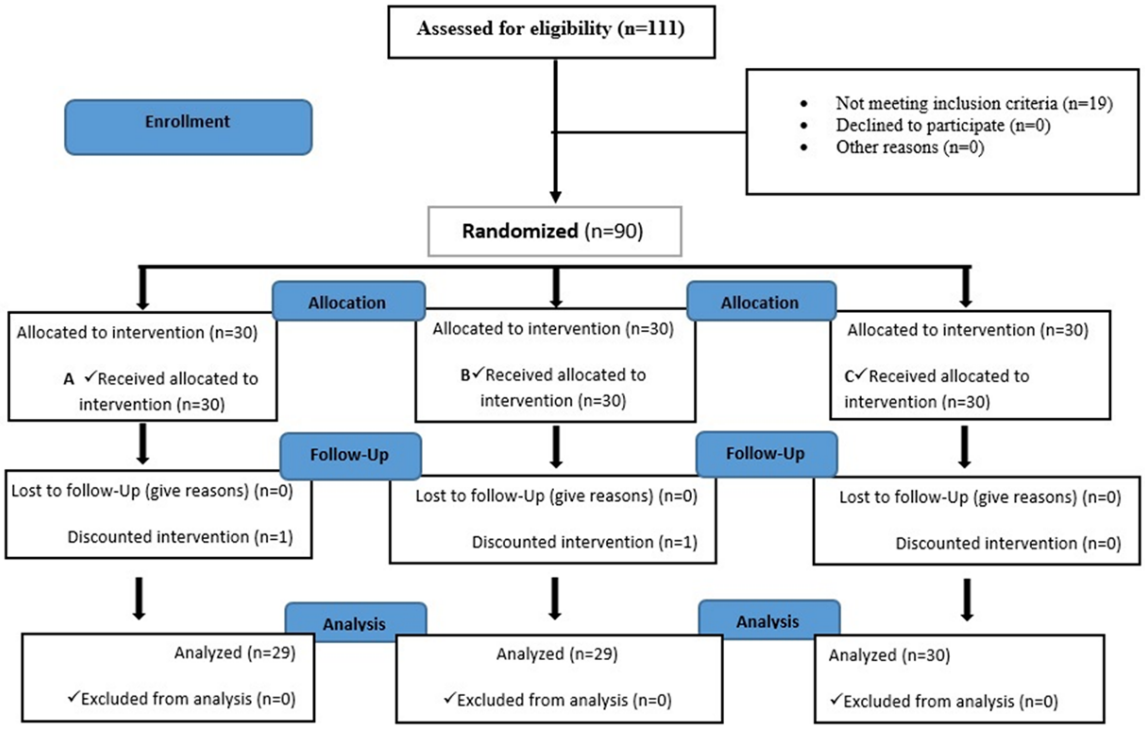


**Figure 1.** CONSRT flow chart of the patients.

• Mean arterial pressure: by pressure monitoring devices (mmHg).

• Arterial oxygenation saturation: by pulse oximetry (percentage).

• The duration of surgery: time interval from surgery initiation until patient's entrance to the recovery room (min).

• The duration of anesthesia: time interval between anesthesia induction and patient's entrance to the recovery room (min).

• Laryngoscopy duration: time interval from an attempt to intubation and successful ventilation via mechanical ventilator device (min).

• Extubation period: the time from the end of surgery to airway extubation (min).

• Recovery time: time interval from patient's entrance to the recovery room to patient's admission to the ward (min).

*Data analysis*

Data were analyzed with Statistical Package for Social Sciences (SPSS) (version 24, SPSS Inc., Chicago, IL). We used repeated measures ANOVA and the significance level in all statistical tests supposed <0.05.

## Results

*Study population*

In this study, of 111 patients, who were candidates for general anesthesia, 19 did not have the inclusion criteria and were not approved. Therefore, 90 patients were randomly assigned to three groups. However, two participants were excluded from the intervention groups, and finally, 88 patients were analyzed (**Figure 1**).

*Demographic and basic data*

The study population comprised 59 women (67.1%) and 29 men (32.9%). The ratio of men to women was 0.49. The mean age of the patients was 41.89±13.97 years. Four patients (4.5%) were in the age group of 18-30 years, 24 patients (27.3%) were in the age group of 30-40 years, 34 patients (38.6%) were in the age group of 40-50 years, 21 patients (23.9%) were in the age group of 50-60, and 5 patients (5.7%)

**Table 1.** The mean values of the studied variables in the groups

| Variables (unit) | Placebo group | | Group 1 | | Group 2 | | *P*-value* |
|---|---|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | Mean | SD | |
| Heart rate (bpm) | 88.06 | 19.30 | 80.28 | 11.14 | 94.76 | 19.61 | 0.008 |
| Systolic blood pressure (mmHg) | 134.17 | 18.55 | 133.75 | 15.09 | 135.73 | 16.60 | 0.893 |
| Diastolic blood pressure (mmHg) | 87.56 | 13.36 | 88.14 | 13.52 | 87.60 | 13.98 | 0.984 |
| Mean arterial pressure (mmHg) | 102.50 | 16.35 | 104.67 | 13.89 | 102.31 | 13.97 | 0.800 |
| Arterial oxygen saturation (mmHg) | 98.96 | 1.47 | 96.92 | 6.49 | 98.93 | 1.43 | 0.085 |

*ANOVA test.

**Table 2.** Comparison of the mean heart rate at baseline before laryngoscopy and at one, three, five, and 10 minutes after the intervention in the three groups

| Heart rate time (bpm) | Code | Placebo | | Group 1 | | Group 2 | | Total | | *P*-value |
|---|---|---|---|---|---|---|---|---|---|---|
| | | Mean | SD | Mean | SD | Mean | SD | Mean | SD | |
| Before laryngoscopy | A | 88.06 | 19.30 | 80.28 | 11.14 | 94.76 | 19.61 | 87.87 | 18.05 | 0.012 |
| One-minute interval | B | 91.86 | 20.03 | 82.00 | 16.54 | 90.56 | 16.31 | 88.28 | 18.06 | 0.043 |
| Three-minute interval | C | 89.80 | 16.59 | 97.85 | 18.89 | 87.23 | 15.54 | 91.48 | 67.67 | 0.010 |
| Five-minute interval | D | 84.56 | 17.40 | 70.75 | 12.75 | 78.23 | 10.66 | 77.98 | 14.87 | 0.004 |
| Ten-minute interval | E | 79.06 | 17.03 | 67.14 | 11.68 | 75.20 | 11.55 | 73.95 | 14.42 | 0.006 |

Bonferroni test (repeated measures test)

| Comparison phase | Placebo group (P=0.04) | | Group 1 (P<0.001) | | Group 2 (P=0.264) | |
|---|---|---|---|---|---|---|
| | Mean difference | *P*-value | Mean difference | *P*-value | Mean difference | *P*-value |
| A:B | -3.800 | 1.000 | -1.714 | 1.000 | 4.200 | 1.000 |
| A:C | -1.733 | 1.000 | -17.571 | 1.000 | 7.533 | 0.167 |
| A:D | 3.500 | 1.000 | 9.536 | 0.001 | 16.600 | 1.000 |
| A:E | 9.000 | 0.309 | 13.143 | 1.000 | 19.567 | 1.000 |
| B:C | 2.067 | 1.000 | -15.857 | 1.000 | 3.333 | 0.752 |
| B:D | 7.300 | 0.325 | 11.250 | 1.000 | 12.400 | 1.000 |
| B:E | 12.800 | 0.001 | 14.857 | 1.000 | 15.367 | 1.000 |
| C:D | 5.233 | 0.251 | 27.107 | 1.000 | 9.067 | 0.002 |
| C:E | 10.733 | 0.001 | 30.714 | 1.000 | 12.033 | 1.000 |
| D:E | 5.500 | 0.228 | 3.607 | 0.103 | 2.967 | 0.061 |

were in the age group of 60-65 years. There was no significant difference in mean age (P=0.601). In addition, patients in the two intervention groups were not significantly different regarding sex distribution (P=0.377). The mean HR, SBP and DBP MAP, and $SpO_2$ are presented in **Table 1**. Regardless of the mean heart rate, other variables examined before the intervention showed no significant difference. Nonetheless, there was a significant difference in HR between the study groups before the intervention (P=0.008). Regardless of the mean heart rate, other variables examined before the intervention was not significantly different between the three groups (P>0.05 for all) (**Table 2**).

*Pressure comparison*

The mean systolic blood pressure was not significantly different between the three groups at the start time and one, three, and five minutes after the intervention; however, the mean SBP was significantly different between the three groups at 10 minutes post-intervention. The results of the Bonferroni correction test showed that changes in systolic blood pressure were not significantly different in the placebo group at one, three, five, and 10 minutes after the intervention compared to the baseline. On the other hand, in the two intervention groups, systolic blood pressure followed a decreasing trend. The difference between the baseline

**Table 3.** Measurement and comparison of the mean arterial pressure at baseline right before laryngoscopy and in one-, three-, five-, and 10-minute intervals in the three groups

| Mean arterial pressure (bpm) | Code | Placebo group | | Group 1 | | Group 2 | | Total | | *P*-value |
|---|---|---|---|---|---|---|---|---|---|---|
| | | Mean | SD | Mean | SD | Mean | SD | Mean | SD | |
| Before laryngoscopy | A | 102.5 | 16.35 | 104.67 | 13.89 | 102.31 | 13.97 | 103.137 | 14.68 | 0.699 |
| One minute after the intervention | B | 108.133 | 20.57 | 105.89 | 18.71 | 102.30 | 16.32 | 105.431 | 18.56 | 0.523 |
| Three minutes after the intervention | C | 101.533 | 15.60 | 93.64 | 17.27 | 95.13 | 16.46 | 96.84 | 16.61 | 0.43 |
| Five minutes after the intervention | D | 97.3 | 19.04 | 88.67 | 12.75 | 88.86 | 13.53 | 91.681 | 15.78 | 0.091 |
| Ten minutes after the intervention | E | 97.6 | 18.72 | 88.28 | 14.42 | 84.89 | 11.7 | 90.367 | 16.06 | 0.004 |

Bonferroni test (repeated measures test)

| Comparison phase | Placebo group (P=0.020) | | Group 1 (P<0.001) | | Group 2 (P<0.001) | |
|---|---|---|---|---|---|---|
| | Mean difference | *P*-value | Mean difference | *P*-value | Mean difference | *P*-value |
| A:B | -5.633 | 0.778 | -1.214 | 1.000 | -0.893 | 1.000 |
| A:C | 0.967 | 1.000 | 11.036 | 0.028 | 6.357 | 1.000 |
| A:D | 5.200 | 1.000 | 16.0 | <0.001 | 12.393 | 0.022 |
| A:E | 4.9 | 1.000 | 16.393 | <0.001 | 16.143 | <0.001 |
| B:C | 6.6 | 0.497 | 12.250 | 0.003 | 7.250 | 0.177 |
| B:D | 10.833 | 0.083 | 17.214 | <0.001 | 13.286 | <0.001 |
| B:E | 10.533 | 0.162 | 17.607 | <0.001 | 17.036 | 0.002 |
| C:D | 4.233 | 1.000 | 4.964 | 0.233 | 6.036 | 0.302 |
| C:E | 3.933 | 1.000 | 5.357 | 0.206 | 9.786 | 0.020 |
| D:E | -0.30 | 1.000 | 0.393 | 1.000 | 3.750 | 1.000 |

measurements and examinations performed five and 10 minutes after the intervention was significant in both groups. However, the mean systolic blood pressure difference was insignificant between the baseline and one- and three-minute intervals after the intervention. Overall, the results indicated the effect of the intervention on lowering systolic blood pressure (**Table 3**).

The mean arterial pressure was not significantly different in the three groups at baseline and one, three, and five minutes after the intervention; nevertheless, the mean arterial pressure was significantly different between the three groups at 10 minutes after the intervention. The results of the Bonferroni test showed that changes in the mean arterial pressure of the placebo group were not significantly different at one, three, five, and 10 minutes after the intervention compared to the baseline. The mean arterial pressure decreased in both intervention groups, and the difference between the baseline and five- and 10-minute intervals after the intervention was significant in both groups. Regarding the mean arterial pressure, the difference was not significant between the baseline and one- and three-minute measurements after the intervention. The results showed the effect of the intervention on reducing the mean arterial pressure.

*Comparison of heart rate*

The mean heart rate was significantly different in the three groups before and after the intervention. The results of the Bonferroni test showed that changes in the heart rate of the placebo group were not significantly different at one, three, five, and 10 minutes after the intervention compared to the baseline. The heart rate decreased in both intervention groups, and the difference was significant between the baseline and five- and 10-minute intervals after the intervention. However, the mean heart rate difference between the baseline and one- and three-minute intervals after the intervention was insignificant. Overall, the effect of interventions on reducing heart rate was confirmed. The results revealed the impact of the intervention on lowering heart rate.

*Further evaluations*

A comparison of the mean duration of surgery, anesthesia, laryngoscopy, extubation, and recovery time between the three groups showed that they were significantly different in terms of laryngoscopy duration and extubation period. In other words, the duration of anesthesia was shorter in the placebo group than in the other groups, and the time of extubation was the shortest in group 2. However, there was no sig-

**Table 4.** Comparison of the mean duration of surgery, anesthesia, laryngoscopy, extubation, and recovery in the three groups

| Groups | Surgery duration (minutes) | Duration of anesthesia (minutes) | Laryngoscopy duration (seconds) | Extubation period (minutes) | Recovery time (minutes) |
|---|---|---|---|---|---|
| Placebo | 116.50±7.8 | 122.33±8.1 | 11.50±3.9 | 525.85±7.5 | 65.34±16.6 |
| Group 1 | 119.66±8.0 | 136.06±8.2 | 12.40±5.4 | 20.87±14.9 | 65.35±14.13 |
| Group 2 | 120.00±6.2 | 132.80±6.1 | 15.45±4.5 | 23.96±12.3 | 92.60±49.8 |
| *P*-value | 0.981 | 0.774 | 0.015 | 0.320 | 0.002 |

nificant difference between the groups in terms of the duration of surgery, duration of anesthesia, or recovery time (**Table 4**).

## Discussion

In the present study, the mean heart rate, systolic and diastolic blood pressure, arterial pressure, and arterial oxygen saturation were not significantly different between the three groups. In contrast, the mean heart rate showed a significant difference. In a study by Modir and colleagues investigating the effects of remifentanil and dexmedetomidine on hemodynamic changes in intubated patients, the percentage of increase in systolic and diastolic blood pressure due to endotracheal intubation was lower in the dexmedetomidine and remifentanil groups compared to the other two groups [14].

This result suggests that in patients with normal blood pressure, administration of dexmedetomidine during anesthesia induction stabilizes the blood pressure induced by anesthesia and reduces the hemodynamic response to endotracheal intubation [14]. The present study compared the effects of two doses of dexmedetomidine (1 and 2 μg/kg) with a placebo, which differs from the study by Lee and colleagues; however, the results were similar regarding the effect of dexmedetomidine, and both doses improved the hemodynamic parameters. A comparison of two doses of dexmedetomidine showed that intranasal administration of dexmedetomidine at a dose of 2 μg/kg for 30 minutes before anesthesia positively affected the hemodynamic parameters.

Additionally, in a study by Xu and colleagues in 2016, the effects of remifentanil and dexmedetomidine on hemodynamic changes were similar in intubated patients; nevertheless, patients receiving remifentanil were more likely to experience hypoxia [15]. Although the results of this study are not consistent with the results of the study by Xu and colleagues, the relatively greater effect of dexmedetomidine was reported, which can be used to improve the hemodynamic status of patients after anesthesia induction. The current study also indicated the positive effect of dexmedetomidine on improving the hemodynamic status after anesthesia induction. A comparison of different doses showed the relatively more significant impact of dexmedetomidine at a quantity of 2 μg/kg on improving the hemodynamic quality.

Moreover, a review study by Trifa and colleagues in 2018, evaluating the effect of dexmedetomidine on general anesthesia, showed that administration of dexmedetomidine at a dose of 2 μg/kg during general anesthesia caused severe hemodynamic changes during pediatric anesthesia and surgeries, which majorly contradicts the present findings [16]. Additionally, in a study by Tarıkçı Kılıç in 2018 the effect of dexmedetomidine on hemodynamic changes during anesthesia was investigated. Dexmedetomidine injection led to a reduction in hemodynamic responses, while it had no impact on arterial oxygen or respiratory rate and caused no side effects [17]. The results of this study are in contrast to the present study, which reported the positive effect of dexmedetomidine on improving the hemodynamic status; the cause of the discrepancy between the results may be the type of anesthesia. It should be noted that the anesthesia method in our study was general anesthesia, whereas Tarıkçı Kılıç and colleagues used the spinal anesthesia method. In addition, in the survey by Tarıkçı Kılıç and colleagues, the method of dexmedetomidine administration was infusion, while in the current study, the nasal route was used.

In a study by Mirkheshti and colleagues, the effect of topical dexmedetomidine on hemodynamic changes was investigated in patients undergoing bronchoscopy. It was found that

sudden changes reduce hemodynamic responses and coughing while improving the patient's tolerance and intubation score [18]. Additionally, in a study by Singh and colleagues in 2017, the effects of dexmedetomidine and diltiazem on patients undergoing intubation were evaluated. In this study, systolic and diastolic blood pressure and mean arterial pressure were less significant in the dexmedetomidine group compared to the control and diltiazem groups [19]. Moreover, in a study by Sharma and colleagues in 2017, the effects of 0.5 and 1 μg/kg of dexmedetomidine on hemodynamic changes were examined in intubated patients, indicating the similar effects of these two doses, with no severe hemodynamic changes in either of the groups [20]; this finding is consistent with the present results. Other studies have also reported the sedative effect of nasal dexmedetomidine, as confirmed in the current research [21, 22].

The limitations of this study were the restricted number of studied patients and not comparing these data with other types of medications. However, our results supported using 2 μg/kg of dexmedetomidine. We recommend that further investigations should be performed in this regard.

## Conclusion

According to the present results, the effects of two doses of dexmedetomidine on hemodynamic parameters were similar compared to the placebo group. Comparing these two doses showed that intranasal administration of two μg/kg of dexmedetomidine 30 minutes before anesthesia induction positively affected hemodynamic parameters.

## Disclosure of conflict of interest

None.

**Address correspondence to:** Zahra Kamran, School of Medicine, Isfahan University of Medical Science, Hezar Jarib St., Isfahan, Iran. Tel: +989128047488; Fax: +983137265007; E-mail: Z.kamran72@gmail.com

## References

[1] De Cassai A, Boscolo A, Geraldini F, Zarantonello F, Pettenuzzo T, Pasin L, Iuzzolino M, Rossini N, Pesenti E and Zecchino G. Effect of dexmedetomidine on hemodynamic responses to tracheal intubation: a meta-analysis with meta-regression and trial sequential analysis. J Clin Anesth 2021; 72: 110287.

[2] Gonzalez A and Kimatian S. The basics of anesthesia. Anesthesiology 2018; 129: 1194-1195.

[3] Ghadimi K, Motififard M, Mohammadi R and Zadeh AR. Complete bilateral knee arthroplasty in staged or simultaneous surgeries in patients with osteoarthritis. Int J Burn Trauma 2022; 12: 59.

[4] Tung A, Fergusson NA, Ng N, Hu V, Dormuth C and Griesdale DE. Medications to reduce emergence coughing after general anaesthesia with tracheal intubation: a systematic review and network meta-analysis. Br J Anaesth 2020; 124: 480-495.

[5] Lee S. Dexmedetomidine: present and future directions. Korean J Anesthesiol 2019; 72: 323-330.

[6] Shehabi Y, Howe BD, Bellomo R, Arabi YM, Bailey M, Bass FE, Bin Kadiman S, McArthur CJ, Murray L and Reade MC. Early sedation with dexmedetomidine in critically ill patients. N Engl J Med 2019; 380: 2506-2517.

[7] Zhao Y, He J, Yu N, Jia C and Wang S. Mechanisms of dexmedetomidine in neuropathic pain. Front Neurosci 2020; 14: 330.

[8] Poonai N, Spohn J, Vandermeer B, Ali S, Bhatt M, Hendrikx S, Trottier ED, Sabhaney V, Shah A and Joubert G. Intranasal dexmedetomidine for procedural distress in children: a systematic review. Pediatrics 2020; 145: e20191623.

[9] Moradi Farsani D, Shetabi H, Rafiee Zadeh A and Saffari Rad N. Comparison of tranexamic acid, remifentanil, and hydralazine on the bleeding volume during dacryocystorhinostomy surgery. Int J Physiol Pathophysiol Pharmacol 2022; 14: 177-186.

[10] Zhang J, Liu G, Zhang F, Fang H, Zhang D, Liu S, Chen B and Xiao H. Analysis of postoperative cognitive dysfunction and influencing factors of dexmedetomidine anesthesia in elderly patients with colorectal cancer. Oncol Lett 2019; 18: 3058-3064.

[11] Li A, Yuen V, Goulay-Dufaÿ S, Sheng Y, Standing J, Kwok P, Leung M, Leung A, Wong I and Irwin M. Pharmacokinetic and pharmacodynamic study of intranasal and intravenous dexmedetomidine. Br J Anaesth 2018; 120: 960-968.

[12] Uusalo P, Guillaume S, Siren S, Manner T, Vilo S, Scheinin M and Saari TI. Pharmacokinetics and sedative effects of intranasal dexmedetomidine in ambulatory pediatric patients. Anesth Analg 2020; 130: 949-957.

[13] Miller J, Balyan R, Dong M, Mahmoud M, Lam J, Pratap J, Paquin J, Li B, Spaeth J and Vinks A. Does intranasal dexmedetomidine provide adequate plasma concentrations for sedation

in children: a pharmacokinetic study. Br J Anaesth 2018; 120: 1056-1065.
[14] Modir H, Yazdi B, Moshiri E, Mohammadbeigi A and Afshari S. Efficacy of dexmedetomidine versus remifentanil to blunt the hemodynamic response to laryngoscopy and orotracheal intubation: a randomized clinical trial. Med Gas Res 2018; 8: 85.
[15] Xu T, Li M, Ni C and Guo XY. Dexmedetomidine versus remifentanil for sedation during awake intubation using a Shikani optical stylet: a randomized, double-blinded, controlled trial. BMC Anesthesiol 2015; 16: 1-7.
[16] Trifa M, Tumin D and Tobias JD. Dexmedetomidine as an adjunct for caudal anesthesia and analgesia in children. Minerva Anestesiol 2018; 84: 836-847.
[17] Kılıç ET and Aydın G. Effects of dexmedetomidine infusion during spinal anesthesia on hemodynamics and sedation. Libyan J Med 2018; 13: 1436845.
[18] Mirkheshti A, Memary E, Honar BN, Jalaeefar A and Sezari P. The efficacy of local dexmedetomidine during fiberoptic nasotracheal intubation: a randomized clinical trial. J Anaesthesiol Clin Pharmacol 2017; 33: 209.
[19] Weber V, Abbott TEF and Ackland GL. Reducing the dose of neuromuscular blocking agents with adjuncts: a systematic review and meta-analysis. Br J Anaesth 2021; 126: 608-621.
[20] Sharma J, Purohit S, Bhatia S, Kalra P, Sharma M and Meena R. Awake orotracheal fibre-optic intubation: comparison of two different doses of dexmedetomidine on intubation conditions in patients undergoing cervical spine surgery. Indian J Anaesth 2017; 61: 811.
[21] Wang L, Huang L, Zhang T and Peng W. Comparison of intranasal dexmedetomidine and oral midazolam for premedication in pediatric dental patients under general anesthesia: a randomised clinical trial. Biomed Res Int 2020; 2020: 5142913.
[22] Goswami M, Sangal A, Rahman B and Chawla S. Comparison of the safety and efficacy of dexmedetomidine with midazolam for the management of paediatric dental patients: a systematic review. J Indian Soc Pedod Prev Dent 2021; 39: 233.