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Effect of dexmedetomidine on intrapulmonary shunt in patients with sevoflurane maintained during one-lung ventilation

A case–control study

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Abstract

Background: The effects of dexmedetomidine on the circulatory system are complex. It is difficult to predict its effects on intrapulmonary shunts and hypoxic pulmonary vasoconstriction in patients with one-lung ventilation. This study aimed to investigate the effect of dexmedetomidine on intrapulmonary shunt in patients with sevoflurane during one-lung ventilation.

Methods: Forty patients requiring thoracoscopic lobectomy were randomly divided into the dexmedetomidine group (Group D, n = 20) and the normal saline group (Group N, n = 20). The arterial partial pressure of oxygen (PaO_2), pulmonary shunt fraction (Qs/Qt), mean end-tidal sevoflurane concentration, mean arterial pressure, and heart rate were compared between the 2 groups at 3 time points: (i) after 5 minutes of two-lung ventilation (T0), (ii) after 30 minutes of one-lung ventilation (OLV) (T1), and (iii) after 45 minutes of OLV (T2). The dosage of sevoflurane from the beginning of OLV to T2 was calculated.

Results: There were no significant differences in age, body mass index, and FEV1/FVC between Groups D and N ($P > .05$). At T0, T1, and T2, the PaO_2 levels of Group D and Group N were similar ($P > .05$), and the PaO_2 levels of Group D and Group N decreased after OLV. The Qs/Qt level of Groups D and N were similar at T0 ($P > .05$), and the level of Groups D and N at T1 and T2 was higher than that at T0. The Qs/Qt of Group D was statistically significantly lower than that of Group N at T1 and T2 ($P < .05$).

Conclusion: Compared with the control group, we found that dexmedetomidine can reduce the intrapulmonary shunt fraction and improve the body's status during OLV.

Abbreviations: BIS = bispectral index monitoring, HPV = hypoxic pulmonary vasoconstriction, HR = heart rate, MAP = mean arterial pressure, OLV = one-lung ventilation, PaO_2 = partial pressure of oxygen.

Keywords: dexmedetomidine, intrapulmonary shunt, one-lung ventilation, video-assisted thoracic surgeries

1. Introduction

One-lung ventilation during general anesthesia can improve the surgical field of vision, which is often used in thoracic surgeries.[1–3] Still, it leads to the increase of intrapulmonary shunt and the occurrence of hypoxemia simultaneously,[4,5] which increases the incidence of perioperative adverse events and the mortality of patients.[6] Hypoxic pulmonary vasoconstriction (HPV) is the primary compensatory mechanism of the body against the pulmonary shunt, which is to divert the pulmonary perfusion blood from the non-ventilated area to the ventilated area, thus reducing pulmonary shunt and improving hypoxemia.[7–9] Anesthetics is one of the critical factors affecting HPV, and anesthesiologists must develop an anesthetic plan with minimal HPV inhibition for patients requiring 1-lung ventilation.[10,11] Dexmedetomidine is a highly selective α_2 adrenergic receptor agonist, which can directly stimulate peripheral α_2 receptors to induce vasoconstriction and increase blood pressure, and also act on central α_2 receptors to suppress sympathetic excitation,[12] which could dilate blood vessels and lower blood pressure. Due to the complex effects of dexmedetomidine on circulation, it is difficult to predict its impacts on intrapulmonary shunt and HPV in patients during 1-lung ventilation. Therefore, we intend to investigate the effect of dexmedetomidine on intrapulmonary shunt in patients with sevoflurane maintained during 1-lung ventilation.

2. Patients and methods

2.1. Patients

This is a prospective, multicenter, parallel-group, single-blind randomized controlled trial initiated by researchers, which the

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The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Ethics Committee has approved of the Affiliated Hospital of Binzhou Medical College (KT-023). After written informed consent 1 day before surgery, 40 patients requiring 1-lung ventilation (OLV) for thoracic surgery in Binzhou Medical University Hospital between September 2021 to January 2022 were randomly assigned to receive dexmedetomidine (Group D) or normal saline (Group N) during anesthesia.

2.2. Sample size determined

The sample size was estimated concerning similar published studies.[13] Q_s/Q_t was the primary outcome index of the study, so Q_s/Q_t at the OLV-30 minutes time point in the reference was selected as the index for sample size calculation. The mean value of Q_s/Q_t in the dexmedetomidine group was 24.5 ± 3.5, and the mean value of Q_s/Q_t in the saline group was 30.7 ± 2.8, with an overall standard deviation of approximately 4.5. We performed efficacy analysis using Origin software. When the power is > 0.8, the sample size needs to be > 10 cases.

2.3. Inclusion and exclusion criteria

2.3.1. *Inclusion criteria*. 18–65 years, ASA I-III, patients who would receive 1-lung ventilation for Video-assisted thoracic surgeries.

2.3.2. *Exclusion criteria*. Renal insufficiency, liver dysfunction or ischemic or valvular heart disease, long-term alcohol, opioid, or sedative-hypnotic drug addiction and dependency history, and neuropsychiatric diseases, intubation failure, bispectral index monitoring (BIS) < 40 or BIS > 60 in surgery and $SpO_{2<}$ 90% during the operation.

2.4. Methods

All patients had fasted before surgeries; in the operating theater, ECG, SpO_2, NIBP, and other monitoring were placed. Oxygen inhalation was performed by mask, and a radial artery catheter was placed under local anesthesia. Before the induction, a loading dose of dexmedetomidine was infused continuously at a rate of 0.75ug × kg^{-1} within 10 to 15 minutes in Group D. The same amount of normal saline was infused in Group N. Anesthesia induction was performed with midazolam 0.05 mg/kg, etomidate 0.3 mg/kg, sufentanil 0.5 μg/kg and vecuronium 0.1 mg/kg. After breath was controlled for about 5 minutes, intubation was performed under a visual laryngoscope with a double-lumen tube. The choice of a double-lumen tube depends on the surgical site. The left double-lumen tube was selected for the right thoracotomy, and the right double-lumen tube were chosen for the left thoracotomy. The default size of the catheter is 37F for males and 35F for females. After intubation, a bronchoscopy was performed to adjust the tube position to maintain an appropriate airway pressure and tidal volume. In the maintenance stage, the right internal jugular vein was cannulated, and BIS was performed to evaluate the depth of anesthesia. During the maintenance phase of anesthesia, patients in Group D received dexmedetomidine at a maintenance dose of 0.3 μg/ (kg × h) until 45 minutes after 1-lung ventilation. Patients in group N received the same amount of normal saline. At the beginning of the operation, 1-lung ventilation was immediately performed, and respiratory parameters were set to maintain the end-tidal pressure of carbon dioxide at 30 to 40 mm Hg. The respiratory parameters were adjusted according to blood gas measurements during the operation. The remifentanil dose and sevoflurane concentration were adjusted to maintain BIS between 40 and 60, and vecuronium was injected intermittently.

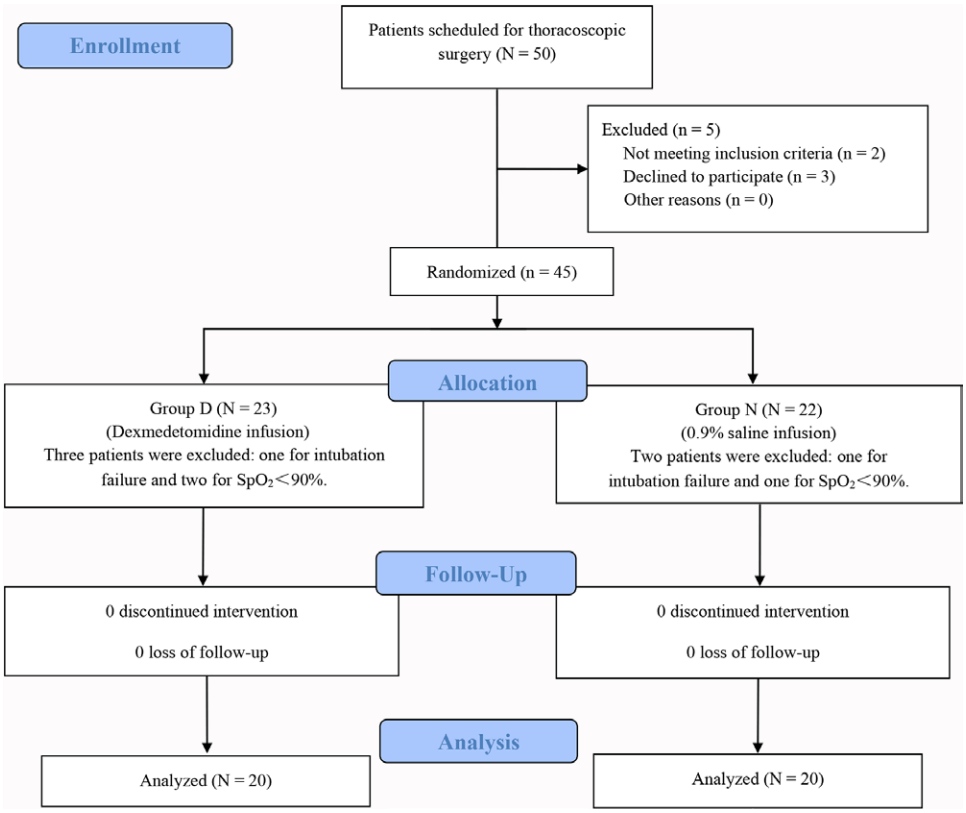

Figure 1. The inclusion flowchart of the patients.

2.5. Outcomes

The arterial partial pressure of oxygen (PaO_2), pulmonary shunt fraction (Q_s/Q_t), mean end-tidal sevoflurane concentration, mean arterial pressure (MAP), heart rate (HR) were compared between the 2 groups at 3-time points; after 5 minutes of 2-lung ventilation (*T*0); after 30 minutes of OLV (*T*1), and; after 45 minutes of OLV (*T*2). Blood gas analysis was performed from the radial artery and internal jugular vein at *T*0, *T*1, and *T*2. The arterial PaO_2, arterial oxygen saturation (SaO_2), hemoglobin (Hb), arterial partial pressure of carbon dioxide ($PaCO_2$), partial venous pressure of oxygen (PvO_2) and venous oxygen saturation (SvO_2) were recorded. The shunt fraction was computed using a standard formula: $Q_s/Q_t = (C'CO_2–CaO_2)/(C'CO_2–CvO_2) \times 100\%$, while $C'CO_2$, CaO_2 and CvO_2 represent the oxygen content of pulmonary end-capillary, arterial and mixed venous blood, respectively. Meanwhile, the average MAP, HR and end-tidal concentration of sevoflurane (%) were recorded at *T*0, *T*1 and *T*2. The dosage of sevoflurane from the beginning of OLV to 45 minutes of OLV was calculated (mL) as well according to the formula: Sevoflurane dosage (mL) = Sevoflurane concentration (%) × gas flow rate (L/minute) × time (minute) × (200.06/3666.24).

2.6. Statistical analysis

The data from the study results were organized and analyzed using SPSS 25.0 software (IBM SPSS, Inc., Chicago, IL). The continuous data were expressed as mean ± SD, and the qualitative data was expressed as rate and frequency. Continuous data were compared using the independent-samples *t*-test, and qualitative data were compared using the χ^2 test. A difference of more than 5% is considered significant ($P < .05$).

3. Results

3.1. Patient details

Fifty patients who were ready for surgery were initially included in this study. Two additional patients were excluded after the strict implementation of inclusion and exclusion criteria; 3 were also excluded because they refused to participate in the study. Subsequently, 1 patient was excluded from the trial group because of failed tracheal intubation and 2 patients with $SpO_2 < 90\%$; 1 patient was excluded from the control group because of failed tracheal intubation and 1 with $SpO_2 < 90\%$. Finally, a total of 40 patients were included in this study. There were 20 patients in the Dexmedetomidine infusion group and 20 in the control group with 0.9% saline infusion (Fig. 1). There were no statistical differences in age, gender, and body mass index between the 2 groups ($P > .05$). The lung function tests were similar in the 2 groups ($P > .05$) (Table 1).

Table 1

Basic information and pulmonary function test results.

Factors	Group D	Group N	*P* value
Age (yr)	51.1 ± 7.9	52.0 ± 5.7	.680
BMI (kg/m^2)	25.5 ± 4.0	25.8 ± 4.3	.838
Male/female	9/11	8/12	.749
FEV1/FVC (%)	84.57 ± 8.15	85.56 ± 5.85	.664
% of predicted FEV1	98.70 ± 10.44	96.88 ± 7.86	.537

Values are presented as mean ± SD, except for male/female (frequency).
FEV1 = forced expiratory vital capacity, FVC = forced vital capacity.

3.2. Oxygenation details

Arterial PaO_2 decreased with the OLV time prolonging, and the levels were similar between Group D and Group N at *T*0, *T*1, and *T*2, with no statistical significance ($P > .05$) (Table 2).

After 5 minutes of total lung ventilation (*T*0), the intrapulmonary shunt fraction (Q_s/Q_t) level was similar between groups ($P > .05$). Q_s/Q_t was higher than *T*0 at 30 minutes OLV (*T*1) and 45 minutes OLV (*T*2) in both groups. At *T*1 and *T*2, Q_s/Q_t was lower in Group D than in group N, with statistically significant differences ($P < .05$), as shown in Table 2.

3.3. Sevoflurane

The average sevoflurane end-tidal concentration (%) of the 2 groups was similar at *T*0 ($P > .05$), while the concentration of group D was lower than that of group N at *T*1, *T*2 ($P < .05$). From the beginning of OLV to *T*2, the dosage of sevoflurane in group D was less than that in group N ($P < .05$), as shown in Table 3.

3.4. Haemodynamics parameters

The MAP in Group D was lower than that in Group N at *T*0, *T*1 and *T*2 ($P > .05$). At *T*0, there was no statistically significant difference in HR between the groups ($P > .05$); at *T*1 and *T*2, the HR level in both groups was lower than that of *T*0. The HR of Group D at *T*1 and *T*2 was lower than that of Group N ($P < .05$) (Table 4).

4. Discussion

We have not found clinical studies that reported the pulmonary effects of dexmedetomidine combined with sevoflurane in patients with 1-lung ventilation. This study aimed to investigate dexmedetomidine's effect on intrapulmonary shunt in patients with sevoflurane maintained during 1-lung ventilation. The results revealed that dexmedetomidine could reduce the intrapulmonary shunt fraction and improve the HPV response during 1-lung ventilation. At the same time, it did not significantly promote the PaO_2 status during 1-lung ventilation. Previous studies have shown that dexmedetomidine combined

Table 2

The details of the oxygenation.

	PaO_2 (mm Hg)			Q_s/Q_t (%)		
Lung ventilation	Group D	Group N	*P* value	Group D	Group N	*P* value
*T*0	441.3 ± 42.10	460.6 ± 45.39	.171	14.36 ± 1.15	14.03 ± 0.96	.325
*T*1	151.35 ± 34.74	157.75 ± 37.98	.581	29.41 ± 4.96	34.35 ± 7.72	.021
*T*2	150.55 ± 35.01	152.15 ± 34.74	.885	29.53 ± 5.04	34.15 ± 7.24	.025

Values are presented as mean ± standard deviations.
PaO_2 = partial pressure of oxygen, *QS/Qt* = intrapulmonary shunt fraction.

with isoflurane can improve HPV and the oxygenation of the body during OLV,[13] which is consistent with our conclusion study.

Dexmedetomidine is an α_2 receptor agonist; studies have shown that vasoconstrictor drugs, such as adrenergic receptor agonists, can enhance HPV,[14,15] and dexmedetomidine may enhance HPV by directly activating peripheral α_2 receptors and thereby causing pulmonary vessel constriction. Dexmedetomidine also acts on central α_2 receptors and inhibits sympathetic responses, which explains the lower MAP and HR at *T*0, *T*1 and *T*2 in Group D. However, there was no difference in HR between groups at *T*0, which may be related to the significant stimulation of the double-lumen tube and the insufficient binding of dexmedetomidine to the central α_2 receptors. Dexmedetomidine has a synergistic effect on sedation. Studies also have proven that dexmedetomidine can reduce the dosage of inhaled and intravenous anesthetics during surgery,[16,17] and the results of this study confirmed that dexmedetomidine reduced sevoflurane dosage during 1-lung ventilation. Sevoflurane inhibits HPV dose-dependent; dexmedetomidine may reduce the dosage of sevoflurane through its synergistic effect, thus alleviating its inhibition of HPV. Xia et al[18] showed in a prospective clinical randomized controlled trial that dexmedetomidine enhances the effect of HPV by reducing the level of oxidative stress in the body during 1-lung ventilation, thereby improving the oxygenation status of patients. In addition, dexmedetomidine reduces the inflammatory response during 1-lung ventilation, thereby reducing lung injury; this effect may be associated with improved intrapulmonary shunting in patients.[19,20]

Patient details and lung function tests were similar in the 2 groups. The baseline is comparable between the groups. After intubation, all patients underwent fiberbronchoscope positioning to adjust the double-lumen tube. We maintained an appropriate airway pressure and peripheral blood oxygen saturation during OLV. Thus, the effect on oxygenation caused by the imperfect alignment of the double-lumen tube is excluded. In addition, there were no statistical differences in PaO_2, Q_s/Q_t and average sevoflurane concentration between the 2 groups at *T*0. Therefore, dexmedetomidine is considered an essential factor affecting intrapulmonary shunt and HPV during 1-lung ventilation in the study. Because the excessive dose of dexmedetomidine can reduce blood pressure and heart rate, which is not conducive to the perfusion of organs and the safety of patients, in the trial, 0.75 μg/kg loading dose and 0.3 μg/ (kg*h) maintaining dose were used for pumping. During OLV, an intrapulmonary shunt is an important factor affecting oxygenation. HPV can help divert blood from the operative lung to the non-operative lung. The intrapulmonary shunt still occurs even in the presence of effective HPV.

This study used Q_s/Q_t and PaO_2 to evaluate body oxygenation. The results showed that Q_s/Q_t in Group D was lower than that in group N during 1-lung ventilation. Still, there was no difference in PaO_2 between the groups, which shows that Q_s/Q_t is more effective in evaluating intrapulmonary shunt than PaO_2. Therefore, we can speculate that the choice of anesthetics is only one of the key factors affecting intrapulmonary shunt in clinical practice; studies have shown that temperature, pH, airway pressure, patient position and cardiac output all impact HPV.[21,22]

This study still has certain limitations. Such as, due to surgical procedures and other reasons, blood gas analysis and data collection were only performed at *T*0, *T*1, and *T*2. In contrast, other time points during anesthesia were not evaluated. Patients were not tested for indicators related to oxidative stress and inflammatory responses during the procedures in this study, and the mechanism of action of dexmedetomidine has not been studied in depth. In addition, there was no comparison of airway pressure and cardiac output between groups. The small sample size study may affect the conclusion's reliability, so multicenter, high-quality, large-sample clinical trials are needed to confirm the decision further.

5. Conclusion

In conclusion, compared with the control group, dexmedetomidine can reduce the intrapulmonary shunt fraction during 1-lung ventilation. Still, there is no statistical significance in the difference in arterial partial pressure of oxygen between groups. Haemodynamic stability and appropriate ventilatory maneuvers may be far more critical for achieving optimal oxygenation during OLV than the anesthetic agent's choice.

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Investigation: Chunzhi Gong.
Methodology: Chunzhi Gong.
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Project administration: Quanyi Zhang.
Software: Fei Yu.

Table 3

Changes in the concentration of sevoflurane.

	Average sevoflurane end-tidal concentration (%)			Dosage of sevoflurane (mL)		
Lung ventilation	Group D	Group N	*P* value	Group D	Group N	*P* value
*T*0	1.01 ± 0.117	1.06 ± 0.111	.215	9.67 ± 0.86	12.94 ± 1.12	<.001
*T*1	1.29 ± 0.078	1.47 ± 0.083	<.001	–	–	–
*T*2	1.30 ± 0.076	1.48 ± 0.083	<.001	–	–	–

Table 4

Haemodynamics parameters.

	MAP (mm Hg)			HR (bpm)		
Lung ventilation	Group D	Group N	*P* value	D	N	*P* value
*T*0	82.80 ± 6.246	88.65 ± 8.518	.018	76.50 ± 8.636	81.10 ± 9.026	.108
*T*1	75.20 ± 4.526	84.60 ± 6.809	<.001	63.0 ± 6.340	72.80 ± 6.685	<.001
*T*2	75.85 ± 4.771	85.55 ± 6.525	<.001	63.75 ± 5.893	73.50 ± 6.245	<.001

Values are presented as mean ± standard deviations.

bpm = beats per minute, HR = heart rate, MAP = mean arterial pressure.

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