



Effect of Dexmedetomidine Combined with Inhalation of Isoflurane on Oxygenation Following One-Lung Ventilation in Thoracic Surgery

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Abstract

Background: One-lung ventilation (OLV) is commonly used during thoracic surgery. At this time, hypoxemia is considered one of the remarkable consequences of the anesthesia management. Hypoxic pulmonary vasoconstriction (HPV) is the defense mechanism against hypoxia.

Objectives: The aim of the present study was to investigate the effect of infusion of dexmedetomidine on improving the oxygenation during OLV among the adult patients undergoing thoracic surgery.

Methods: A total of 42 patients undergoing OLV by general anesthesia with isoflurane inhalation were randomly assigned into two groups: IV infusion of dexmedetomidine at 0.3 microgram/kg/h (DISO) and IV infusion of normal saline (NISO). Three Arterial Blood Gas (ABG) samples were obtained throughout the surgery. Hemodynamic parameters, PaO₂, PaCO₂, and complications at recovery phase were recorded. The collected information was analyzed using SPSS software version 22.

Results: In the dexmedetomidine group, the mean hemodynamic parameters had a significant reduction at 30 and 60 minutes following OLV. Administration of dexmedetomidine resulted in a significant increase in the PaCO₂ and a reduction in the PaO₂ when changing from two-lung ventilation to OLV, where PaO₂ reached its maximum value within 10 minutes after OLV in the DISO group, and it began to gradually increase to the end of operation. The duration of the recovery phase, also complications at the recovery phase decreased significantly in DISO group.

Conclusions: The results of the study showed that, dexmedetomidine may improve arterial oxygenation during OLV in adult patients undergoing thoracic surgery, and can be a suitable anesthetic agent for thoracic surgery.

Keywords: Dexmedetomidine, Hypoxic Pulmonary Vasoconstriction, One-Lung Ventilation, Thoracic Surgery

1. Background

One-lung ventilation (OLV) refers to mechanical separation of the two lungs for independent ventilation of one lung from the other (1, 2) in order to provide a suitable operating space for the surgeon, and to protect the healthy lung against bleeding or edema caused by the damaged lung (3, 4). Nevertheless, OLV can lead to a mismatch in ventilation/perfusion (V/Q) ratio consequently leading to increased intrapulmonary shunt as well as hypoxemia (5, 6). Hypoxic pulmonary vasoconstriction (HPV) is the most important protective mechanism against hypoxemia, based on whether the blood flow shifts from the non-ventilated lung towards the ventilated areas maintaining proper arterial oxygenation (2). Hypoxic pulmonary vasoconstriction is influenced by different factors including changes

in pulmonary pressure, alkalosis, vasodilators, anesthetic agents, etc. (6-8). Among these factors, volatile anesthetic agents have the most significant effect on the HPV. Therefore, administration of drugs with no or minimum inhibitory effects on this vital mechanism is of great significance in the anesthesia management of patients undergoing OLV (9, 10). Dexmedetomidine is a selective agonist of α_2 receptors whose tendency to α_2 receptors is eight times more than that of clonidine. It also has powerful sedative, analgesic, anti-inflammatory, and organ protective properties (11, 12). Dexmedetomidine diminishes sympathetic tone, heart rate (HR), blood pressure, and myocardial oxygen consumption (13). Over the past few years, some studies have investigated the effect of dexmedetomidine on OLV whose results have been very diverse and controversial; and currently, there is not much information about

the effects of dexmedetomidine on HPV as well as the extent of oxygen saturation during OLV (3, 5).

2. Objectives

The present study was carried out to evaluate the effect of dexmedetomidine infusion on improving the oxygenation during OLV in adult patients undergoing thoracic surgery.

3. Methods

After acquiring the permission from the Ethics Committee and registration of the trials (IRCT201610174731N15), 42 cases with the American Society of Anesthesiologists' (ASA) physical status I, II, aged 20 - 60 who were undergoing elective thoracic surgery were included in the study from November 2016 to January 2018. The exclusion criteria involved liver or kidney dysfunction, end-stage chronic obstructive pulmonary disease (COPD), severe heart block, and uncontrolled hypertension. An informed written consent was taken from the patients. Enrolled patients were randomly assigned into two groups: IV infusion of dexmedetomidine plus isoflurane inhalation (DISO) and IV infusion of normal saline plus isoflurane inhalation (NISO). Both patients and anesthesiologists were blinded to the identity of the study drug (dexmedetomidine or placebo). The patients did not receive any pretreatment before entering to the operation room. All patients were hydrated with 200 mL of normal saline before induction of anesthesia and routine monitoring was performed on all patients including noninvasive blood pressure (NIBP), SPO₂, and ECG. As to postoperative pain relief, an epidural thoracic catheter was inserted before inducing intravenous anesthesia through midline approach using the loss of resistance technique. Until the end of operation, no drug was administered. Anesthetic induction included fentanyl 2 $\mu\text{g}\cdot\text{kg}^{-1}$, intravenous propofol (2 - 3 mg/kg) followed by atracurium 0.5 mg/kg to facilitate endotracheal intubation. After induction of anesthesia, 0.5 mL/kg bolus of the solution (0.3 $\mu\text{g}/\text{kg}$ of dexmedetomidine or placebo) was injected intravenously within 10 minutes. After completion of the bolus dose, constant infusion of dexmedetomidine or placebo 0.9 mL/kg/h (0.3 $\mu\text{g}/\text{kg}/\text{h}$) was initiated. Maintenance of anesthesia was performed using isoflurane titrated to achieve a BIS of 40 - 60 and remifentanyl (1 0.1 - 0.2 $\mu\text{g}/\text{kg}/\text{min}$) was titrated to maintain the hemodynamic stability. Lung isolation was performed using a double-lumen tube. Proper positioning of the tube was checked by the stethoscope and using fiber-optic bronchoscopy before and after positioning the patient into lateral position. Mechanical ventilation was applied in OLV

with a tidal volume (TV) of 8 mL/kg, respiration rate (RR) of 12 rpm, I:E = 1:2, FiO₂ 100%. The respiration rate was adjusted to maintain end-tidal CO₂ (EtCO₂) at around 35 - 40 mmHg. The OLV was initiated after the pleura was opened. SpO₂ less than 90% was considered hypoxia, and accordingly possible causes (hemodynamic imbalance, air leakage, and malpositioning etc.) were examined and care was taken care subsequently. In case of refractory hypoxia, PEEP of 10 cm H₂O was applied to the ventilating lung and if continued, the lung was ventilated periodically with positive pressure. Three arterial blood gas (ABG) samples were obtained at three intervals: T1:10 min after induction of anesthesia and before OLV; T2:10 min after starting the OLV; and T3:60 min after performing the OLV. Also in the end of the procedure patients were successfully extubated. The data obtained from the study were evaluated using descriptive statistical methods (mean \pm standard deviation, frequency, and percentage) plus paired samples *t*-test, repeated -measures ANOVA, and independent samples *t*-test. To ensure the normality of the data distribution, Kolmogorov-Smirnov test was utilized. The data were analyzed using SPSS software version 22. In this study, a P value of < 0.05 was considered as statistically significant.

4. Results

In this study, 42 adult patients requiring OLV for thoracic surgery were included. No patient was excluded from the research. The demographic characteristics of the patients are presented in Table 1. Patients did not have significant difference in terms of gender, physical status, ASA class, type of operation, and body weight. In investigating the hemodynamic parameters (Table 2) before and during OLV, no significant difference was observed in the systolic and diastolic blood pressure values as well as the mean arterial pressure or heart rate between the two study groups. However, at 30 minutes and 60 minutes post OLV, a significant decline was observed in the parameters of mean arterial blood pressure and heart rate in the DISO group ($P = 0.04$, $P = 0.00$, respectively). Nevertheless, SpO₂ and EtCO₂ did not show any significant difference between the groups. The results obtained in the ABG from three stages showed that, PaO₂ decreased insignificantly in both groups (Table 3). The OLV resulted in a significant decline in the PaO₂ when shifting from two-lung ventilation to OLV in both groups, where PaO₂ reached its minimum value within 10 min following OLV in DISO group. The reduction in the PaO₂ was greater in DISO group than the NISO group throughout OLV, and it was not statistically significant. Nevertheless, hypoxemia was recorded in both groups. Finally, PaCO₂ had a significant difference between the groups following OLV ($P = 0.00$) ($P = 0.02$). Fi-

nally, there was a significant difference in terms of the incidence of complications during the recovery between the two groups. Patients in the DISO group had the following symptoms: 45% pain, 5% nausea and pain, 5% high blood pressure and pain, yet the remaining 45% had no complications. Patients in the normal saline group suffered from 30% pain, 25% nausea and pain, 15% pain and shivering, 30% high blood pressure with pain. There was nobody who experienced any complication (Table 4).

Table 1. Patient Characteristics and Perioperative Data

	DISO Group (N = 21)	NISO Group (N = 21)	P Value
Age (years)	51 ± 12	46 ± 16	0.71
Gender (M/F)	16/5	16/5	1.00
Weight (kg)	65.2 ± 12	64.6 ± 15	0.892
BMI (kg/m ²)	32.1 ± 1	23 ± 1.6	0.51
ASA (I/II/III)	12/6/3	7/13/1	0.98
Operation time (min)	178.46 ± 55	150.83 ± 61	0.209

5. Discussion

Hypoxia during OLV is considered as an important concern throughout thoracic anesthesia. Hypoxic pulmonary vasoconstriction is a defense mechanism against hypoxia reducing the shunt (14, 15). In the present study, there was no significant difference in the demographic data of the patients and improvement was demonstrated in oxygenation during OLV in the DISO group. The results from the Bugeat et al. study indicated that demographic data and baseline characteristics were not statistically significant and also dexmedetomidine infusion improved oxygenation and lung mechanics in patients with restrictive lung disease (14). These findings are in line with our study. Xia et al. investigated the effect of intravenous injection of dexmedetomidine on arterial oxygenation and intrapulmonary shunt during the OLV, and found the changes in the ventilation/perfusion ratio in patients during the OLV. They also suggested that initiation of OLV is associated with a significant increase in the intrapulmonary shunt and reduction of the PaO₂ (5). These findings aren't in line with our study. Investigation of hemodynamic parameters of the patients in the present study showed that, the value of mean arterial pressure, and heart rate decreased significantly in DISO group at 30 minutes and 60 minutes. Several previous studies suggested that dexmedetomidine treatment is associated with a significant decline in the HR and MAP during surgery, confirming that dexmedetomidine can inhibit sympathetic drive and diminish the HR and

MAP. Tanskanen et al. found that infusion of dexmedetomidine (0.4 µg/kg/h) causes the stability of heart rate and blood pressure compared to the placebo (16). Nevertheless, Amano et al. reported that, dexmedetomidine administration might be associated with bradycardia, which may even lead to cardiac arrest (17).

The results obtained from three stages of ABG sampling revealed that, arterial oxygen saturation diminished in both groups; nevertheless, the difference was not significant. Accordingly, PaO₂ reached its minimum value at 10 min following OLV in DISO group. Thereafter, PaO₂ began to rise at 60 min following OLV, which could be due to the effect of HPV. Hickey (7) indicated that, HPV reaches its maximum effect in 15 min leading to diminished pulmonary shunt, normalization of the ventilation/perfusion ratio, and improved oxygenation (7). Therefore, in our study, the trivial effect of dexmedetomidine on the PaO₂ observed in the DISO group could be attributed to the inhibitory effect of isoflurane on the HPV (Table 2). Kernan et al. showed that dexmedetomidine did not cause any significant changes in the oxygenation during the OLV. They employed desflurane for maintenance of anesthesia. They supposed that, trivial improvement in the oxygenation with dexmedetomidine may be due to the minor effect of dexmedetomidine, which might have decreased the concentration of desflurane and its subsequent inhibitory effect on the HPV (18), which was in line with our study. Some studies have evaluated the effects of volatile agents (isoflurane, desflurane, and sevoflurane) and dexmedetomidine on the gas exchange states in animal or human models undergoing the OLV. Volatile anesthetic agents have been found to inhibit the HPV and enhance the intrapulmonary shunt; which are in accordance with our study (5, 15, 19, 20). The present study also suggested that PaCO₂ increased in DISO group and had a significant difference with that of NISO group (P = 0.00) (P = 0.02). It can be concluded that dexmedetomidine may cause more respiratory depression. On the other hand, it is believed that, since these changes in levels were within the normal range of variation in the ETCO₂ and PaCO₂ (30 - 45 mmHg), and although these differences are statistically significant, it is not clinically feasible to defend the respiratory depression performance of dexmedetomidine. Scott and Rui investigated the effect of dexmedetomidine on the arterial oxygenation and intrapulmonary shunt during one-lung ventilation, and indicated that the changes were in the normal range (30 - 45 mmHg) (5, 18). Also, there was a significant difference in terms of complications at recovery phase between the two groups (Table 4). At recovery phase, complications including pain, shivering, elevated blood pressure, and nausea occurred less frequently in the dexmedetomidine group. Patients in this group needed less recovery

Table 2. Comparison of Hemodynamics, SpO₂, EtCO₂ in Two Groups of DISO and NISO

Parameters	Before-OLV	OLV-10	P Value	OLV-30	P Value	OLV-60	P Value
HR (beats/min)							
DISO	89 ± 12	81 ± 15	0.108	82 ± 13 ^{a,b}	0.006	72 ± 10 ^b	0.016 ^a
NISO	91 ± 12	86 ± 15	0.329	87 ± 12	0.965	95 ± 13	0.099
P Value	0.069	0.330		0.021		0.006	-
MAP (mmHg), mean ± SD							
DISO	92 ± 13	88 ± 24	0.115	84 ± 10 ^{a,b}	0.031	73 ± 23 ^{a,b}	0.021
NISO	91 ± 15	96 ± 18	0.098	88 ± 10	0.671	89 ± 15	0.130
P Value	0.756	0.671		0.006		0.022	-
SpO₂ (mmHg), mean ± SD							
DISO	97.5 ± 0.2	96.5 ± 0.8	0.883	96 ± 0.8	0.220	98 ± 1	0.188
NISO	96.2 ± 2	97 ± 0.3	0.391	96 ± 1	0.805	97 ± 0.3	0.088
DISO	97.5 ± 0.2	96.5 ± 0.8	0.883	96 ± 0.8	0.220	98 ± 1	-
EtCO₂ (mmHg), mean ± SD							
DISO	-	36 ± 20	-	38 ± 9	-	38 ± 7	-
NISO	-	35 ± 30	-	37 ± 7	-	37 ± 8	-
P Value	-	0.220	-	0.132	-	0.291	-

^aP < 0.05 versus Before-OLV^bP < 0.05 versus NISO group**Table 3.** Arterial Blood Gas Analysis in Both Groups

Parameters	DISO Group, Mean ± SD	NISO Group, Mean ± SD	P Value
ABG #1			
PaO ₂	172.6 ± 111	176.6 ± 124	0.915
PaCO ₂	43.57 ± 9	39.74 ± 6	0.132
ABG #2			
PaO ₂	102.5 ± 56	149.9 ± 104	0.082
PaCO ₂	44.25 ± 7	37.17 ± 1	0.004 ^a
ABG #3			
PaO ₂	118.4 ± 52	122.6 ± 71	0.832
PaCO ₂	43.03 ± 6	38.11 ± 8	0.044 ^a

^aP < 0.05 DISO versus NISO group

time than the control group as well. Therefore, administration of dexmedetomidine as an alternative drug for the management of anesthesia might be suitable as no or very few considerable complications occur during the recovery of patients. Lee et al. reported that dexmedetomidine administration could improve the quality of recovery and decrease the pain, postoperative nausea and vomiting, opioid consumption, and hospital stay (21). Furthermore, Le Bot et al. in a systematic review suggested that generally, dexmedetomidine administration can be associated with

less requirement of anesthetic agents, better quality of recovery, and diminished analgesic requirement during the recovery; whereas, it has no effect on the duration of recovery stay (22).

5.1. Conclusions

The results of the current study revealed that, the administration of dexmedetomidine along with isoflurane during the OLV may lead to improved oxygenation. The improved oxygenation in patients receiving dexmedetomidine led to less requirement of volatile anesthetic (isoflurane) agent. Furthermore, dexmedetomidine administration can be associated with very few complications during the recovery phase and therefore, it can be considered as a suitable drug for patients undergoing thoracic surgery.

Footnotes

Authors' Contribution: Somayah Asri and Hamzeh Hosseinzadeh developed the original idea and the protocol, abstracted and analyzed data, wrote the manuscript, and is a guarantor. Mahmood Eydi, Marzieh Marahem, Abbasali Dehghani, and Hassan Soleimanpour contributed to the development of the protocol, abstracted data, and prepared the manuscript.

Clinical Trial Registration Code: IRCT201610174731N15.

Table 4. Complication During Recovery in Two Groups of DISO and NISO

Parameters	Groups		Total	P Value
	DISO	NISO		
Complication During Recovery				
Pain				
Count	9	6	15	< 0.001 ^a
% within	45.0%	30.0%	30.0%	
Pain and nausea				
Count	0	5	5	0.671
% within	0.0%	25.0%	12.5%	
Pain and shivering				
Count	1	3	4	0.130
% within	5.0%	15.0%	10.0%	
Pain and high BP				
Count	1	6	7	0.756
% within	5.0%	30.0%	17.5%	
No complication				
Count	9	0	9	0.098
% within	45.0%	0.0%	30.0%	
Total				
Count	20	20	40	
% within	100.0%	100.0%	100.0%	

^aP<0.05 DISO versus NISO group

Conflict of Interests: The authors declared no conflict of interest.

Ethical Approval: IR.TBZMED.REC.1395.506.

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Informed Consent: Informed written consent was taken from the patients.

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