Cardiovascular Topics

Sevoflurane- and propofol-based regimens show comparable effect on oxygenation in patients undergoing cardiac valve replacement with cardiopulmonary bypass

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Abstract

Background: Our study aimed to compare the effects of sevoflurane- and propofol-based anaesthetic regimens on oxygenation during the early period of cardiopulmonary bypass (CPB) in patients undergoing cardiac valve-replacement surgery.

Methods: Patients undergoing mechanical mitral, aortic or double valve replacement were enrolled and randomly divided into two groups: the sevoflurane-based anaesthetic regimen group consisted of patients who received 1–3% sevoflurane inhalation during anaesthesia maintenance and the propofol-based anaesthetic regimen group consisted of patients who received 6–10 mg/kg/h of propofol infusion during anaesthesia maintenance. The partial pressure of oxygen/fraction of inspired oxygen (PaO_2/FiO_2), respiratory mechanics and haemodynamics were recorded during CPB.

Results: Forty-two patients met the eligibility criteria for the study. The groups did not differ in terms of clinical and demographic characteristics, and pre- and intra-operative features. Changes in oxygenation were mild (mean PaO_2/FiO_2 from 358 ± 82 to 471 ± 106 mmHg) within one hour of CPB in our patients. There were no differences in PaO_2/FiO_2, respiratory mechanics and haemodynamics between the sevoflurane and propofol groups.

Conclusion: In patients undergoing cardiac valve replacement with CPB, lung injury was mild, and sevoflurane- and propofol-based anaesthetic regimens showed similar effect on oxygenation, respiratory mechanics and haemodynamics during the early stage of CPB.

Keywords: oxygenation, sevoflurane, propofol, cardiac valve replacement, cardiopulmonary bypass

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During cardiopulmonary bypass (CPB), the lung is subjected to ischaemia/reperfusion injury and systemic inflammatory response syndrome.[1] Pulmonary complications with variable severity are common after cardiac surgery with CPB. However, with improvement in membrane oxygenation and the development of extracorporeal circulation, the incidence of lung injury has declined.[2]

Fast-track cardiac care has been advocated in recent years, including a complex intervention of several components of care during cardiac anaesthesia and in the postoperative period. It has been demonstrated that fast-track anaesthetic techniques for cardiac surgery contribute to a shorter intensive care unit (ICU) stay.[3]

Experimental evidence has documented that propofol, a widely used intravenous drug for fast-track anaesthetic regimens, can improve lung function in endotoxin-induced lung injury.[4] Volatile anaesthetics are frequently employed in cardiothoracic surgery, however, the effects of inhalational anaesthetic agents on pulmonary oxygenation remain controversial.

Recent studies have demonstrated that sevoflurane or isoflurane could impair oxygenation in oleic acid-induced lung injury in dogs.[5,6] However, in endotoxin-induced lung injury in rats, sevoflurane improved oxygenation compared to propofol.[7] Furthermore, in thoracic aortic occlusion-induced lung injury in pigs, sevoflurane and propofol showed a similar effect on oxygenation.[8] These results indicate that the effects of sevoflurane on oxygenation vary with different lung injury models.

The purpose of this study was to evaluate the severity of the insult on lung oxygenation and the effects of sevoflurane- and propofol-based anaesthetic regimens on oxygenation during the early stage of CPB in patients undergoing cardiac valve replacement surgery. We hypothesised that lung injury would not be severe and a sevoflurane-based anaesthetic regimen could not impair oxygenation compared to a propofol-based regimen during the early period of CPB.

Methods

This prospective, randomised study was approved by the local institutional ethics committee. Written informed consent was obtained from every patient. The study was conducted according to the Declaration of Helsinki.

Patients undergoing mechanical mitral, aortic or double valve replacement (ASA III) were screened for eligibility. Exclusion criteria included patients with relevant pulmonary disorders such

as pulmonary oedema, pneumonia, bronchial asthma, acute respiratory distress syndrome (ARDS), those with pre-operative pulmonary therapy or pre-operative detected pathological lung-function tests [vital capacity (VC), forced expiratory volume in one second (FEV_1) and blood gas analysis], and those with an ejection fraction of less than 30%, significant hepatic disease (alanine aminotransferase or aspartate aminotransferase > 150 IU/l), renal failure (creatinine > 200 µmol/l), or history of seizure, and stroke.

Patients were randomly divided into two groups using sealed, opaque assignment envelopes as follows: the sevoflurane group, a sevoflurane-based anaesthetic regimen, and the propofol group, a propofol-based anaesthetic regimen. In both groups, anaesthesia was induced with midazolam (0.05 mg/kg) and sufentanil (1 µg/kg). Anaesthesia was maintained with sufentanil (1 µg/kg/h) combined with a continuous intravenous infusion of propofol (6–10 mg/kg/h) in the propofol group, or with 1–3% sevoflurane in the sevoflurane group, based on bispectral index monitoring (maintained at 40–60).

Tracheal intubation was facilitated by administration of 0.15 mg/kg cisatracurium besylate. After endotracheal intubation, patients were mechanically ventilated on a volume-controlled mode with fraction of inspired oxygen (FiO_2) of 0.5, inspiratory:expiratory ratio (I:E) of 1:2, extrinsic positive end-expiratory pressure ($PEEP_e$) of 0 cm H_2O, frequency of 10–12 breaths/min and tidal volume (TV) of 8 ml/kg. To keep arterial blood gases within the physiological range, the respiratory rate (RR) was adjusted with the guidance of end-tidal CO_2 monitoring and intermittent arterial blood gas analyses.

Standard CPB was established with aortic and both vena caval cannulations. The priming solution contained Ringer's lactate solution, 6% HAES–steril (130/0.4), sodium bicarbonate, mannitol and heparin with a target of 24–25% haematocrit.[9] During CPB, systemic hypothermia of 28–30°C and a pump flow of 2.4–2.5 l/min/m^2 were applied. Patients were transferred to ICU after surgery.

Haemodynamics and respiratory mechanics were recorded at baseline, before CPB, at 15 min after declamping, and at five, 30 and 60 min after cessation of CPB. The partial pressure of oxygen/fraction of inspired oxygen (PaO_2/FiO_2) was calculated and recorded at baseline, 15 min after declamping, and at five, 30 and 60 min after cessation of CPB.

Statistical analysis

Results are expressed as mean ± SD. Data of haemodynamics, respiratory mechanics and PaO_2/FiO_2 were analysed using repeated-measures ANOVA. Differences in clinical characteristics and parameters at each time point between the groups were analysed by the independent samples *t*-test for continuous variables or chi-squared test for categorical variables. Statistical analysis was performed with the SPSS software package (version 18; SPSS Inc, Chicago, IL). Significance was assumed at $p < 0.05$.

Table 1. Demographic, pre- and intra-operative data of the patients

Variables	*S group* (n = *21*)	*P group* (n = *21*)	p-*value*
Age (years)	44.6 ± 9.2	45.0 ± 10.4	0.909
Gender (M/F)	15/6	14/7	0.739
Weight (kg)	54.5 ± 6.4	54.9 ± 9.1	0.859
NYHA classification (*n*)			
Class II	5	4	0.707
Class III	16	17	
CPB time (min)	106 ± 28	97 ± 33	0.433
Time of cross-clamping (min)	63 ± 21	58 ± 26	0.340

Data are presented as mean ± standard deviation or number as appropriate. S: sevoflurane; P: propfol; NYHA: New York Heart Association; CPB: cardio-pulmonary bypass.

Table 2. Haemodynamic variables of the study groups

Variables	*Baseline*	*Pre-CPB*	*15 min after declamping*	*5 min post-CPB*	*30 min post-CPB*	*60 min post-CPB*
HR, beats/min						
Sevoflurane	73 ± 24	88 ± 20	93 ± 20	94 ± 19	92 ± 17	87 ± 15
Propofol	73 ± 19	93 ± 17	98 ± 16	101 ± 7	86 ± 13	85 ± 15
MAP, mmHg						
Sevoflurane	71 ± 12	62 ± 9	56 ± 5	63 ± 5	66 ± 8	68 ± 8
Propofol	75 ± 9	58 ± 10	60 ± 8	64 ± 10	69 ± 6	74 ± 6
CVP, mmHg						
Sevoflurane	6.4 ± 6.1	6.6 ± 4.3	5.2 ± 5.0	10.2 ± 3.1	10.1 ± 2.9	9.4 ± 2.2
Propofol	5.0 ± 3.9	6.2 ± 3.2	6.2 ± 3.9	8.7 ± 4.0	9.5 ± 4.0	10.6 ± 3.6

Data are presented as mean ± standard deviation. HR: heart rate; MAP: mean arterial pressure; CVP: central venous pressure; CPB: cardiopulmonary bypass.

Results

Patient clinical and demographic characteristics, and pre- and intra-operative features are listed in Table 1. Forty-two patients were enrolled in the study, with 21 in each group. The sevoflurane group included 15 males and six females weighing 54.5 ± 1.4 kg, with a mean age of 44.6 ± 2.0 years, and the propofol group comprised 14 males and seven females weighing 54.9 ± 2.4 kg, with a mean age of 45.0 ± 2.7 years ($p = 0.739$, 0.859 and 0.909, respectively, by chi-squared test and independent samples *t*-test). With regard to NYHA classification, there were five class II patients in the sevoflurane group and four in the propofol group, and 16 class III patients in the sevoflurane group and 17 in the propofol group ($p = 0.707$ by chi-squared test). The intra-operative characteristics such as CPB time and time of cross-clamping were not different between the two groups ($p = 0.433$ and 0.340, respectively, by independent samples *t*-test).

Changes in haemodynamic variables are shown in Table 2. There were no differences in heart rate (73 ± 24 vs 73 ± 19 beats/min, $p = 0.962$ by independent samples *t*-test), mean arterial pressure (71 ± 12 vs 75 ± 9 mmHg, $p = 0.258$ by independent samples *t*-test) and central venous pressure (CVP) (6.4 ± 6.1

Table 3. Mechanical variables of the study groups

Variables	*Baseline*	*Pre-CPB*	*15 min after declamping*	*5 min post-CPB*	*30 min post-CPB*	*60 min post-CPB*
PIP, cm H_2O						
Sevoflurane	16.6 ± 3.3	16.9 ± 3.0	18.9 ± 4.2	17.0 ± 3.8	16.0 ± 2.9	17.0 ± 2.7
Propofol	16.3 ± 2.7	16.6 ± 2.1	16.8 ± 2.2	16.0 ± 2.6	15.5 ± 2.1	16.5 ± 1.9
mPaw, cm H_2O						
Sevoflurane	6.2 ± 1.3	6.2 ± 1.0	6.5 ± 0.8	6.4 ± 1.2	5.7 ± 1.7	6.4 ± 1.6
Propofol	5.8 ± 0.7	5.8 ± 0.5	6.3 ± 0.7	5.9 ± 0.8	5.6 ± 0.5	5.8 ± 0.7
iPEEP, cm H_2O						
Sevoflurane	2.7 ± 0.9	2.6 ± 1.0	2.9 ± 0.9	3.0 ± 0.9	3.0 ± 0.9	3.1 ± 1.0
Propofol	2.5 ± 0.5	2.6 ± 0.5	2.8 ± 0.5	2.5 ± 0.5	2.5 ± 0.5	2.6 ± 0.5
DLC, ml/cm H_2O						
Sevoflurane	39.6 ± 6.6	39.1 ± 4.9	33.6 ± 7.4	40.3 ± 6.0	41.4 ± 4.7	37.7 ± 6.3
Propofol	41.0 ± 7.9	41.7 ± 6.3	41.6 ± 5.4	41.4 ± 5.8	41.2 ± 7.3	38.3 ± 6.9

Data are presented as mean ± standard deviation. TV: tidal volume; PIP: peak inspiratory pressure; mPaw: mean airway pressure; iPEEP: intrinsic positive end-expiratory pressure; DLC: dynamic lung compliance.

vs 5.0 ± 3.9 mmHg, p = 0.485 by independent samples t-test) between the sevoflurane and propofol groups at baseline. These haemodynamic variables were similar in both groups before CPB, at 15 min after declamping, and five, 30 and 60 min post-CPB (p = 0.787, 0.179, and 0.720, respectively, by repeated-measures ANOVA).

Changes in respiratory mechanics are shown in Table 3. At baseline, peak inspiratory pressure (PIP), mean airway pressure (mPaw), intrinsic positive end-expiratory pressure (iPEEP) and dynamic lung complicance (DLC) were not different between the sevoflurane and propofol groups (p = 0.795, 0.445, 0.608 and 0.486, respectively, by independent samples t-test). These mechanical variables were similar in each group before CPB, at 15 min after declamping, and five, 30 and 60 min post-CPB (p = 0.625, 0.561, 0.326 and 0.342, respectively, by repeated measures ANOVA).

As shown in Fig. 1, PaO_2/FiO_2 was not different between the sevoflurane and propofol groups at baseline (423 ± 90 vs 459 ± 57 mmHg, p = 0.242 by independent samples t-test). There was also no difference in PaO_2/FiO_2 between the groups at 15 min after declamping (411 ± 125 vs 471 ± 106 mmHg), and five (454 ± 52 vs 454 ± 32 mmHg), 30 (440 ± 76 vs 457 ± 31 mmHg) and 60 min (358 ± 82 vs 360 ± 97 mmHg) post-CPB (p = 0.477 by repeated-measures ANOVA).

Discussion

Our study showed that there were no differences in PaO_2/FiO_2, respiratory mechanics and haemodynamics during CPB in patients undergoing cardiac valve replacement when a sevoflurane- or propofol-based anaesthetic regimen was applied. This is the first investigation to evaluate the difference in oxygenation between an inhaled and intravenous anaesthetic regimen in cardiac surgery with CPB.

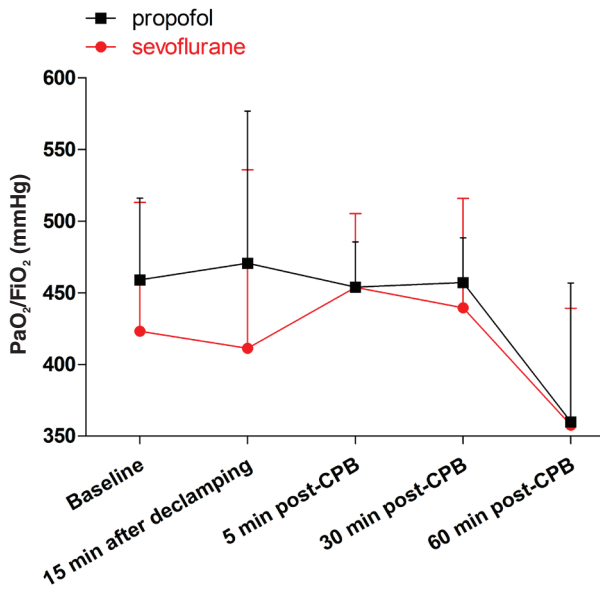

Fig. 1. Changes in PaO_2/FiO_2 at baseline, 15 min after declamping, and five, 30 and 60 min post-CPB. Red indicates the sevoflurane group, black indicates the propofol group (p = 0.477 by repeated-measures ANOVA).

The results of this study showed that the oxygenation index of PaO_2/FiO_2 was not significantly decreased (> 400 mmHg at 15 min after declamping, and at five and 30 min post-CPB, and ~ 360 mmHg at 60 min post-CPB) compared with the respective baselines in the sevoflurane- and propofol-based groups, indicating that lung injury was mild during the early period of CPB in our patients undergoing cardiac valve replacement surgery.

Volatile anaesthetics are frequently employed in cardiothoracic surgery. Early clinical investigations showed during one-lung ventilation (OLV) there was no difference in oxygenation when sevoflurane or propofol was administered in patients undergoing open thoracic surgery.[10,11] This is consistent with our results of a similar effect on oxygenation by sevoflurane- and propofol-based anaesthesia in cardiac valve replacement surgery. However, in another OLV by Cho,[12] desflurane impaired arterial oxygenation compared with propofol anaesthesia in patients with thoracoscopic surgery. The discrepancy regarding the effects on oxygenation by volatile anaesthetics and propofol during OLV in thoracic surgical patients may be ascribed to different volatile anaesthetics (sevoflurane vs desflurane) and thoracic surgical manner (with or without chest opened).

In animal studies, controversy exists regarding the effects of inhalational anaesthetic agents on oxygenation when compared to intravenous anaesthetic propofol. Voigtsberger,[7] Schläpfer[13] and Kellner[14] demonstrated that sevoflurane administration led to a better oxygenation compared to propofol administration in a rat model of lipopolysaccharide (LPS)-induced mild acute lung injury (ALI) (mean PaO_2/FiO_2 ~ 400–500 mmHg after two or three hours of LPS insult). However, in a recent study, the authors found there was no difference in oxygenation between isoflurane- and propofol-based anaesthetic regimens in a dog model of OLV,[15] which is consistent with the finding by Karci *et al.*[16] that sevoflurane and propofol showed comparable effects on PaO_2 in a rat model of OLV.

In our oleic acid-induced canine severe ALI model (mean PaO_2/FiO_2 < 200 mmHg), although the oxygenation was worse in sevoflurane-sedated dogs compared with propofol-sedated dogs during a six-hour mechanical ventilation,[5] possibly via sevoflurane-induced pulmonary vasodilation and its inhibition of hypoxic pulmonary vasoconstriction (HPV),[17] no difference was found in oxygenation between seveflurane and propofol at five and six hours following mechanical ventilation.[5] Different models and subjects may account for literature discrepancies in terms of the effects of sevoflurane compared to propofol on oxygenation in animal experiments.

Our study has limitations. A one-hour observation period after CPB with sevoflurane- or propofol-based cardiac anaesthesia may be too short. Our results reflect only the early time effect on oxygenation by both anaesthetic regimens during CPB. The long-term effect of sevoflurane- or propofol-based anaesthesia on gas exchange deserves further investigation in patients undergoing cardiac surgery with CPB.

Conclusion

In patients undergoing cardiac valve replacement with CPB, the changes in PaO_2/FiO_2 and lung injury were mild, and sevoflurane-

or propofol-based anaesthesia showed a similar effect on oxygenation, respiratory mechanics and haemodynamics during the early stage of CPB. Both sevoflurane- and propofol-based regimens can be used in cardiac anaesthesia.

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