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SCIENTIFIC ARTICLE

Comparison of the effect of sevoflurane and propofol on oxygenation during gradual transition to one-lung ventilation

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Abstract

Background: It is known that hypoxic pulmonary vasoconstriction increases as a result of intermittent regional hypoxic challenges. The aim of this study was to compare the effects of sevoflurane and propofol on oxygenation and shunt fraction during one-lung ventilation in a novel model of hypoxic preconditioning before one-lung ventilation.

Methods: Sixteen Wistar-albino rats were anesthetized intra-peritoneally before venous and arterial cannulations and tracheotomized. The animals were randomly allocated to receive either sevoflurane 2% or 10 mg/kg/h propofol infusion and ventilated with 100% oxygen at an inspiratory rate of 80 breaths/min for 30 min. Three cycles of one-lung ventilation and two-lung ventilation were performed and one-lung ventilation was continued for 15 min. Arterial blood gas samples were obtained as follows: after cannulation and tracheotomy, following 30 min of treatment with sevoflurane or propofol, and at the 5th and 15th min of one-lung ventilation.

Results: The PaO₂ levels were higher and shunt fractions were lower in rats receiving propofol compared to rats treated with sevoflurane but the difference was not significant; the two groups were comparable in terms of PaCO₂.

Conclusions: The similar effects of sevoflurane and propofol on PaO₂ during one-lung ventilation following hypoxic preconditioning may be due to other causes beside the inhibition of hypoxic pulmonary vasoconstriction. Gradual transition to one-lung ventilation is a novel technique for preconditioning experiments for one-lung ventilation.

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Introduction

During one-lung ventilation (OLV), the operated lung not only remains atelectatic, but also hypoperfused because of

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hypoxic pulmonary vasoconstriction (HPV), which is a protective mechanism that diverts pulmonary blood flow away from the lung regions with low alveolar oxygen tensions to better ventilated areas of the lung, and reduces the intrapulmonary shunt and systemic hypoxia.¹⁻³ In order to maximize HPV in the non-ventilated lung, repeated intermittent cycles of deflation-inflation to the lung (hypoxic preconditioning (HP)) are recommended during the initiation of one lung ventilation.⁴⁻⁶

the cannula was pulled back for two-lung ventilation (TLV). The animals were ventilated with an inspired oxygen fraction (FIO₂) of 100%, and a respiratory rate of 80 breaths/min during this period. The rats were subjected to OLV following three cycles of 1-min OLV and 1-min TLV. This procedure was performed in all the animals before the investigations commenced. Arterial blood gases were collected at the 5th and 15th minutes of OLV and the shunt fraction was calculated.

The shunt fraction was calculated using the formula:

$$\frac{Q_s}{Q_t} \text{ (shunt fraction)} = (5.8 \times \text{RI}) + 6.7, \text{ where RI was the respiratory index.}$$

$$\text{(a) RI} = \frac{\text{PAO}_2 - \text{PaO}_2}{\text{PaO}_2}$$

$$\text{(b) PAO}_2 = ([\text{PB} - \text{PH}_2\text{O}] \times \text{FIO}_2) - \text{PaCO}_2$$

Although it is generally accepted that volatile anesthetics inhibit HPV and may promote hypoxemia in a dose-dependent manner during OLV,^{2,7,8} IV anesthetics including propofol, inhibit HPV to a small degree.^{8,9}

The overall objective of the present study was to determine the efficacy of HP using a new model of 'gradual transition' to OLV as defined in a previous study,⁷ before the initiation of OLV and to compare the effects of sevoflurane and propofol during the procedure.

Materials and methods

The animals were handled in accordance with the principles of laboratory animal care and all the experimental procedures were approved by the Research Commission for the Care and Use of Laboratory Animals of School of Medicine, Dokuz Eylul University.

Sixteen Wistar-albino rats (weighing 312–382 g) were anesthetized by intraperitoneal injection of ketamine (40 mg/kg) and xylazine (5 mg/kg) prior to venous and arterial cannulations.

The femoral vein was then cannulated with a polyethylene tube for infusion of the agents; the same cannula was also used to infuse saline continuously at a rate of 3 mL kg⁻¹ h⁻¹. The femoral artery on the other side was similarly cannulated to measure the blood pressure and monitor the arterial blood gases. Following tracheotomy, a 16-gauge cannula was inserted into the trachea and connected immediately to the mechanical ventilator (*Kent Scientific Pressure-controlled Ventilator*) and the animals were allowed to ventilate in a pressure-controlled mode with an inspired oxygen fraction (FIO₂) of 100%, and a respiratory rate of 60 breaths/min. To eliminate artifacts from spontaneous breathing movements, paralysis was induced with 0.1 mg/kg rocuronium bromide.

Following a 15-min stabilization period, blood was withdrawn for measurement of arterial blood gasses. The animals were randomly allocated to receive either 2% sevoflurane through a calibrated vaporizer (Group S; n = 8) or 10 mg/kg/h propofol infusion (Group P; n = 8) for 30 min after the stabilization period. At the end of 30 min, the tracheal cannula was pushed forward and it was confirmed that the tip was in the bronchus, the lung was ventilated for 1 min and that

PB = barometric pressure (760 mmHg at sea level); PH₂O = partial pressure of water (47 mmHg); PAO₂ = alveolar partial pressure of oxygen, PaO₂ = arterial partial pressure of oxygen, PaCO₂ = arterial partial pressure of carbon dioxide, FIO₂ = inspiratory oxygen fraction.

We used the method suggested by Koessler et al. and Peyton et al.^{10,11} The calculation was done with the formula where RI (Respiratory Index) = $\{[(\text{PB} - \text{PH}_2\text{O}) \times \text{FIO}_2] - \text{PaCO}_2 - \text{PaO}_2\} / \text{PaO}_2$.

Statistical analyses

All the results were expressed as means ± standard deviation. The scattered parameters were expressed by the SE values. The SPSS 11.0 for Windows was used for the statistical analyses. The Kolmogorov–Smirnov test was used to evaluate the intergroup differences.

The statistical tests were carried out with the significance level set at $p < 0.05$.

Results

The intermittent cycles of deflation-inflation before OLV were studied in 16 rats allocated randomly to treatment with sevoflurane inhalation or propofol infusion.

There were no significant differences in the blood gas analysis and shunt fraction among the protocol groups, either at the end of stabilization period, or after treatment with sevoflurane or propofol.

Following 30 min of anesthesia, marked decreases in arterial oxygen tensions (mean ± SE) were observed in the propofol and sevoflurane groups 5 min after the onset of OLV (101.48 ± 12.37 and 77.08 ± 6.17, respectively). The decrease was 29% and 38% in the propofol and the sevoflurane groups, respectively, and this decrease was not significant between the groups ($p = 0.074$). After 15 min, the decrease in oxygenation was more pronounced (mean 71.65 ± 5.39 [57.90–103.10] and 66.01 ± 4.19 [56.50–100.08]). Consistently, the PaO₂ values were higher in the propofol group for the duration of OLV (Fig. 1).

Similarly, arterial carbon dioxide levels showed an increase with initiation of OLV in rats treated with propofol and those treated with sevoflurane at 5 min (35.44 ± 2.9;

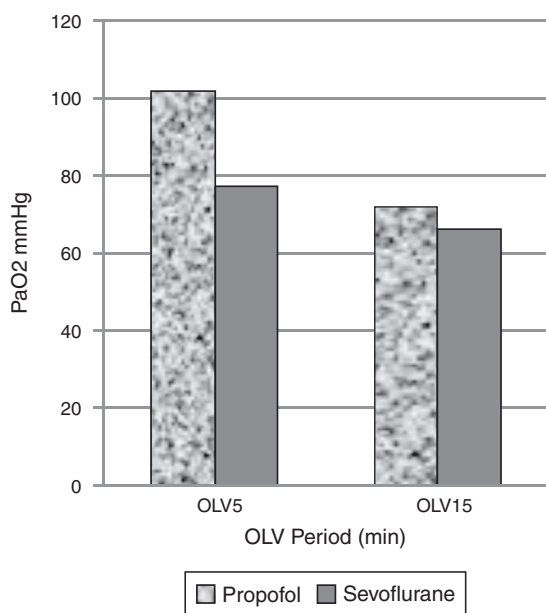


Figure 1 Time-related changes in arterial partial pressure of oxygen during one-lung ventilation.

41.62 ± 2.05, respectively), and 15 min (38.27 ± 2.36; 47.54 ± 2.54, respectively). Consequently, the pH values decreased and the difference between the groups was significant at 5 min (7.41 ± 0.3 and 7.34 ± 0.02; $p=0.022$, respectively) (Fig. 2). The difference was not apparent at the end of 15 min (7.38 ± 0.2 and 7.31 ± 0.02; $p=0.052$).

After gradual transition to OLV, the Q_s/Q_t did not show a significant difference, depending on the anesthetic agent. The pulmonary shunt fraction (Q_s/Q_t) increased from 28.53 ± 1.91 to 42.67 ± 3.87 in the rats treated with propofol; the increase was from 40.61 ± 7.25 to 53.72 ± 4.20 in the sevoflurane group in 5 min of OLV. The Q_s/Q_t change from 5 to

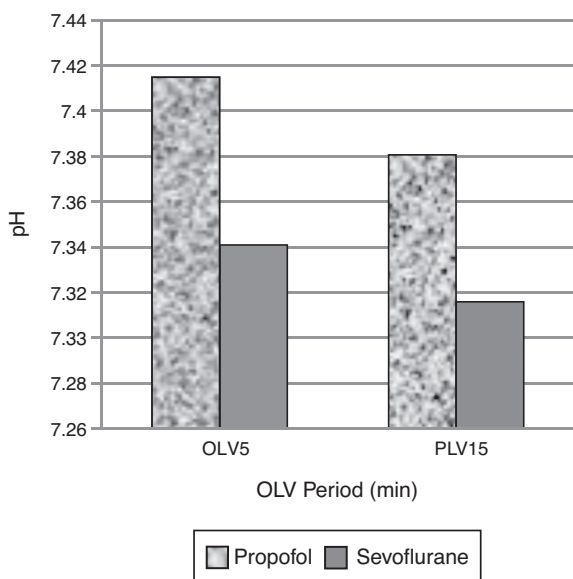


Figure 2 Time related changes in arterial partial pressure of arterial pH during one-lung ventilation. * $p < 0.05$ propofol anesthesia compared to sevoflurane anesthesia.

15 min of OLV (57.31 ± 3.53 and 61.18 ± 4.20 in the propofol and the sevoflurane groups, respectively) was not significant between the two anesthetic regimens.

Discussion

The present study has shown that sevoflurane and propofol at the doses used, had similar effects on arterial oxygenation and shunt fraction during OLV in the rat model of HP.

In previous animal studies, it was concluded that intermittent hypoxia increases the HPV and that the results have important implications for the conduct of HPV experiments and interpretation of blood-gas changes during OLV.⁴⁻⁶ Similarly, Singh et al.¹² demonstrated for the first time that preconditioning with a low dose of cobalt was advantageous in protecting the lung and the brain by attenuating hypobaric hypoxia-induced oxidative injury. In an attempt to increase the tolerance to hypoxemia that would develop during OLV, we examined the effect of an unique model for preconditioning, namely 'gradual transition' to OLV.

HP is defined as a rapid and reversible pro-adaptive response to mild hypoxic exposure that protects the cells from subsequent hypoxic or ischemic insult, and it is reported to occur in two temporally distinct phases, the early and the late phases. Hypoxic protection by early preconditioning occurs within minutes, peaks in about an hour, and lasts for about 4 h.¹³ Therefore, for the first time, we used three consecutive 1-min OLV and TLV cycles before a longer period of OLV in order to allow the tissues to adapt to the forthcoming hypoxemia. In an animal model of HP, Shukla et al.¹⁴ demonstrated that acute exposure to hypobaric hypoxia led to an increase in the lung water content, total protein and albumin leakage in lavage fluids. However, when the animals were exposed to hypoxia after HP, a significant decrease in the lung water content as well as the serum total protein and albumin leakage was observed. The previous adaptation induced by HP resulted in increased tolerance to lethal hypoxia.

The effect of sevoflurane and propofol with regard to oxygenation and shunt fraction during OLV following preconditioning was also investigated. Despite numerous reports^{15,16} about the decrease of oxygenation and the increase of shunt fraction due to inhibition of HPV with inhalational anesthetics agents, some¹⁷⁻¹⁹ have indicated the opposite. Glasser et al.² concluded that attenuation of HPV is not a general characteristic of all inhalational anesthetics. Furthermore, in their clinical investigation, Abe et al.⁹ demonstrated that propofol improved the oxygenation and shunt fraction during OLV compared to volatile anesthetics. According to our results in rats receiving propofol or sevoflurane, the decrease in arterial oxygenation was parallel to the increase in shunt fraction among transition to OLV, but the groups did not differ in this respect. Although the PaO₂ values (Fig. 1) were higher and the shunt fractions were lower in the propofol group compared to the rats treated with sevoflurane, the difference between the groups never reached a significant level. OLV caused an increase in PaCO₂, which was accompanied by an adequate decrease in pH, significant only at 5 min. We believe that the choice of anesthesia did not affect the observed increase in carbon dioxide levels and the decrease of pH.

We propose two reasons for the results of our study. First, as De Conno et al.²⁰ recently described, the volatile anesthetic sevoflurane has an immunomodulatory role in patients undergoing OLV with a significant decrease in inflammatory mediators. Their analysis has shown an almost exponential increase in inflammatory mediators in correlation with the OLV time in the propofol group. Interestingly, a significant correlation was observed between CRP and the OLV time in the propofol group, this was clearly attenuated in the sevoflurane group. Secondly, since hypoxic protection by early preconditioning occurs within minutes,¹³ we used 1-min cycles of deflation and inflation. However, recently, Duan et al.²¹ used a protocol in which the rats inhaled hypoxic air mixture for 5 min followed by 10 min of air inhalation. The methodological differences between the two studies may explain the discrepancy between the results.

The onset of OLV is characterized by development of a significant intrapulmonary shunt through the collapsed lung with the potential for intraoperative hypoxemia. Absence of a further decrease in oxygenation or increase in shunt fraction from 5 to 15 min of OLV may indicate that the maximum HPV was reached in 5 min. These findings are consistent with observations made by Chen et al.⁴ who reported that the maximum HPV was reached at the initiation of hypoxia and no further increase was observed with repeated hypoxia episodes. Conversely, Marshall and Marshall¹⁵ showed that in the presence of methylene blue, there is a hypoxic pulmonary vasoconstrictor response, which is potentiated with time. Pirlo et al.⁵ found that repeated (2–4 times) intermittent hypoxic challenges to a lobe of the lung potentiated and finally maximized the lobar HPV. Thus, putting aside the question of the time-alone factor, intermittent hypoxia has been reported to increase HPV in a quantitative manner.

Abe et al.⁹ concluded that propofol improved oxygenation during single-lung ventilation (OLV) compared to volatile anesthetics. There is a possibility, however, that oxygenation during OLV may improve with time. Accordingly, Ishikawa et al.²² showed that after starting OLV, mean PaO₂ rapidly decreased and gradually increased thereafter.

The ventilation technique is important if we are to decrease the incidence of hypoxemia during OLV. Thus, a careful ventilatory strategy was adopted in this study in order to avoid additional stress factors to the inflammatory response triggered by OLV. It has been reported that pressure-controlled ventilation in rats offers a decelerating flow pattern, which results in a more homogenous distribution of tidal volume, recruits the poorly ventilated lung regions and improves oxygenation.^{3,23} Moreover, lung trauma is attenuated when the peak and plateau transalveolar airway pressures are controlled.^{3,24}

In summary, sevoflurane administered at a concentration of 2% resulted in comparable changes in the shunt fraction as did propofol in rats during the 'gradual transition' to OLV. Similarly, PaO₂, and PaCO₂ levels did not differ between the groups. Changes in the shunt fraction during OLV may probably result from sources other than the attenuation of the HPV response. Hemodynamic changes, pulmonary perfusion and in particular, appropriate ventilatory strategies that prevent alveolar collapse may be more important for obtaining optimal arterial oxygenation during OLV than either the anesthetic agent of choice or the preconditioning maneuvers. 'Gradual transition' to OLV in rats is a unique model

for HP and our results indicate that longer periods of OLV may be required.

Conflicts of interest

The authors declare no conflicts of interest.

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