The Effects of Sevoflurane and Propofol on Oxygenation and Lung Perfusion During One-Lung Ventilation in an Animal Model

Wpływ znieczulenia z udziałem sewofluranu lub propofolu na utlenowanie krwi i perfuzję płucną podczas wentylacji jednego płuca – doświadczenia z użyciem modelu zwierzęcego

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Abstract

**Background.** Thoracic surgery often requires one-lung ventilation. During one-lung ventilation, arterial oxygenation depends on the distribution of lung perfusion between the ventilated and the non-ventilated lung.

**Objectives.** This study investigates the effects of sevoflurane and propofol on pulmonary perfusion and arterial oxygenation during one-lung ventilation in living animals at comparable mean arterial pressures.

**Material and Methods.** A prospective study with a crossover design involving 12 pigs was carried out at the Institute for Experimental Animals, University of Jena, Germany. After the induction of anesthesia, a left-sided double-lumen tube was inserted via tracheotomy. One-lung ventilation was started with 1.0 FiO2, and anesthesia was continued with either propofol or sevoflurane (2.6% end-tidal concentration). After stabilization, the hemodynamic parameters and oxygenation were recorded, and differential lung perfusion was measured with colored microspheres. Then the anesthetic was changed and, after another stabilization period, the measurements were repeated.

**Results.** The arterial oxygenation, mixed venous pO2, non-ventilated lung perfusion and shunt fraction were comparable during one-lung ventilation with both agents, whereas cardiac output was reduced during sevoflurane anesthesia (p < 0.05).

**Conclusions.** In a clinically relevant animal model of one-lung ventilation, sevoflurane, as compared with propofol, did not increase the non-ventilated lung perfusion and shunt fraction and did not worsen arterial oxygenation (Adv Clin Exp Med 2011, 20, 3, 249–253).

**Key words:** thoracic surgery, one-lung ventilation, propofol, sevoflurane, lung perfusion.

Streszczenie

**Wprowadzenie.** Chirurgia klatki piersiowej wymaga często wentylacji jednego płuca. Podczas wentylacji jednego płuca utlenienie krwi tętniczej jest zależne od ukrwienia płuca wentylowanego i niewentylowanego.

**Cel pracy.** Określenie wpływu sewofluranu lub propofolu na perfuzję płucną i utlenowanie krwi tętniczej podczas wentylacji jednego płuca w zwierzętach w celu oceny wpływów na perfuzję płucną, ukrwienie oraz utlenienie krwi tętniczej.

**Materiał i metody.** W badaniu poszczególnych grup zwierząt w wybranych warunkach technicznych użycie wentylacji jednego płuca, w której jedno płuco wentylowano, a drugie nie wentylowano, a następnie analiza postępujących zmian w parametrach ukrwienia i utlenienia krwi tętniczej.

**Wyniki.** W badaniu poszczególnych grup zwierząt w wybranych warunkach technicznych analizowano wpływ wentylacji jednego płuca, w której jedno płuco wentylowano, a drugie nie wentylowano, a następnie analiza postępujących zmian w parametrach ukrwienia i utlenienia krwi tętniczej.

**Konkluzje.** W badaniu poszczególnych grup zwierząt w wybranych warunkach technicznych analizowano wpływ wentylacji jednego płuca, w której jedno płuco wentylowano, a drugie nie wentylowano, a następnie analiza postępujących zmian w parametrach ukrwienia i utlenienia krwi tętniczej.
Oxygenation during one-lung ventilation (OLV) depends on the distribution of lung perfusion between the ventilated and the non-ventilated lung. Lung perfusion is regulated by hypoxic pulmonary vasoconstriction (HPV), which diverts blood flow from non-ventilated areas to ventilated areas. Whereas in vitro intravenous anesthetics do not depress HPV, all clinically used volatile anesthetics impair HPV [1–4]. In vivo the effects of volatile or intravenous anesthetics on oxygenation during OLV are less predictable [5–7]. Therefore this study was undertaken to compare the effects of sevoflurane in a minimal alveolar concentration (MAC) of 1.0 with a similar dose of propofol on differential lung perfusion and oxygenation in a pig model of OLV.

**Material and Methods**

After obtaining approval from the local Animal Care Committee (Landesverwaltungsamt Thuringen, Germany) 12 female pigs (German land race, 29 ± 7 kg) were studied at the Institute for Experimental Animals, University of Jena, Germany, using similar methods as in our earlier studies on OLV [8–12].

Anesthesia was induced in the premedicated animals (ketamine 500 mg IM) with propofol (2–3 mg/kg IV) and pancuronium (0.15 mg/kg IV). The trachea was orally intubated with a 7.0–8.0 ID endotracheal tube (Safety Flex™, Mallinckrodt, Athlone, Ireland). During the preparation, mechanical ventilation was adjusted to keep end-tidal CO$_2$ tension (etCO$_2$) at approximately 32–36 mm Hg. Anesthesia was maintained with a 1:1 mixture of nitrous oxide and oxygen, sevoflurane 2.6% (end-tidal, measured by Physioflex™, Draeger, Luebeck, Germany), and continuous infusion of remifentanil (10–20 µg × kg$^{-1}$ × h$^{-1}$) and pancuronium (0.1–0.2 mg × kg$^{-1}$ × h$^{-1}$). The left femoral artery was surgically exposed and a 4-F fiberoptic-tethermistor catheter (Pulsioath, Pulsoon Medical Systems, Munich, Germany) was advanced 20–25 cm into the abdominal aorta. An accessory lumen of the sheath was connected via a pressure transducer to a monitor (AS3, Datex, Helsinki, Finland) for continuous recording of arterial blood pressure; the aortic thermodilution catheter was connected to a computer system (COLD-Z021, Pulsion Medical Systems, Munich, Germany), which allowed cardiac output calculation using the Stewart-Hamilton equation. CO measurements using this transpulmonary thermodilution technique were performed in triplicate with 10 ml cold saline and averaged for each time point.

A pulmonary artery catheter (Baxter, Irvine, USA) was passed through the right external jugular vein. The tip of the pulmonary artery catheter was positioned just beyond the pulmonary valve to ensure placement in the main pulmonary artery. Additionally, a central venous catheter was placed in the right internal jugular vein. Then a tracheotomy was performed and, using fiberoptic guidance, the orotracheal tube was replaced by a specially designed left-sided 39 Ch double-lumen tube (DLT; Mallinkrodt, Athlone, Ireland). This DLT ensured that the right upper bronchus could also be ventilated or accessed through the tracheal limb. After the DLT placement, the animals were moved into the left decubitus position on a Warmtouch blanket (Mallinkrodt, El Paso, USA), ventilation to the right lung was stopped and an 8.0 ID endotrachéal tube was passed through a right-sided mini-thoracotomy into the right pleural space to serve as access for a thoracoscopy.

During the study, correct DLT placement was verified by continuous dual capnography. Bronchoscopy and thoracoscopy were repeated at the end of each study phase, followed by a single recruitment maneuver of the ventilated lung.

After the preparation, remifentanil and N$_2$O were discontinued and FiO$_2$ was adjusted to 1.0. One-lung ventilation of the left lung was continued with 2.6% sevoflurane (1 MAC). The infusion of pancuronium (0.1–0.2 mg × kg$^{-1}$ × h$^{-1}$) was continued throughout the experiment without changing the dosage. After 30 minutes, measurements of mean arterial pressure and heart rate during 1 MAC sevoflurane were recorded as the baseline measurement.

At that point the actual study period started: Anesthesia was continued either with sevoflurane (2.6% i.e. 1 MAC) or with propofol, in random order. Propofol was dosed so that the mean arterial pressure remained within the range (±10%) of 1 MAC sevoflurane anesthesia at the baseline measurement.

**Wyniki.** Utenowanie krwi tętniczej, ciśnienie parczalne tlenu we krwi żyłnej mieszanej, perfuzja niewentylowane-go płucu i wewnętrzpluwny przeciek prawo-łewy były w przypadku obu środków znieczulających porównywalne, a pojemność minutowa serca była zmniejszona w znieczuleniu z użyciem sevofluranu (p < 0.05).


**Słowa kluczowe:** chirurgia klatki piersiowej, wentylacja jednego płucu, propofol, sevofluran, perfuzja płucna.

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urements (The dose of propofol needed to achieve this in the animals was 29 ± 5 mg × kg⁻¹ × h⁻¹). After an equilibration time of at least 30 minutes, hemodynamic measurements were started if the heart rate, blood pressure and end-tidal anesthetic concentration varied by no more than ±10% for at least 20 minutes. Arterial blood and mixed venous blood were analyzed using an automated blood gas analyzer (ABL 715, Radiometer Copenhagen, Copenhagen, Denmark). Starting with the fourth animal (i.e., in nine of the twelve animals), at the end of this time period colored microspheres (see below) were administered through a central venous line for the measurement of pulmonary perfusion.

Then the anesthetic was changed and the second study period started. After a renewed equilibration time of at least 30 minutes, the same measurements were taken and microspheres were administered. After that the pigs were sacrificed with a lethal dose of potassium chloride and the thorax was opened surgically to remove the lungs.

The pigs received 15 ml/kg of body-warm balanced electrolyte solutions during induction and preparation; this was continued at a rate of 10 ml × kg⁻¹ × h⁻¹ during the study period.

Ventilation during OLV was provided by a constant volume/pressure ventilator (Physioflex™, Draeger, Luebeck, Germany). The ventilation pressure was set at 25 cm H₂O, the expiratory pressure (PEEP) was set at 5 cm H₂O, and the respiratory frequency was varied to achieve an end-tidal CO₂ of 32–36 mm Hg.

The microsphere technique: The technique of microsphere measurements in pigs has already been presented and discussed in detail elsewhere [13]. Briefly: 1.2 × 10⁶ colored microspheres (Dye-Trak, Triton Technology, San Diego, USA) with a diameter of 15 µm were injected slowly over 120 seconds via the central venous catheter at the end of each of the two experimental phases. The lungs of the sacrificed animals were dissected, and digested in a concentrated potassium hydroxide (KOH) solution. To retrieve the microspheres, the digested samples were filtered; the microspheres were then washed with a 2% Tween 80 solution and ethanol. The dye was removed from the microspheres by adding 150 µl dimethylformamide as a solvent, and the photometric absorption of each dye solution was determined with a spectrophotometer (Model 7500, Beckman Instruments, Fullerton, USA). The number of microspheres was calculated using the specific absorbance value of the different dyes. The percentage of right lung perfusion was calculated as the proportion of the number of microspheres

<table>
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<tr>
<th>Table 1. Cardiopulmonary parameters during one-lung ventilation</th>
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<tr>
<td><strong>Propofol</strong></td>
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<td>HR – 1/min</td>
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<td>MAP – mm Hg</td>
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<td>PVO₂ – mm Hg</td>
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<td>SvO₂ – %</td>
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<td>Qs/Qt – %</td>
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<td>Vt – ml</td>
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<tr>
<td>RR – /min</td>
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<td>PAW – cm H₂O</td>
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Means ± standard deviation; HR = heart rate; MAP = mean systemic arterial pressure; PAP = mean pulmonary artery pressure; CVP = central venous pressure; CO = cardiac output; RL perfusion = right lung perfusion, measured in 9 of the 12 pigs; Qs/Qt = intrapulmonary shunt; Vt = tidal volume; RR = respiratory rate; PAW = peak airway pressure.
obtained from right lung in relation to the total number of microspheres.

The statistical analysis of data was performed with the "Statistical Packet for the Social Sciences" SPSS (version 11.5, SPSS Inc., Chicago, USA) using the Wilcoxon signed-rank test. All data are expressed as means (± standard deviation). A stepwise linear regression analysis was performed with the factors CO, SvO\textsubscript{2}, shunt fraction, perfusion of the non-ventilated lung and the type of anesthetic. A p value of < 0.05 was considered statistically significant.

**Results**

Tidal volume, respiratory frequency and peak airway pressure were comparable during sevoflurane and propofol anesthesia. PaO\textsubscript{2} and PaCO\textsubscript{2} during OLV with propofol were not different compared with sevoflurane. Although MAP, CVP, PAP, HR, and SvO\textsubscript{2} were comparable during sevoflurane and propofol anesthesia, CO was significantly lower during sevoflurane anesthesia. Perfusion of the non-ventilated lung and shunt fraction did not differ between the two anesthetics. (Table 1). PaO\textsubscript{2} during OLV, regardless of anesthetic, correlated negatively with shunt fraction and perfusion of the non-ventilated lung (p < 0.01; r = –0.6) but not with SvO\textsubscript{2} or CO.

**Discussion**

In this animal model of OLV, oxygenation and shunt fraction during intravenous anesthesia with propofol were the same as during inhalational anesthesia using 1 MAC sevoflurane.

The results of this study are comparable with the results of most of the clinical studies comparing sevoflurane and propofol during OLV in patients, and it may help to explain the results of those studies [5–7]: If sevoflurane influences HPV during OLV, one would expect that the perfusion of the non-ventilated lung would be higher than when using propofol. However, in the current study, perfusion of the non-ventilated lung during propofol anesthesia was comparable with perfusion during sevoflurane anesthesia. This may seem contradictory and surprising at first glance, but the current authors have observed similar results in previous studies. For example, in one study, increasing the concentration of inhalational anesthetics from 0.5 to 1.5 MAC during OLV led to a stepwise decrease in perfusion of the non-ventilated lung and to a concomitant decrease in shunt fraction [9]. Our present and previous studies do not suggest that sevoflurane has no effect on HPV; rather, they suggest that the direct effects of sevoflurane on HPV are modified by the concurrent indirect effects of sevoflurane on hemodynamic parameters. In the current study, CO was lower during inhalational anesthesia with sevoflurane. It is well known that a decreased blood flow leads to a preferential increase in the perfusion of the normoxic (ventilated) lung [14]. One can speculate that oxygenation during OLV with sevoflurane might have been lower if sevoflurane and propofol had been compared at the same level of cardiac output. In a clinical setting, however, cardiovascular stability is mostly judged by heart rate and mean arterial pressure. It was therefore decided to compare the drugs in accordance with these parameters and not with CO.

In conclusion, this experiment on intact animals demonstrates that oxygenation during OLV with intravenous anesthesia is comparable with oxygenation during inhalational anesthesia. The direct effects of anesthetics on HPV as measured during in vitro experiments may be counteracted in vivo by the indirect effects of these drugs on hemodynamic parameters such as CO.

**References**


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