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ORIGINAL

Haemodynamic changes after induction of anaesthesia with sevoflurane vs. propofol

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ABSTRACT

Inhalation induction with sevoflurane would appear to offer several objective advantages compared to induction with propofol. In our study, the hemodynamic results of sevoflurane vs. propofol induction in patients undergoing thoracotomy were studied. In a prospective, randomized, blinded study 24 patients were randomly allocated to one of 2 groups: sevoflurane (S) and propofol (P) (n=12 each). For hemodynamic monitoring the LIDCO plus system was used. Patients in group S were induced into anaesthesia with sevofluran, remifentanil and vecuronium, whereas patients in group P with propofol, remifentanil and vecuronium. The anaesthesia was maintained with the same agents. Hemodynamic stability was guided using a special algorithm. The goal was oxygen delivery index (DO2I) > 500 mL min-1 m-2. According to the algorithm, patients received colloids or vasoactive drugs. Hemodynamic parameters were recorded before induction, 3 minutes after induction and 3 minutes after intubation and commencement of one lung ventilation. The consumption of vasoactive drugs and colloids and the time from the beginning of induction to intubation were documented. No statistically significant differences in measured hemodynamic parameters, remifentanil and colloid consumption between the S and P group were found. In group P, statistically more ephedrine was used (S: 4.2, P:20.8, p<0.05). Patients undergoing thoracotomy induced with sevoflurane are circulatory more stable than those induced with propofol.

Key words: thoracotomy, one lung ventilation, cardiac index, Systemic Vascular Resistance Index (SVRI)

Introduction

According to the literature, inhalation induction of anaesthesia with sevoflurane would appear to offer several objective advantages over induction with propofol: induction with sevoflurane is significantly slower compared to propofol, it is associated with a lower incidence of apnoea, less time is needed to establish spontaneous ventilation, induction complications are uncommon, and the majority of patients find induction with sevoflurane more acceptable. (1,2)

In the past, inhalation anaesthetics, including sevoflurane, were not considered ideal for use in thoracic surgery, since they were believed to reduce hypoxic pulmonary vasoconstriction, thereby increasing the "shunting" of non-oxygenated blood during one lung ventilation (OLV) and causing hypoxia. (3) This view has been refuted by several studies. (4-6)

During OLV, hypoxic vasoconstriction results in hypoxia of the lung parenchyma in the non-ventilated lung. A recent study focusing on lung injury caused by OLV in pigs showed congested vasculature in the deflated non-ventilated lung. This could be the result of an inflammatory response to hypoxia. Sevoflurane decreases hypoxic pulmonary vasoconstriction and the degree of hypoxic injury. (7)

Since sevoflurane has a protective effect on the heart, it could have a similar effect on lung tissue. Sevoflurane also has favourable effects on the inflammatory response which is triggered by OLV. Due to these properties, it is increasingly used in open lung surgery. (8-11)

The maintenance of haemodynamic stability is very important in open lung surgery. These are generally very complex operations, performed in patients with associated cardiovascular illnesses, in whom haemodynamic instability is a common problem. (12) One of the most sensitive phases (in terms of haemodynamics) during an open lung operation is the induction of anaesthesia and the beginning of one lung ventilation. (13) In our study, we compared the haemodynamic effects of sevoflu-

rane and propofol during this phase of thoracotomy. A similar comparison has not been performed, to our knowledge. Our working hypothesis was that patients anaesthetized with sevoflurane, would have greater circulatory stability than patients anaesthetized with propofol.

Patients and methods

This study was designed as a pilot study to be conducted in preparation for a larger study. The protocol was approved by the National Medical Ethics Committee of the Republic of Slovenia. Twenty-four patients according to the American Society of Anaesthesiologists classification (ASA) II-III patients admitted for an elective anterolateral thoracotomy during a period of 2 months were enrolled after giving written informed consent. We chose this time interval and includeAd as many patients as were gathered during this period because we had no idea of the values for power analysis. Each patient was randomly allocated to one of two induction groups using a computer-generated sequence with sealed envelopes. Patients with a history of malignant hyperthermia or adverse reaction to inhalation anaesthetics or propofol were excluded from the study. Patients with severe chronic obstructive pulmonary disease (Forced expiratory Volume in first second (FEV1) <40% of predicted value), anaemia (Hb<100 g L^{-1}) or contraindications for use of a LiDCO haemodynamic monitor were also excluded.

One hour before surgery, all patients were premedicated with 5 mg of oral diazepam (Apaurin, Krka, d.d., Slovenia). An intravenous catheter, a central venous catheter, and a radial artery catheter were introduced into the forearm opposite the side of surgery. Arterial blood was withdrawn for determination of haemoglobin, blood gas and serum sodium levels needed for calibration of a LiDCO Plus haemodynamic monitor (LiDCO, London, UK). (14,15)

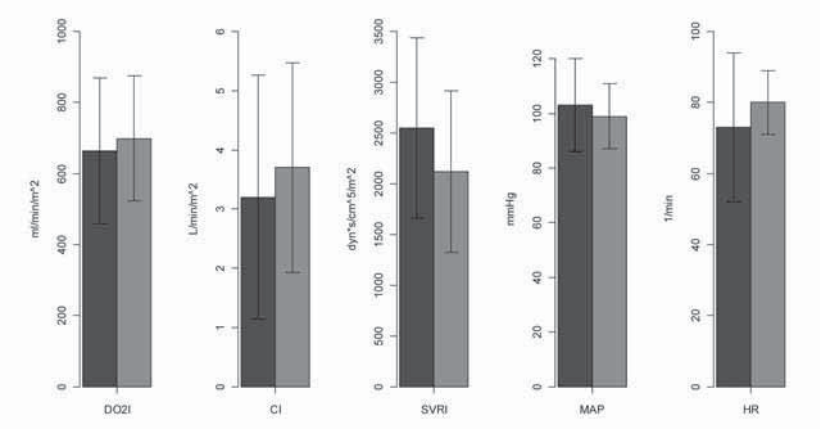
The LiDCO monitor was connected to the patient before induction of anaesthesia. (For calibration of the system, 0.3 mL of lithium chloride was injected into the central or the peripheral venous line, and the lithium concentration in arterial blood was recorded by withdrawing blood past a lithium sensor attached to the arterial line. Following calibration with the cardiac output value, the system calculated the beat-to-beat cardiac output (CO) by analyzing the arterial blood pressure trace. (14,15) It was calibrated according to the manufacturer' instructions. The baseline haemodynamic parameters were then recorded.

The study was carried out by two anaesthesiologists, one was responsible for induction of general anaesthesia, and the other for monitoring. The latter, who was unaware of the patients' distribution between the two groups, guided the former, indicating when to administer additional anaesthetics, vasoactive drugs or fluids.

Before induction, all patients received oxygen for 1 min from a clear plastic face mask at a flow rate of 5 L min^{-1}. In one group of patients, induction was performed with 8% sevoflurane (Sevorane, Abbott Laboratories d.o.o., Illinois, USA). In the second group, 1% propofol (Fresenius Kabi, Germany) was injected at a dose of 1.5-2.5 mg kg^{-1}. Remifentanil 0.5 μg kg^{-1} (Ultiva, GlaxoSmithKline d.o.o., UK) was administered to both groups. When the bispectral index (BIS) value decreased below 60%, vecuronium bromide 0.1 mg kg^{-1} (Norcuron, Organon) was injected.

Monitoring included continuous electrocardiogram (leads II and V5), heart rate, invasive arterial blood pressure, BIS, central venous pressure (CVP), pulse oximetry, end-tidal carbon dioxide ($ETCO_2$), inspired oxygen concentration (FiO_2), peak and plateau airway pressures, tidal volume, and minute ventilation. The following haemodynamic parameters were measured by the LiDCO Plus system: oxygen delivery index (DO_2I), cardiac index (CI), stroke volume variation (SVV), and systemic vascular resistance index (SVRI).

Haemodynamic management was performed using the goal-directed therapy approach. A DO_2I value of ≥500 mL min^{-1} m^{-2} was selected as the target value. (15) The primary outcome for oxygen delivery was based on the available data as a likely optimum between accomplishing the desired effect and avoiding possible consequences of a higher CO. (15) SVV was used as a dynamic marker of fluid responsiveness to guide haemodynamic management. (16) If DO_2I decreased below



CI, cardiac index; DO_2I, oxygen delivery index; HR, heart rate; MAP, mean arterial pressure; SVRI, systemic vascular resistance index.

Figure 1. The extent of the change in DO2I, CI, SVRI, MAP and HR at the various points with sevoflurane (blue) and propofol (pink).

500 ml min^{-1} m^{-2} with SVV exceeding 10%, a colloid solution consisting of 6% hydroxyethyl starch 130/0.4 in 0.9% sodium chloride (Voluven R, Fresenius Kabi, Germany) was administered at a rate of 20 ml kg^{-1} h^{-1} until SVV fell below 10%. If DO_2I failed to reach 500 ml min^{-1} m^{-2} with fluid alone, one or more 5 mg boluses of ephedrine hydrochloride (0.5% Efedrin, Central Pharmacy of the University Medical Centre Ljubljana) were administered. The same treatment, i.e. one or more 5 mg boluses of ephedrine hydrochloride, was given if SVRI decreased below 1500 dyn s cm^{-5} m^2. According to Hensley et al, ephedrine causes appreciable increases in CO, blood pressure and contractility, and also slight increases in SVR and heart rate. (17)

One lung ventilation was performed via a double-lumen endobronchial tube (Broncho-Cath, Mallinckrodt). A Cato volume cycled ventilator (Dräger, Lübeck, Germany) was used with the tidal volume set to 8 mL kg^{-1} of ideal body weight, the inspiratory-to-expiratory ratio to 1:2, and the positive end-expiratory pressure to 5 cmH_2O. Arterial haemoglobin oxygen saturation was maintained above 98% by administering 80-100% oxygen. $ETCO_2$ levels were kept in the range of 3 to 6 kPa by adjusting the tidal volume and the respiratory rate.

Anaesthesia was maintained with 2% sevoflurane in one group of patients. In the second group, propofol was administered at a rate of 100-200 μg kg^{-1} min^{-1}. Both groups received remifentanil at a rate of 0.2 μg kg^{-1} min^{-1}. If the mean arterial pressure and/or heart rate increased by 30%, the patient would receive an additional bolus of 0.5 μg $kg^{-1}$of remifentanil. The depth of anaesthesia was controlled by BIS monitoring. If the BIS value remained above 60, the patient would either be given an additional bolus of 0.5 mg kg^{-1} of propofol or would continue to receive sevoflurane in the initial concentration (8%).

Haemodynamic parameters were recorded after induction (3 min after BIS fell below 60 and 3 min after the patient was intubated and one lung ventilation was started. The time from the beginning of induction to the second recording of the haemodynamic parameters, the consumption of colloid solutions, and the consumption of ephedrine were documented.

Statistical Analysis

The null hypothesis under test was that sevoflurane and propofol do not differ significantly in their haemodynamic effects when used for induction of anaesthesia in patients undergoing thoracotomy. Accordingly, the primary outcome measure was the amount of supplemental ephedrine and colloids required to maintain the oxygen delivery index above 500 mL min^{-1} m^{-2}.

Statistical analysis was performed using a statistical software package San Jose, CA. The normal distribution of data was first evaluated with the Kolmogorov-Smirnov test. Continuous variables were then analyzed using Student's t-test or the Mann-Whitney u-test depending on data distribution. Categorical variables were analyzed with the contingency table analysis and Fisher's exact test. A P value $\leq$ 5% was considered significant. Continuous variables were presented as mean ($\pm$SD) or median (range), while categorical variables were presented as count (%).

Results

There were no significant differences in age, weight, height, gender, ASA physical status distribution, or duration of induction between the two groups (table 1).

The baseline haemodynamic data (DOI_2, CI, SV, SVV, SVRI, Mean arterial pressure (MAP), heart rate (HR), CVP) also did not differ significantly between the two groups, as evident from table 2.

The CI, MAP, HR and SVRI values recorded after induction and clamping of one lumen of the Carlens tube are presented in table 3. DO_2I was maintained above 500 mL min^{-1} m^{-2} in all patients, and its values did not differ significantly between the two groups. However, the amount of ephedrine needed to maintain DO_2I above the target value was significantly greater in the propofol group (20.8$\pm$5.2 mg) compa-

Table 1. Anthropometric characteristics and duration of induction in the two studied groups.

	Sevoflurane group	Propofol group	p
Age (year)	52.7$\pm$14.6	60.9$\pm$9.4	0.16
Weight (kg)	77.6$\pm$13.5	81.9$\pm$15.2	0.49
Height (cm)	174.3$\pm$9.5	172.8$\pm$9.5	0.73
Sex (f/m)	5/7	4/8	x
ASA physical status 1/2/3/4 (n)	0/4/8	0/5/7	x
Duration of induction (min)	6.95$\pm$2.5	7.1$\pm$2.3	0.89

ASA, American Society of Anaesthesiologists.
Values are means $\pm$ SD or count. There were no statistically significant differences observed between groups.

Table 2: Baseline haemodynamic data.

	Sevoflurane group	Propofol group	p
DO_2I ($mL\ min^{-1}\ m^{-2}$)	664±206	699±177	0.53
CI ($L\ min^{-1}\ m^{-2}$)	3.2±2.06	3.7±1.77	0.23
SVRI ($dyn\ s\ cm^{-5}\ m^2$)	2550±886	2120±797	0.27
MAP (mmHg)	103±17	99±12	0.51
HR (min^{-1})	73±21	80±9	0.38

CI, cardiac index; DO_2I, oxygen delivery index; HR, heart rate; MAP, mean arterial pressure; SVRI, systemic vascular resistance index.
Values are means ± SD. There were no statistically significant differences observed between groups.

red to the sevoflurane group (4.2±1.3 mg) (P = 0.03). The amount of colloids infused did not differ significantly between the two groups (289 mL vs. 189 mL, respectively, P = 0.19).
No patients needed additional boluses of remifentanil. The BIS values showed no differences in depth of anaesthesia between the two groups (table 4).
In figure 1 you can see the extent of the change in DO_2I, CI, SVRI, MAP and HR at the various points with sevoflurane (blue) and propofol (pink).

Discussion

Our study showed that patients anaesthetized with sevoflurane were haemodynamically more stable than patients given propofol, since the amount of ephedrine needed to maintain haemodynamic stability was lower in the sevoflurane group than in the propofol group (table 3).
A similar conclusion was reached by Thwaites et al. who found that the mean arterial pressure was more stable when anaesthesia was induced with sevoflurane as compared to propofol. (1)
Unlike Thwaites et al. who concentrated on MAP, we also measured several other haemodynamic parameters, which enabled us to examine more specifically the influence of sevoflurane on haemodynamics.
Our study was performed on patients undergoing open lung surgery. As we know, lung disease requiring thoracotomy is very often associated with other diseases, especially with cardiovascular disorders. An open lung operation is a complicated procedure, which often results in circulatory instability with consequent tissue hypoperfusion. (18) One lung ventilation, carried out during these operations, frequently leads to serious complications. It would thus be advantageous to use anaesthetics that have the least effect on haemodynamics.
In our study, haemodynamic parameters were measured after the induction of anaesthesia and at the beginning of one lung ventilation, when haemodynamic instability is especially frequent. (18) After induction, the haemodynamic values in both groups of patients decreased by about 30% but remained within the normal range. However, the patients anaesthetized with propofol required substantially more ephedrine to maintain the haemodynamic parameters within the normal range and thus ensure normal tissue perfusion. This means that the patients in the propofol group were haemodynamically less stable than the patients in the sevoflurane group.
The cardiovascular effects of sevoflurane are similar to those of isoflurane. (19-21) Sevoflurane causes a dose-dependent depression of right ventricular function. (22) Propofol is believed to cause a reduction in systolic and diastolic arterial pressures by lowering SVRI and afterload. (23) Some studies on people and animals showed that it had no influence on CI, (23-25) while in others it caused a reduction in CI. (26,27) Its haemodynamic effects depend on the speed of administration and on associated cardiovascular diseases. (26,28). Filipovic et al. observed that sevoflurane had no effect on left ventricular relaxation, while propofol influenced it to a certain extent. However, neither sevoflurane nor propofol caused a clinical diastolic dysfunction. (29) Fredman et al. established that although the mean arterial pressure values were similar after induction with sevoflurane or propofol, the use of sevoflurane was associated with consistently lower heart rate. (30) Similar conclusions about the effects of sevoflurane on heart rate and mean arterial pressure were reached by Ebert et al. (20)
Ephedrine, used in this study, has a non-selective stimulating effect on alpha and beta adrenergic receptors. By using more specific substances, like noradrenalin and dobutamine, and ensuring their targeted administration while changing individual haemodynamic parameters, we could have confirmed that propofol was more potent in reducing CI or SVRI. However, these substances may be administered only in the form of infusion at very low doses. Consequently, it would have been difficult to titrate their effects during the short time that was available in this study. We will be able to use them in our further research when we compare the haemodynamic effects of sevoflurane and propofol throughout the duration of thoracotomy.
In the present study, bispectral index was measured in all patients to prevent achieving better circulatory stability at the expense of awareness and pain. Blood pressure and heart rate were also monitored. The BIS values ranged between 40 and 60, while BP and HR did not increase by more than 30% above the baseline value. None of the patients needed an additional bolus of analgesics. The rate of infusion of remi-

Table 3. Haemodynamic parameters measured after induction and after tube clamping.

	Sevoflurane group	Propofol group	P
CI after induction ($L\ min^{-1}\ m^{-2}$)	2.0 ± 1.87	2.6 ± 2.8	0.19
CI after clamping ($L\ min^{-1}\ m^{-2}$)	2.6 ± 1.4	3.0 ± 2.0	0.30
MAP after induction (mmHg)	75 ± 12	76 ± 21	0.88
MAP after clamping (mmHg)	86 ± 14	91 ± 18	0.54
HR after induction (min^{-1})	70 ± 11	62 ± 18	0.18
HR after clamping (min^{-1})	77 ± 9	78 ± 10	0.82
SVRI after induction ($dyn\ s\ cm^{-5}\ m^2$)	2816 ± 771	2437 ± 898	0.31
SVRI after clamping ($dyn\ s\ cm^{-5}\ m^2$)	2722 ± 725	2382 ± 898	0.35
Ephedrin given (mg)	4.2±1.3	20.8±5.2	0.03

CI, cardiac index; HR, heart rate; MAP, mean arterial pressure; SVRI, systemic vascular resistance index.

Values are means ± SD. There were no statistically significant differences observed between groups.

Table 4. Bispectral index (BIS) after induction and after tube clamping.

	Sevoflurane group	Propofol group	P
BIS after induction	44±2.1	43±1.5	0.88
BIS after clamping	43±1.7	44±0.9	0.79

BIS, bispectral index.

Values are means ± SD. There were no statistically significant differences observed between groups

fentanil, calculated according to body weight, was the same in both groups.

Until recently, the use of inhalation anaesthetics in lung surgery has been questioned because of the possibility of reversing hypoxic vasoconstriction in the non-ventilated lung and thus causing hypoxia. (3) Several recent studies have refuted this view, and sevoflurane has been increasingly recognized as a suitable anaesthetic for thoracotomy due to its positive effects on the cardiovascular system, respiratory organs and inflammatory response. (8 -11)

Our study could have been improved by continuous recording of haemodynamic parameters throughout the induction of anaesthesia. This would have enabled us to determine the minimum and the maximum values of the haemodynamic parameters studied, and to examine more specifically the action of the two anaesthetic agents.

It would be useful to record and analyze the haemodynamic effects of propofol and sevoflurane throughout the duration thoracotomy, and to measure their effect on the inflammatory response by determining cytokine levels in the blood.

This study serves as a pilot study for a larger investigation in which we plan to examine more closely the haemodynamic effects and anti-inflammatory activity of sevoflurane in patients undergoing thoracotomy.

Conclusion

Our pilot study showed that sevoflurane is superior to propofol in terms of haemodynamic stability, which is evident from a lesser consumption of ephedrine during the induction of anaesthesia. However, further studies will be needed to evaluate the impact of sevoflurane on haemodynamic stability and on the inflammatory response throughout the duration of anaesthesia in patients undergoing thoracotomy with one lung ventilation.

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