Vpliv intravenskega ali inhalacijskega uvoda v anestezijo na prenos kisika pri starostnikih, operiranih zaradi kolorektalnega raka

Effects of intravenous and inhalation induction of anesthesia on oxygen delivery in elderly patients undergoing colorectal surgery

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Ključne besede:
Propofol, sevofluran, uvod v anestezijo, prenos kisika, starostnik.

Key words:
Propofol, sevoflurane, induction of anesthesia, oxygen delivery, elderly.

Članek prispel / Received
22. 5. 2018
Članek sprejet / Accepted
14. 3. 2021

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Izvleček

Namen: *Uvod v splošno anestezijo z direktno laringoskopijo in vstavitvijo dihalne cevke je postopek, ki lahko močno vpliva na prenos kisika. Hitra in pravilna izbira učinkovin ter njihovih odmerkov za vzdrževanje prenosa kisika pripomore k izboljšanju izida zdravljenja.*
Namen raziskave je bil primerjati vpliv propofola in sevoflurana v uvodu v anestezijo na prenos kisika pri starostnikih, anesteziranih zaradi operacije debelega črevesja.
Metode: *V raziskavo smo vključili 40 bolnikov, starejših od 65 let, uvrščenih po ASA v 2. in 3. skupino, ki so bili programsko operirani na debelem črevesju. Glede na anestetik so bili bolniki naključno razdeljeni v propofolsko skupino (skupina P) ali sevofluransko skupino (skupina S)*
Rezultati: *Po uvodu v anestezijo so*

Abstract

Purpose: *The induction of anesthesia with direct laryngoscopy and orotracheal intubation are two interventions, which can influence oxygen delivery. Rapid adjustments of treatment to restore oxygen delivery are crucial to improving the outcomes for patients.*
The aim of this study was to compare the effects of induction of anesthesia with propofol and sevoflurane on oxygen delivery in elderly patients undergoing colorectal surgery.
Methods: *We studied forty patients with physical status II or III, according to the American Society of Anesthesiology, who were older than 65 years and undergoing elective surgery for resection of colorectal carcinoma. The patients were randomly divided into the propofol group (P-group) and sevoflurane group (S-group), according to the anesthetic received*

se srčna frekvenca, srednji arterijski pritisk, minutni volumen srca in indeks prenosa kisika statistično značilno zmanjšali v obeh skupinah v primerjavi z izhodiščno vrednostjo. Po uvodu v anestezijo se je srčna frekvenca statistično značilno hitreje zmanjšala v skupini P. Takoj po vstavitvi dihalne cevke so se srčna frekvenca, srednji arterijski pritisk, minutni volumen srca in indeks prenosa kisika statistično značilno povečali v skupini S, vendar že naslednjo minuto ta razlika med skupinama ni bila več statistično značilna.

Po vstavitvi dihalne cevke so bili srčna frekvenca, srednji arterijski pritisk, minutni volumen srca in indeks prenosa kisika statistično značilno znižani v obeh skupinah v primerjavi z izhodiščno vrednostjo.

Zaključek: *V uvodu v anestezijo pri starostniku imata propofol in sevofluran klinično primerljiv učinek na prenos kisika.*

for the induction of anesthesia.

Results: *After induction of anesthesia, heart rate, mean arterial pressure, cardiac output and the oxygen delivery index significantly decreased in both groups compared to the baseline values. Following induction of anesthesia, the decrease in heart rate was significantly more rapid in the P-group.*

Immediately after orotracheal intubation, heart rate, mean arterial pressure, cardiac output and the oxygen delivery index significantly increased in the S-group, but one minute later these diferences were not statistically significant. Heart rate, mean arterial pressure, cardiac output and the oxygen delivery index were significantly lower after orotracheal intubation in both groups, compared to baseline.

Conclusion: *Propofol and sevoflurane are clinically comparable in the induction of anesthesia in elderly patients according to the effect on oxygen delivery.*

INTRODUCTION

Oxygen delivery (DO_2) is an important parameter that represents the amount of oxygen delivered to the tissues per minute and is determined by oxygen saturation of arterial blood, hemoglobin, and cardiac output (CO). The oxygen delivery index (DIO_2) is DO_2 standardized to the patient's body surface area (BSA).

Oxygen supply and demand are imbalanced in several acute pathophysiological changes that may lead to increase mortality due to the switch to anaerobic metabolism and tissue hypoxia (1-7). Numerous studies have shown that maintaining proper DO_2 reduces mortality and complications both in critically ill patients and in patients who require major surgery (1-8). Measuring DO_2 allows appropriate selection of medications and their doses, and rapid adjustment of therapy according to patient requirements (1, 2, 7, 8).

The induction of anesthesia with direct laryngoscopy and orotracheal intubation (OTI) are two interventions that can influence DO_2 in two opposite ways. OTI is a very painful procedure, which can trigger the release of stress hormones and activate the sympathetic nervous system, leading to an increase in systemic vascular resistance (SVR), mean arterial pressure (MAP), heart rate (HR) and the emergence of arrhythmias (17, 38).

Intravenous or inhaled anesthetics used for induction of anesthesia, cause depression of the central nervous system, which is different between the anesthetics, because their actions on different parts of the central nervous system vary. Depression of the sympathetic nervous system can influence the cardiovascular system. They also have a direct vasodilator effect, depress the myocardium and inhibit the baroreceptor reflex, and decrease SVR and MAP. When MAP and SVR are reduced, the baroreceptor reflex compensates by increasing HR; therefore, CO is only minimally reduced (8, 11, 18-21).

Studies comparing propofol and sevoflurane have demonstrated a small decrease in MAP and HR before OTI and a small increase in MAP and HR during and immediately after OTI following induction with sevoflurane (15, 16, 22-31).

Elderly patients with anatomical and physiological changes are a particularly vulnerable group and can develop hemodynamic instability during the induction of anesthesia. A decrease in the DIO_2 can rapidly lead to tissue hypoxia, including hypoxia of the central nervous system and myocardium (8-17).

The aim of the present prospective single-blind study

was to compare the effect of propofol and sevoflurane on the DIO_2 during the induction of anesthesia in elderly patients undergoing major surgery. The goal of the study was to determine what type of induction anesthesia allows more stable functioning of the circulatory system in the elderly.

METHODS

We studied forty patients with physical status II or III, according to the American Society of Anesthesiologists physical status classification system, who were older than 65 years and undergoing elective surgery for the resection of colorectal carcinoma. The study was approved by the National Medical Ethics Committee. All the patients were informed of the aims of the study and its protocols, and provided written consent to participate in the study.

Patients with an allergy or sensitivity to volatile anesthetics or to propofol, with known or suspected genetic susceptibility to malignant hyperthermia, chronic abusers of illicit substances or alcohol and patients with aortic insufficiency, intraaortic balloon pump, arrhythmias and vasoconstriction of peripheral veins due to poor reliability of LidcoRapid monitoring were excluded from the study.

The patients were randomly divided into two groups by a person not involved in the study by choosing a sealed envelope. The propofol group (P-group) received propofol and the sevoflurane group (S-group) received sevoflurane for the induction of anesthesia.

Patients were orally premedicated with midazolam 7.5 mg 60 minutes before the induction of anesthesia. A blood sample was collected for the measurement of serum hemoglobin (Hb) before the induction of anesthesia. An epidural catheter at level Th 10-11 and an arterial catheter were inserted in all patients, which allowed invasive continuous monitoring of DIO_2 values with the LidcoRapid device, which included the patented and clinically verified algorithm PulseCo. MAP, DIO_2, HR, SVR and cardiac index (CI) were obtained by constant analysis of the pulse wave from beat to beat.

For patients in the S-group, a circle CO_2 absorber circuit with a 3-L reservoir bag was used. The circuit was primed with sevoflurane 8% in a 2:1 ratio of nitrous oxide to oxygen at a fresh gas flow rate of 6 l/min for 1 minute.

During the induction of anesthesia, patients in both groups received the analgesic fentanyl 2 µg/kg. One minute later, the face mask was placed over the mouth and nose of the patients in the S-group and they started breathing the mixture of 100% oxygen and sevoflurane 8 vol %. When 4.5% end tidal concentration of sevoflurane was reached, the concentration of sevoflurane was reduced to 4%.

One minute after fentanyl application, patients in the P-group received a total of 2 mg/kg propofol.

Following the loss of eyelash reflexes, patients in both groups received 0.6 mg/kg rocuronium. One minute after the application of rocuronium, OTI was performed and mechanical ventilation with a tidal volume of 6-8 ml/kg was started to maintain end tidal CO_2 concentration between 4 and 4.5 kPa. In both groups, anesthesia was maintained with sevoflurane at the concentration of 1 MAC at a 40:60 ratio of nitrous oxide to oxygen at a fresh gas flow rate of 2 l/min.

The bispectral index (BIS), MAP, HR, CI, SVR, and Hb saturation (SpO_2) were continuously measured and the DIO_2 was calculated two minutes before and fifteen minutes after orotracheal intubation according to the formula:

$$DIO_2 = (CO \times SpO_2 \times Hb) / BSA$$

During the period of measurements, we registered the number of cardiovascular side effects necessitating rescue treatment and the dose of rescue medication. Hypertension was defined as a MAP greater than 85 mmHg. Hypotension was defined as a MAP lower than 65 mmHg. Tachycardia was defined as a heart rate higher than 90 beats/min and bradycardia as a heart rate lower than 40 beats/min. Rescue medication was started when the duration of cardiovascular events exceeded 1 minute. Hypertonic events and/or tachycardia were treated with increments of fentanyl 2 µg/kg. Hypotonic events were treated with increments of phenylephrine 25 µg to maintain MAP above 65 mmHg. Rescue medication for bradycardia was increments of atropine at 0.5 mg until HR increased.

The obtained data were processed using the IBM

SPSS program and the use of relevant statistical tests. Demographic data and baseline values were compared using the t-test for independent samples. The ANOVA test was used to process repeated measurements of the variables, thus comparing the values of the variables between and within groups. P values <0.05 were considered statistically significant.

RESULTS

In this study, 40 patients were randomly allocated into the sevoflurane group (S-group) or propofol group (P-group, Figure 1). There were no statistically significant differences between the groups in terms of age, gender, weight, height, Hb, MAP, HR, CO, and DIO_2 (Table 1).

Time to loss of palpebral reflex (T_{LPR}) and time to orotracheal intubation (T_{OTI}) were statistically significantly longer in the S-group (Table 2). Statistically significantly higher BIS values at the loss of palpebral reflex (BIS_{LPR}) and before OTI (BIS_{OTI}) were observed in the S-group (Table 2).

Before and during the induction of anesthesia until insertion of the breathing tube, there were no statistically significant differences between the groups in terms of SpO2, MAP, CO and DIO_2 values.

HR, MAP, CO and DIO_2 significantly decreased after the induction of anesthesia in both groups compared to baseline values (Table 3). Following the induction of anesthesia, the decrease in HR was significantly more rapid in the P-group (Table 3). Immediately after OTI, the HR, MAP, CO and DIO_2 significantly increased in the S-group compared to the P-group, but after one minute these differences were not statistically significant (Table 3).

The DIO_2 was significantly lower after OTI compared to baseline (Table 3, Figure 2). After anesthesia induction, the DIO2 increased in both groups, but was significantly higher in the S-group than in the P-group (Table 3, Figure 2).

SpO_2 values ranged between 98% and 100% over the measured time period.

We observed hypotension, which required rescue medication in 12 patients in the S-group and in 10 patients in the P-group, but the difference was not

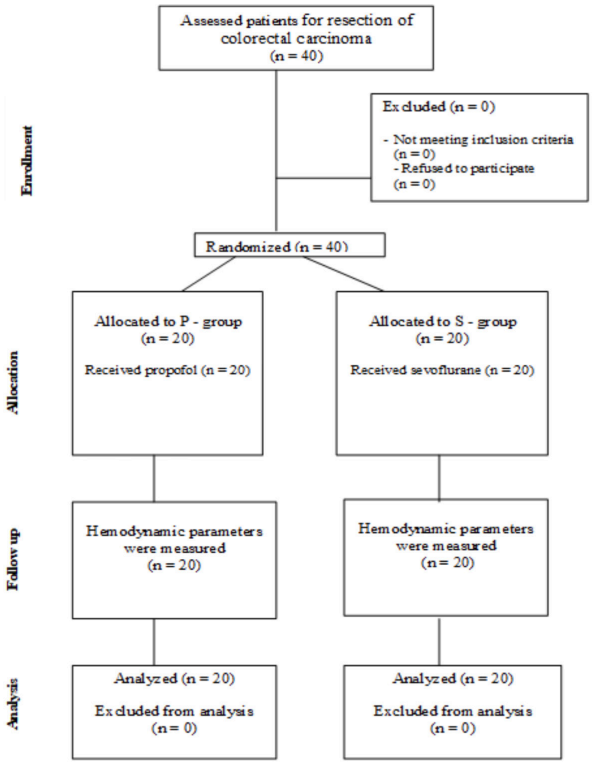

Figure 1. *Study flow diagram*

Table 1. *Demographic data and baseline values of the hemodinamic parameters.*

	P-group (n = 20)	S-group (n = 20)	P
Age (years)	71.2±6.2	71.5±6.5	0.88
Gender (Female/Male) (n)	8/12	8/12	0.48
Weight (kg)	72.3±15.9	73.6±13.9	0.78
Height(cm)	167.1±7.3	169.4±9.2	0.39
Hb before induction (mmol/l)	122.4±15.9	122.9±17.4	0.92
MAP before induction (mmHg)	99.6±12.8	101.2±11.9	0.69
HR before inductio (min-1)	69.8±9.3	70.9±11.1	0.72
CO before induction (ml/min)	3.1±0.9	3.4±1.0	0.28
DIO_2 before induction(ml/min/m²)	497.5±167.6	550.5±182.1	0.34

*Legend: Data is the mean value ± standard deviation; n = absolute number; * P < 0,05 compared between groups; HR = heart rate; CO = cardiac output; Hb = serum hemoglobin concentration; DIO_2 = oxygene delivery index; MAP = mean arterial pressure*

Table 2. *Time to loss of palpebral reflex (T_{LPR}), time to orotracheal intubation (T_{OTI})), BIS at loss of palpebral reflex (BIS_{LPR}) and BIS before orotracheal intubation (BIS_{OTI}).*

Time	P-group	S-group	p
T_{LPR}(s)	111.6±9.5*	144.8±21.7*	< 0.05
T_{OTI}(s)	172.1±9.9*	205.4±22.7*	< 0.05
BIS_{LPR} (s)	64.9±8.7*	80.0±8.1*	< 0.05
BIS_{OTI}(s)	31.8±6.6*	54.3±10.7*	< 0.05

*Legend: Data is the mean value ± standard deviation; * P < 0.05 compared between groups*

statistically significant, and the cumulative dose of phenylephrine was not significantly different between the groups (Table 4). We observed bradycardia, which required rescue medication in 2 patients in the P-group and in 7 patients in the S-group, which was significantly different, and the cumulative dose of atropine was also significantly different between the groups (Table 4). None of the patients developed hypertension or tachycardia during the study period.

DISCUSSION

The aim of this study was to compare the effects of propofol and sevoflurane on the DIO_2 in elderly patients during induction of anesthesia and for 15 minutes after OTI, and to determine which anesthetic provided greater stability of the circulatory system. A number of

Table 3. *Hemodynamic parameters before the induction of anesthesia, 1 and 2 minutes after the start of induction, before and immediately after orotracheal intubation and 2, 4, 6, 8, 10 and 15 minutes after orotracheal intubation.*

Time	MAP (mmHg)		HR (beat/min)		CO (ml/min)		DIO_2 (ml/min/m²)	
	P-group	S-group	P-group	S-group	P-group	S-group	P-group	S-group
baseline value	100±13	101±12	70±9	71±11	3.1±1.8	3.4±1.1	497±167	550±182
1 min after induction	97±12	98±13*	67±9*‡	71,±12‡	3.0±0.8	3.4±1	493±167	545±187
2 min after induction	81±13*	82±16*	66±10*	67±12*	2.5±0.8*	2.7±1.0*	424±163*	440±179*
before OTI	70±17*	71±12*	62±10*	64±12*	1.7±0.7*	2.1±0.8*	279±110*	338±127*
after OTI	74±15*‡#	86±17*‡#	70±13‡#	81±17‡#	1.9±0.5*‡#	2.7±1.0*‡#	319±102*‡#	454±190*‡#
2 min after OTI	70±15*	76±15*	65±14*	67±13	1.9±0.7*	2.2±0.7*	315±122*	366±126*
4 min after OTI	69±12*	70±11*	64±12*	60±10*	1.7±0.7*	1.9±0.7*	288±118*	318±117*
6 min after OTI	67±12*	64±8*	61±10*	58±8*	1.7±0.6*	1.8±0.6*	273±101*	290±98*
8 min after OTI	64±12*	62±7*	60±10*	56±8*	1.6±0.5*	1.7±0.6*	264±92*	271±87*
10 min after OTI	66±9*	63±9*	57±9*	57±9*	1.5±0.5*	1.7±0.5*	250±88*	274±88*
15 min after OTI	64±8*	61±8*	56±8*	57±8*	1.5±0.4*	1.6+0.5*	241±79*	263±79*

*Legend: Data is the mean value ± standard deviation; n = absolute number; * P < 0.05 compared to baseline value; ‡ p < 0.05 between group comparison; # p < 0.05 compared to value before OTI; HR = heart rate; CO = cardiac output; MAP = mean arterial pressure; DIO_2 = oxygene delivery index; OTI = orotracheal intubation*

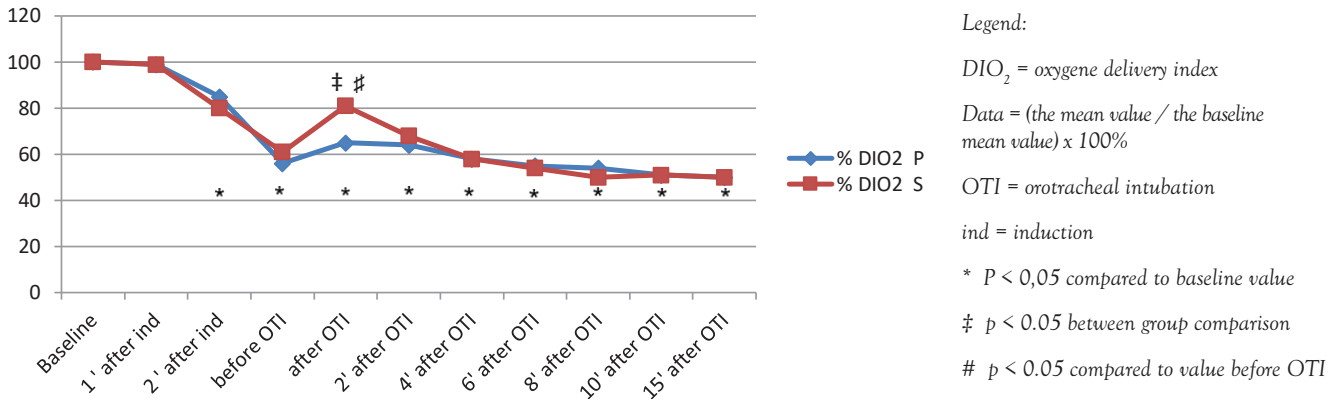

Figure 2. *Changes in oxygene delivery index (DIO_2) before the induction of anesthesia, 1 and 2 minutes after the start of induction, before and immediately after orotracheal intubation and 2, 4, 6, 8, 10 and 15 minutes after orotracheal intubation .*

Table 4. *Commulative dose of the rescue medications.*

Time / rescue medication	P-group	S-group	p
Phenylephrine (mcg)	45.0±66.7	67.5±74.8	0.322
Atropine (mg)	0.05±0.1‡	0.2±0.3‡	< 0.05

Legend: Data is the mean value ± standard deviation

‡ P < 0.05 compared between groups

studies which investigated the influence of anesthetic drugs during induction of anesthesia on the function of the circulatory system, both in adults and exclusively in the elderly, were limited to the study of MAP and HR changes during the induction of anesthesia (15, 16, 22-31). Only a few studies have compared the effect of propofol and sevoflurane on CO or DO_2 (32-35).

Studies that compared intravenous induction of anesthesia with propofol and sevoflurane demonstrated greater stability of the circulatory system following induction with sevoflurane; a lower decrease in MAP and HR before OTI and a lower increase in MAP and HR between and immediately after OTI were observed. Following the induction of anesthesia with sevoflurane or propofol, we observed significant decreases in MAP, HR, and CO, which caused a statistically significant decrease in the DIO_2, without statistically significant differences between the S-group and P-group.

Husedzinovic et al. compared the effect of sevoflurane and propofol on the contractility of the heart muscle in adult patients using transesophageal echocardiography, and reported statistically significant higher values of the stroke volume after the induction of anesthesia in the group receiving sevoflurane (32). Nishikawa K et al. proved that propofol compared to sevoflurane has a greater negative inotropic effect on the heart in the elderly (33).

Based on our results we cannot confirm that sevoflurane allows more stable MAP and DIO_2 during the induction and after OTI.

We observed a significantly more rapid decrease in HR after induction of anesthesia in the P-group in the first minute, but after that and up to OTI no statistically significant differences in HR were noted between the groups. However, patients in the S-group showed significantly more bradycardia events, requiring more rescue doses of atropine (Table 3 and 4). This was attributed to the inhibitory effect of high concentrations of sevoflurane on the baroreceptor reflex (34). On the other hand, propofol should inhibit cardiac parasympathetic nerves depending on the dose (35).

Despite the satisfactory depth of anesthesia, according to the BIS values, statistically significant increases in HR, MAP, and CO were observed after OTI in the S-group compared to the P-group, but these diferences were subsequently not statistically significant (Table 3).

Based on the present results we cannot confirm the results by Dwivedi et al. and Bharti et al., who reported

greater stability of the circulatory system during and after OTI with sevoflurane induction; however, only MAP and HR were compared in these studies (36, 37). Nevertheless, despite the increase in DIO_2 in the S-group after OTI, the average DIO_2 value remained just below the lower limit of the desired value of 520 – 600 ml/min/m2 (1). The DIO_2 in the P-group was even lower and achieved only 60% of the baseline value. According to the present results, we suggest using a lower dose of propofol during induction, as propofol decreases the DIO_2 significantly more than sevoflurane. We agree with studies recommending titration of the propofol dose according to the BIS to achieve greater hemodynamic stability (39). We cannot support the use of a continuous infusion of phenylephrine or noradrenaline to increase MAP and improve hemodynamic stability during induction, as these drugs may further decrease the DIO_2.

The time to loss of palpebral reflex and the OTI was statistically significantly longer in the S-group, but still within a clinically acceptable time frame. Similar results were also observed by other researchers (22-25).

In conclusion, propofol and sevoflurane are clinically comparable in the induction of anesthesia in elderly patients according to the effect on oxygen delivery. Inhalation induction with sevoflurane offers no advantage over intravenous induction with propofol, with respect to hemodynamic stability and oxygen delivery in elderly patients undergoing major surgery.

CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest to declare.

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