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Hemodynamic Differences in Sevoflurane Versus Propofol Anesthesia

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A B S T R A C T

The aim of the study was to compare the effect of sevoflurane and propofol anesthesia on myocardial contractility during laparotomic cholecystectomy using transesophageal echo-Doppler. In the study, 40 patients were randomized into two groups, depending on whether they received sevoflurane or propofol anesthesia. Heart rate, cardiac index, stroke volume, left ventricular ejection time and acceleration were measured 10 minutes after induction of anesthesia, 1 minute and 25 minutes after incision. The results were analyzed using paired t-test and ANOVA. Significantly lower values were found for all parameters after the initial measurement ($p<0.05$). In the sevoflurane group, stroke volume decreased from 66±6.2 ml/beat to 65±6.4 ml/beat and to 63±5.6 ml/beat 1 minute and 25 minutes after incision respectively. In the propofol group changes were from 64 ml/beat to 58±10.5 ml/beat to 58±8.6 ml/beat. Stroke volume was significantly higher in the sevoflurane than in the propofol group ($p<0.05$). Sevoflurane anesthesia allows a better hemodynamic stability during laparotomic cholecystectomy.

Key words: *sevoflurane, propofol, echocardiography, transesophageal, hemodynamics, cholecystectomy*

Introduction

Nowadays, an anesthesiologist can use numerous intravenous or inhalation anesthetics, which allow many combinations and ways of usage. The introduction of total intravenous anesthesia and the use of volatile induction/maintenance anesthesia has led to the reintroduction of »single-agent« anesthesia and the elimination of the transition phase between the induction and the maintenance. The advantages of total intravenous anesthesia versus volatile induction/maintenan-

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ce anesthesia are still the subject of many investigations, but, on the other hand, the principle of »single-agent« anesthesia in relation to balanced anesthesia is still the subject of extensive investigations[1,2]. Many studies have investigated the pharmacokinetics and pharmacodynamics of various anesthetic agents, but only a small number of them have investigated anesthetic repercussions on myocardial contractility[3].

Sevoflurane was first described in 1972 and introduced in clinical use in Japan in 1990, in Germany in 1995 and in the United States (USA) in 1996. Compared with older inhalation agents, such as desflurane or halothane, the most important property of sevoflurane is its low blood/gas partition coefficient of 0.69, which results in a rapid wash-in and wash-out. Furthermore, sevoflurane depresses cardiovascular function and myocardial contractility, similarly to isoflurane, but less than halothane and enflurane.

Modern principles of anesthesia have made some new starting points in the anesthesiologist profession. A faster awakening from general anesthesia, a better control of anesthesia deepness and the cost/benefit ratio are the advantages of sevoflurane in comparison with intravenous anesthesia, especially in short surgeries[2].

There are still many controversies on the impact of sevoflurane versus propofol on cardiovascular stability. Some authors have not found any differences between sevoflurane and propofol[2,4], whereas others favor one anesthetic over the other because of their alleged good action on hemodynamic stability[5].

The aim of this study was to compare the effect of sevoflurane and propofol on myocardial contractility. The investigated drugs were administered using a noninvasive technique of transesophageal echo -Doppler (TEED) during laparotomic cholecystectomy.

Patients and Methods

Patients

In a prospective randomized clinical study, forty patients were monitored between April 10 and December 1, 2002. The Hospital Ethical Committee had approved the study protocol. All the participants had been informed about the investigation and had signed the Informed Consent before the surgery. Of forty patients included in the study, 20 were randomly assigned to the sevoflurane group: 10 male and 10 female subjects, aged between 25 and 64 years (median value 45). Other 20 patients, 10 male and 10 female, aged between 35 and 62 (median value 49), formed the propofol group. Before the measurements body surface area (BSA) was calculated for each patient, and its median values were calculated for each group. It was 1.9 m^2 (1.7–2.3 m^2) in the sevoflurane group and 1.8 m^2 (1.7–2.0 m^2) in the propofol group.

All the study subjects had to conform to the following preoperative inclusion criteria: a laparotomic cholecystectomy for which general anesthesia and tracheal intubation, not longer than one hour, were indicated. Finally, all the patients were classified using the ASA physical status in the class I and class II.

The exclusion criteria were: any confirmed esophagus disease that could compromise the insertion of TEED (such as a confirmed esophageal carcinoma, esophagitis or dilated distal venous plexus of the esophagus)[6]. Furthermore, excluded were also all patients in whom preoperative data on a suspected development of malignant hyperthermia on halogenated anesthetics in earlier anesthesias were unclear.

Anesthesia

All patients received premedication half an hour before the surgery. As premedication, midazolam (Dormicum®, F.

Hoffman-La Roche Ltd., Basel, Switzerland), in an IM dose of 0.07–01 mg/kg was prescribed. For the induction of anesthesia, both patient groups received the same protocol: propofol (Propofol®, Fresenius Kabi South Africa Ltd., Vorna Valley, Midrand) 1–2 mg/kg IV, fentanyl (Fentanyl®, Janssen Pharmaceutica, Beerse, Belgium) 3–5 μg/kg IV, and pancuronium -bromide (Pavulon®, N. V. Organon, Oss, the Netherlands) 0.08–0.12 mg/kg IV.

For the maintenance of anesthesia in the sevoflurane group, 35% of O_2 and 65% of air were used, up to the total gas-flow of 3 L/min and 1.5–3% of sevoflurane (Sevorane®, Abbott Laboratories, S.A., Abbott Park, IL, USA) to achieve approximately 2.0% of the minimal alveolar concentration (MAC).

In the propofol group, patients received a complete protocol of intravenous maintenance of anesthesia. Anesthesia was established by continuous infusion of propofol in the dose of 100 μg/kg/min, accompanied by usual doses of the 35% O_2 and 65 % of air up to the total gas-flow of 3 L/min. If it was necessary, both groups received bolus doses of fentanyl 2–3 μg/kg and 0.02 mg/kg of pancuronium-bromide.

Transesophageal echo-Doppler

Immediately after the induction of anesthesia, the transducer of TEED probe HemoSonic™100 Hemodynamic Monitor (Arrow International®) was inserted through the mouth or the nose and positioned in the esophagus, at the approximate level of Th5-Th6 thoracic vertebrae[7]. At this level, the aorta runs parallel with the esophagus for about 5 cm and the highest density of signal in TEED probe can be achieved.

Before the insertion of the transesophageal echo-Doppler transducer, a disposable biocompatible sterile elastomer sheath is mounted on it. The sheath is filled with a sterile ultrasound gel that ensures the transmission of ultrasound waves without air interposition. The transducer with the sheath is compressed by the naturally contracting esophageal wall, which immobilizes the transducer in the esophagus, directing the ultrasound sensors towards their aortic target[8]. The transducer-sheath assembly can be used with a naso-gastric tube inserted *in situ*, without disturbing echo-Doppler signals[9,10].

The cylindrical transducer handle can rotate axially under external manual control. Finally, the transducer handle is secured by a fixed arm attached to the operating table or bedside.

Hemodynamic monitoring

Hemodynamic parameters measured were the following: heart rate (HR), cardiac index (CI), stroke volume (SV), left ventricular ejection time (LVET) and, finally, acceleration (Acc) as a sensitive indicator of global LV performance and myocardial contractility[11]. Acceleration measures the rate of change of blood velocity just at the moment of the aortic valve opening[12,13]. Mean arterial pressure (MAP) was measured by means of a noninvasive technique using the arm tourniquet cuff, automatically cuffed every minute by the pressure monitor device.

Measurements were performed three times during anesthesia. The initial measurement was performed 10 minutes after the induction of anesthesia. The second measurement was performed 1 minute after the incision and the final measurement 25 minutes after the incision.

Statistics

Computational statistics was done using SPSS for Windows (release 7.5, SPSS Inc., Chicago, IL, USA). Numerical data were presented by means and standard deviations. Initial measurements between patient groups were compared using paired t-test, while all measurements were simultaneously compared using general

linear model (GLM) analysis of variance for repeated measurements (ANOVA). Using this model, between- subject statistics was accomplished to test the difference in parameter values between two patient groups, while within-subject statistics was done to compare repeated measurements. If the differences were significant, initial parameter values were compared with repeated measurements (contrast). Both statistics obtained using ANOVA were presented with the values of F-distribution and probability p. In all the tests only two-tailed p-values lower than 0.05 were considered significant.

Results

In the initial measurement of hemodynamic parameters there was no statistical significance between the patient groups (Table 1).

The initial values of all measured hemodynamic parameters were statistically significantly higher in comparison with the values estimated during the next two measurements (Table 2, within-subject effect, $p<0.001$ for all).

A statistically significant decrease of HR was observed. In the sevoflurane group, HR decreased from 75 beats/min to 70 beats/min and to 69 beats/min respectively ($p=0.001$) and in the propofol group, a similar statistically significant decrease in the HR was found – from 76 beats/min to 75 beats/min in both latter measurements ($p=0.001$). Although all three measurements showed lower values of HR in the sevoflurane group, these values were not statistically significantly different in comparison with HR values in the propofol group (Table 2, $p=0.090$).

The values of CI, Acc and SV showed the signs of myocardial depression in all the estimated values, when compared with the initial values of these parameters in both groups of patients. Cardiac index values decreased from 2.44 L/min/m^2 in the initial measurement, through 2.09 L/min/m^2 to 2.08 L/min/m^2 in the propofol group. In the sevoflurane group, CI decreased from 2.42 L/min/m^2 in the initial measurement to 2.21 L/min/m^2, and to 2.13 L/min/m^2 respectively (Table 2).

The initial acceleration value in the propofol group was 7.63 m/s^2, and this value decreased to 6.81 m/s^2 and to 6.46 m/s^2 over the measurements. The values of acceleration in the sevoflurane group changed from 7.38 m/s^2 in the initial measurement, through 6.92 m/s^2, to 6.82 m/s^2 (Table 2). Neither CI nor Acc showed statistically significant difference when compared between two groups ($p=0.348$ for CI, and $p=0.780$ for Acc), although the decrease of CI and Acc were strongly expressed in the propofol group.

In the sevoflurane group, stroke volume values were higher than in the propofol group. The measured values chan-

TABLE 1
HEMODYNAMIC VALUES (MEAN ± SD) AT INITIAL MEASUREMENT IN PATIENTS IN SEVOFLURANE (N=20) AND PROPOFOL GROUP (N=20)

Hemodynamic parameters	Patient groups		Statistics	
	Sevoflurane	Propofol	t	p
Heart rate (beats/min)	75 ± 7	76 ± 8	–0.273	0.786
Cardiac index (L/min/m^2)	2.42 ± 0.13	2.44 ± 0.20	–0.379	0.707
Acceleration (m/s^2)	7.38 ± 1.29	7.63 ± 0.82	–0.719	0.477
Left ventricular ejection time (ms)	413 ± 6.29	411 ± 10.80	0.716	0.479
Stroke volume (ml/beat)	66 ± 6.2	64 ± 8.9	0.659	0.514

TABLE 2
PARAMETER VALUES IN SEVOFLURANE (N=20) AND PROPOFOL GROUP (N=20)

Variable	Patient groups		Measurements (X±SD)			Statistics[a]	
			Initial	After incision 1 min.	25 min.	Between-subject effect F	p
Heart rate (beats/min)		Sevoflurane	75±7	70±7	69±7	3.0	0.090
		Propofol	76±8	75±9	75±8		
	Statistics[b]	Within-subject effect (F, p)	9.8, p<0.001				
		Within-subject contrast (F, p)	11.9, p<0.001	12.0, p<0.001			
Cardiac index (L/min/m^2)		Sevoflurane	2.42±0.13	2.21±0.19	2.13±0.15	0.90	0.348
		Propofol	2.44±0.20	2.09±0.21	2.08±0.19		
	Statistics[b]	Within-subject effect (F, p)	145.43, p<0.001				
		Within-subject contrast (F, p)	255.11 p<0.001	248.53 p<0.001			
Acceleration (m/s^2)		Sevoflurane	7.38±1.29	6.92±0.84	6.82±0.98	0.08	0.780
		Propofol	7.63±0.82	6.81±0.63	6.46±0.67		
	Statistics[b]	Within-subject effect (F, p)	46.58, p<0.001				
		Within-subject contrast (F, p)	38.92 p<0.001	59.32 p<0.001			
Stroke volume (mL/beat)		Sevoflurane	66±6.2	65±6.4	63±5.6	4.26	0.046
		Propofol	64±8.9	58±10.5	58±8.6		
	Statistics[b]	Within-subjects effect (F, p)	17.06, p<0.001				
		Within-subject contrast (F, p)	14.54 p<0.001	22.30 p<0.001			
Left ventricular ejection time (ms)		Sevoflurane	411±10.80	407±12.15	407±9.75	0.55	0.464
		Propofol	413±6.29	411±6.54	407±6.06		
	Statistics[b]	Within-subjects effect (F, p)	16.43, p<0.001				
		Within-subject contrast (F, p)	5.93 p<0.001	30.88 p<0.001			

[a] Between subject statistics in repeated measures analysis of variance
[b] Within subject statistics in repeated measures analysis of variance

ged from 66 ml/beat in the initial measurement to 65 ml/beat and to 63 ml/beat in the sevoflurane group at the end of the measurement, while the values in the propofol group decreased from 64 ml/beat to 58 ml/beat for both measurements. Stroke volume was statistically significantly higher in the sevoflurane group in comparison with the propofol group (between-subject effect; $F = 4.26$, $p<0.05$).

Finally, there was no statistical significance in the reduction of LVET values between the groups. Lower values were observed in the sevoflurane group (411 ms in the initial measurement, and reduced to 407 ms in both later measurements) than in the propofol group, where the initial value was 413 ms and decreased to 411 ms and to 407 ms respectively (between-subject effect; $F = 0.55$, $p =0.464$).

Discussion

In literature, there is a small number of studies, which compare the influence of sevoflurane and propofol on myocardial contractility. Hemodynamic effects of sevoflurane and propofol have been well documented in animals[14] and healthy humans, but not significantly higher values of SV in sevoflurane anesthesia than in propofol anesthesia. Statistical significance was not noted in the increase of CI in the sevoflurane group compared to the propofol group. This observation could be explained by the higher heart rate in the sevoflurane group. A depressive anesthetic action on myocardial function in the present study was confirmed by the finding of LVET and Acc reduction. These reductions were strongly expressed in the propofol group, but without statistical significance when compared with the sevoflurane group.

Regardless of a negative inotropic effect, in both patient groups there was no registered significant hypotension (lowering of the MAP for more than 20% in relation with the initial values), or need for the drug treatment of hypotension.

The clinical implication of this observation, that propofol and sevoflurane impair left ventricular inotropy, but improve myocardial function by Frank-Sterling mechanism was corroborated in the present investigation.

Similarly to the present results, Ozkose et al.[4] reported bradycardia during the use of sevoflurane and propofol in patients undergoing neurosurgical procedures.

In contrast to Junckenhofel et al.[1], our results did not confirm a better hemodynamic stability during propofol anesthesia, in comparison with sevoflurane, or hypotension in either study group[15].

Our findings of higher values of SV, constant values of Acc and lower heart rate with previously known cardioprotective effect on the myocardium[16] in the sevoflurane group suggest that sevoflurane could be the anesthetic of choice in abdominal surgery, especially in patients with a previously known compromised cardiovascular function[17].

Thwaites et al.[18] studied sevoflurane and propofol as induction agents for the day-case cystoscopy in 102 patients. In contrast to the present study, these authors had found an increase of HR with each agent, but without significant differences between their groups. This finding could be explained by the absence of adequate premedication in their study. Increased HR values were also reported by El-Orbany et al.[19]. An increase in HR or the development of tachycardias during anesthesia could be hemodynamically considerable, because, they can produce myocardial ischemia, especially in patients with a previously compromised cardiovascular function[20,21].

Inada et al.[22] reported an increase in heart rate, pulmonary capillary wedge

pressure, mean pulmonary arterial pressure and systemic vascular resistance, as a response to the surgical incision at 1.5 MAC. Due to this, the authors concluded that sevoflurane at 1.5 MAC could not prevent the hemodynamic response to the surgical incision.

On the other hand, sevoflurane, as an inhalation anesthetic, has a different pharmacodynamic effect from intravenous anesthetics. In contrast to intravenous anesthetics, sevoflurane advantages lie in the induction to anesthesia, awakening prudence, maintenance of anesthesia and, finally, a lower price compared with other anesthetics[18]. All these reasons make sevoflurane one of good alternatives and substitutions for propofol.

The limitation of this study is that could not be possible to perform exact estimation of patients' response on incision. Both effects of incision and anesthetics, for now, it is not possible to clearly separate. This part will be of interest for further investigations. Further limitations of this study were a small number of patients and, because of the type of surgical procedure, a specific patient population.

In conclusion, sevoflurane ensures a better patient hemodynamic stability in comparison with propofol during laparotomic cholecystectomy.

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HEMODINAMSKE RAZLIKE SEVOFLURANSKE I PROPOFOLSKE ANESTEZIJE

S A Ž E T A K

Cilj ispitivanja bio je usporediti učinak sevofluranske i propofolske anestezije na kontraktilitet miokarda tijekom kolecistektomije pomoću transezofagusnog eho-Doplera. U ovome ispitivanju 40 bolesnika randomizirano je prema vrsti anestezije na sevofluransku i propofolsku skupinu. Hemodinamski parametri: frekvencija srca, indeks srca, udarni volumen, izbačajno vrijeme lijevoga ventrikula i akceleracija izmjereni su 10 minuta nakon indukcije anestezije, 1 minuta i 25 minuta nakon incizije. Rezultati su analizirani parnim t-testom i analizom varijance. Znakovito su snižene sve vrijednosti hemodinamskih parametara unutar obiju skupina bolesnika izmjerene 1 minuta i 25 minuta nakon incizije ($p<0.05$). U sevofluranskoj skupini udarni volumen smanjio se sa 66±6.2 mL/udarac na 65±6.4 mL/udarac i 63±5.6 mL/udarac nakon 1 minute i 25 minuta nakon incizije. U propofolskoj skupini udarni volumen smanjio se sa 64±8.9 mL/udarac na 58±10.5 mL/udarac i 58±8.6 mL/udarac. Udarni volumen bio je znakovito veći u sevofluranskoj nego u propofolskoj skupini ($p<0.05$). Sevofluranska anestezija osigurava bolju hemodinamsku stabilnost tijekom kolecistektomije.