The effects of sevoflurane and propofol on cerebral hemodynamics during intracranial tumors surgery under monitoring the depth of anesthesia

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Summary. *Hemodynamic effects during cerebral tumor resection surgery under monitoring the depth of anesthesia and during recovery in sevoflurane- or propofol-anesthetized patients have not been previously compared.*

Objective. To compare cerebral hemodynamic changes using transcranial Doppler sonography during sevoflurane or propofol anesthesia under state entropy (SE) monitoring, and during recovery period.

Material and methods. In a randomized manner, 130 patients received sevoflurane (group T-S) or propofol (group T-P) to maintain SE at 40–50. Cerebral blood flow velocity (Vmean) in the middle cerebral artery was evaluated at baseline, after tracheal intubation, opening of the dura mater, tumor resection, skin closure, extubation, and two hours after extubation. Cerebrovascular resistance index (RAP), estimated cerebral perfusion pressure (eCPP), and cerebral blood flow index (CBFI) were calculated off-line.

Results. During surgery SE was 40.6 (SD, 8.1) in the group T-S and 44.0 (SD, 7.4) in the group T-P. Blood pressure was significantly higher in the group T-P. Compared to the baseline, Vmean decreased by 16.6% and 23.5% in the groups T-S and T-P, respectively (P<0.05). RAP and eCPP were higher in the group T-P versus the group T-S: 28.9% and 5.2%, respectively, above the baseline for RAP (P<0.005) and 3.2% and 16.9% below the baseline for eCPP (P<0.005). CBFI was below the baseline by 20.1% and 24.0% in the groups T-S and T-P, respectively (P>0.05). After the extubation and 2 hours later, Vmean recovered comparably with no differences in RAP, eCPP, or CBFI between the two groups.

Conclusions. At the comparable depth of anesthesia for intracranial tumors surgery and during recovery, sevoflurane had no major effect on cerebral circulation measured by transcranial Doppler sonography as compared with propofol. Our results add to current knowledge on the safety of sevoflurane in neuroanesthesia.

Introduction

Anesthesia for intracranial neurosurgical procedures must provide hemodynamic stability, maintenance of cerebral perfusion pressure, control of intracranial pressure, producing slack brain and good conditions for surgery. Anesthesiologists must plan smooth emergence, rapid awakening, and early neurological assessment of the patient in the postoperative period.

Both volatile and intravenous anesthetic agents are used for maintenance of anesthesia during neurosurgical procedures. Balanced general anesthesia with sevoflurane or propofol has been widely accepted as anesthetic management for patients undergoing craniotomy for supratentorial intracranial tumors surgery because both of them demonstrate similar characteristics for anesthetic induction, maintenance, emergence time, and early cognitive function (1, 2). Cerebral vasodilatory effect of sevoflurane is dose dependent and less evident when compared with other inhalational agents (3–5). Conversely, propofol is not associated with a significant modification of cerebral hemodynamics and demonstrates possible avoidance of the undesirable effects in neuroanesthesia (6–8). What anesthetic, inhalational or intravenous, is preferable for craniotomies is still under discussion (9–11).

Transcranial Doppler ultrasonography (TCD) is

a noninvasive tool allowing for bedside monitoring to determine blood flow velocities indicative of changes in vascular caliber. Aaslid and colleagues introduced TCD for monitoring blood flow velocity in the basal cerebral arteries in 1982 (12) and described the method for estimation of cerebral perfusion pressure from arterial blood pressure and transcranial Doppler recordings in 1986 (13). Transcranial Doppler ultrasonography can be useful pre-, intra-, and postoperatively helping to recognize the development of cerebral vasospasm or increased intracranial pressure (ICP) and disturbance of cerebral blood flow (CBF) before the onset of its clinical effects (14, 15).

The aim of this prospective randomized study was to compare the influence of sevoflurane and propofol on cerebral hemodynamic changes measured by TCD during intracranial tumor surgery at the same depth of anesthesia.

Material and methods

The study protocol was approved by the Local Bioethics Committee of the Lithuanian University of Health Sciences (former Kaunas University of Medicine), Lithuania, in 2006. The study was prospectively carried out at the Department of Anesthesiology and the Department of Neurosurgery, Hospital of the Lithuanian University of Health Sciences. Inclusion criteria for patient enrollment were as follows: ASA status I–III, age of 18–75 years, Glasgow Coma Scale (GCS) score of 15, first-time elective surgery for supratentorial intracranial tumors. Exclusion criteria were as follows: recraniotomy, severe intracranial hypertension (more than 5-mm midline shift on the computed tomography scan with altered sensorium), the history of cerebrovascular disorders, GCS score <15, body mass index >30, pregnancy, known allergy to any anesthetic agent, history of drug or alcohol abuse, family or personal history of malignant hyperthermia.

After giving written informed consent, 135 patients were enrolled into the study. Using sealed, opaque envelopes, patients were allocated to one of the two study groups to be anesthetized with either sevoflurane (group T-S) or propofol (group T-P). Five patients (3 in the sevoflurane group and 2 in the propofol group) were later excluded due to lack of an acoustic window for the Doppler measurements. Thus, 130 patients completed the study.

Anesthesia. All the patients received 7.5-mg midazolam for premedication orally 1–1.5 h before anesthesia induction. After preoxygenation with 100% oxygen, anesthesia was induced with 1–2.5 mg/kg of propofol and 2–3 μg/kg of fentanyl. Muscle relaxation was induced with 0.06–0.09 mg/kg of pipecuronium according to neuromuscular transmission monitoring, and patient's trachea was intubated.

During surgery in the group T-S, end-tidal concentration of sevoflurane was maintained at 0.5–1.8%. In the group T-P, the rate of continuous propofol infusion was 1.5–8.5 mg·kg^{-1}·h^{-1}. The dose of sevoflurane and propofol was titrated to maintain surgical level of the depth of anesthesia (value of state entropy index, 40–50).

All the patients were given fentanyl at a rate of 1–3 μg·kg^{-1}·h^{-1} and bolus of 1 μg/kg if indicated. Pipecuronium at a dose of 1–2 mg was administered to maintain the train-of-four (TOF) ratios below 10%. The patients were mechanically ventilated with an air/oxygen mixture (FiO$_2$ 0.35–0.4) to mild hypocapnia or normocapnia (end-tidal CO$_2$ [ET-CO$_2$], 30–35 mm Hg). An infusion of isotonic saline (10±3 mL·kg^{-1}·h^{-1}) was started for all the patients after arrival to the operating room. At the end of surgery, residual neuromuscular blockade was antagonized with 2-mg neostigmine and 1-mg atropine. Fentanyl infusion was stopped after skin closure, while the administration of sevoflurane and propofol was continued until head bandaging was completed. After emergence, all patients were extubated and followed up in an intensive care unit (ICU).

Intraoperative monitoring included continuous electrocardiogram, heart rate (HR), noninvasive systolic (SBP), diastolic (DBP), and mean (MBP) arterial blood pressures, peripheral oxygen saturation (SpO$_2$), ET-CO$_2$, end-tidal anesthetic agent (ET$_{SEVO}$), core temperature in the middle of the esophagus (T).

The depth of anesthesia (state entropy, SE, and response entropy, RE) was measured by entropy module E-Entropy® in Avance Carestation®. SE values vary between 0 (suppressed EEG activity) and 91 (indicating an awake state). RE values vary between 0 and 100. The recommended range for adequate anesthesia for both the parameters is from 40 to 60 (16). Following induction of anesthesia and until emergence, we aimed to maintain anesthesia level between 40 and 50 for all the patients.

Monitoring of cerebral hemodynamics. A 2-MHz transcranial Doppler ultrasound probe of portable TCD system Smart-Lite™ (Rimed Ltd, Raanana, Israel) was used to measure the time-averaged systolic (Vsyst), diastolic (Vdiast), and mean (Vmean) blood flow velocities in the middle cerebral artery. After patient's arrival to the operating room, the middle cerebral artery was insonated on the opposite side as craniotomy through the temporal window. The best signal was obtained at the depth of 45–55 mm and confirmed using standard criteria (12). The place of the Doppler transducer was marked on the skin, and the probe was secured in position using a specially designed holder so that the angle of insonation remained constant throughout the study

period. Measurements were taken continuously and recorded at selected time points as required by the study protocol. We calculated cerebral hemodynamic parameters based on the following equations introduced by Aaslid et al. (13), modified by Belfort et al. (17), and used by others (18, 19) off-line:

Estimated cerebral perfusion pressure (eCPP)= Vmean×(MBP-DBP)/(Vmean−Vdiast);

Resistance area product (RAP)=MBP/Vmean;

Cerebral blood flow index (CBFI)=eCPP/RAP.

Measurements were recorded at seven time points: point 1, arrival to the operating room (baseline); point 2, after induction and tracheal intubation at the surgical level of the depth of anesthesia (after intubation); point 3, after craniotomy and opening of the dura mater; point 4, after intracranial tumor resection; point 5, end of surgery after skin closure; point 6, after extubation and early neurological assessment (after extubation); and point 7, two hours after extubation in the intensive care unit (ICU).

Statistical analysis. We calculated that approximately 49 patients would be needed to detect a 10-cm/s difference of Vmean between the groups with the power of 90% and α level of 0.05, with the assumed SD of 15 cm/s in the outcome variables. The data were recorded on a computer using SPSS for Windows 13.0.1 statistical software (SPSS Inc., Chicago, IL, USA). Parameters were evaluated using the Kolmogorov-Smirnov test for the normality of distribution and Levene's test for homogeneity. Data were expressed as mean and standard deviation (SD). The mean intraoperative value (study points 3, 4, and 5) was calculated and compared between the groups using Student t test. Significant differences between groups were expressed as the mean difference and confidence interval (95% CI). The mean percentage difference from baseline was calculated and compared using Student t test between the study groups. For the assessment of changes within the same group and differences between groups at each time point, a paired t test was used.

The χ^2 test was used for nonparametric data. The differences were considered statistically significant when P values were less than 0.05.

Results

One hundred thirty patients were recruited (65 in each group). There were no statistically significant differences between the two groups with respect to demographical characteristics (sex, age, BMI), ASA physical status, duration of anesthesia and surgery (Table 1).

During anesthesia, the mean end-tidal sevoflurane concentration (ET_{SEVO}) was 1.12% (SD, 0.31%), and propofol was administered at a mean rate of 4.32 mg·kg^{-1}·h^{-1} (SD, 1.36 mg·kg^{-1}·h^{-1}). The relative consumption of fentanyl was 2.19 μg·kg^{-1}·h^{-1} (SD, 0.52) in the group T-S and 2.46 μg·kg^{-1}·h^{-1} (SD, 0.50) in the group T-P ($P<0.005$). Changes in the SE and RE throughout the study period are shown in Table 2. Anesthesia was slightly deeper in the group T-S.

Intraoperative ET-CO$_2$ and core temperature, systolic and diastolic blood pressures, systolic and diastolic blood flow velocities are shown in Table 2.

The mean blood pressure throughout the study is shown in Fig. 1. The mean (SD) blood pressure during the maintenance of anesthesia (study points 3, 4, and 5) was 89.9 mm Hg (9.9 mm Hg) in the group T-S and 99.6 mm Hg (10.6 mm Hg) in the group T-P ($P<0.005$) with a mean difference of 9.6 mm Hg (95% CI, 6.1–13.2 mm Hg) and it was by 12.7% below the baseline in the group T-S compared to 2.7% in the group T-P ($P<0.005$). After the extubation, MBP recovered and was 1.7% below the baseline in the group T-S and 0.6% below the baseline in the group T-P ($P>0.05$). Two hours after the extubation, MBP was 12.0% and 8.9% below the baseline, respectively ($P>0.05$).

The mean flow velocities in the middle cerebral artery are shown in Fig. 2. Vmean decreased in the same manner in both the groups. During surgery, the mean (SD) Vmean (study points 3, 4, and 5) was 43.7 cm/s (12.3 cm/s) in the group T-S and

Table 1. Demographical data, ASA physical status, and duration of anesthesia and surgery

Variable	Group T-S (n=65)	Group T-P (n=65)	P value
Sex: Female, n (%)	42 (64.6)	45 (69.2)	0.58
Male, n (%)	23 (35.40)	20 (30.8)	
Age, mean (SD), years	50.7 (14.7)	53.7 (13.6)	0.24
Body mass index, mean (SD), kg/m^2	26.0 (3.2)	25.0 (3.1)	0.09
ASA class I, n (%)	9 (13.8)	8 (12.3)	
ASA class II, n (%)	47 (72.4)	48 (73.9)	0.97
ASA class III, n (%)	9 (13.8)	9 (13.8)	
Duration of surgery, mean (SD), min	185.0 (58.7)	182.7 (53.7)	0.81
Duration of anesthesia, mean (SD), min	234.3 (69.8)	228.7 (58.5)	0.62

Group T-S, brain tumor resection under sevoflurane anesthesia; group T-P, brain tumor resection under propofol anesthesia.

Table 2. Changes in the absolute values of physiologic and hemodynamic parameters throughout the study period

| Variable | Group | Baseline (1) | After intubation (2) | Maintenance of anesthesia | | | After extubation (6) | 2 h after extubation (7) |
				After dura mater opening (3)	After tumor resection (4)	After skin closure (5)		
SE	T-S	87.7 (2.1) #	40.7 (10.3)*	40.9 (8.1)*#	41.3 (9.1)*	39.8 (10.1)*#	86.0 (3.6)*	ND
	T-P	88.3 (1.7)#	43.8 (8.4)*	44.2 (8.1)*#	43.5 (8.1)*	44.2 (9.1)*#	86.7 (3.2)*	ND
RE	T-S	97.1 (1.8)	42.5 (10.3)*	42.4 (8.5)*	43.0 (9.5)*	42.0 (10.9)*#	95.7 (3.5)*	ND
	T-P	97.2 (1.7)	45.6 (8.4)*	45.5 (9.7)*	45.9 (8.4)*	47.1 (9.5)*#	95.5 (3.7)*	ND
ET-CO$_2$, mm Hg	T-S	ND	31.12 (2.66)	30.09 (1.43)*	30.72 (1.70)	30.72 (1.76)	ND	34.4 (3.3)[a]*
	T-P	ND	31.20 (2.50)	30.25 (1.71)*	30.75 (1.70)	31.15 (2.02)	ND	34.5 (3.9)[a]*
Temperature, °C	T-S	ND	36.45 (0.25)	36.18 (0.26)*	36.30 (0.28)*	36.49 (0.30)	ND	36.68 (0.23)*
	T-P	ND	36.41 (0.29)	36.17 (0.28)*	36.31 (0.34)*	36.49 (0.32)	ND	36.65 (0.23)*
SBP, mm Hg	T-S	136.4 (21.2)	112.5 (19.9)*	119.3 (18.5)*#	120.6 (15.1)*#	114.5 (14.9)*#	137.4 (18.3)	124.5 (16.1)*
	T-P	136.6 (19.3)	111.1 (18.0)*	131.9 (19.1)#	134.8 (17.1)#	128.5 (17.0)*#	136.7 (17.1)	128.4 (15.7)*
DBP, mm Hg	T-S	80.3 (11.2)	66.4 (12.1)*	71.9 (11.4)*#	72.8 (11.9)*#	69.3 (12.2)*#	78.5 (10.8)	73.3 (11.5)*
	T-P	80.1 (10.5)	67.0 (12.4)*	78.0 (12.5)#	79.9 (11.0)#	76.3 (12.6)*#	78.4 (11.6)	74.6 (10.1)*
Vsyst, cm/s	T-S	73.3 (18.6)	58.0 (15.7)*	60.0 (18.2)*	60.6 (18.1)*	62.0 (19.3)*	84.7 (23.9)*	82.4 (23.7)*
	T-P	77.2 (20.6)	59.1 (16.0)*	58.6 (16.8)*	59.9 (18.9)*	60.8 (16.9)*	87.6 (23.8)*	84.7 (22.7)*
Vdiast, cm/s	T-S	33.0 (9.4)	24.7 (7.6)*	26.6 (8.8)*	27.7 (8.9)*	28.2 (9.1)*	38.8 (12.0)*	33.9 (9.5)
	T-P	35.4 (10.0)	25.6 (7.6)*	25.8 (7.0)*	27.3 (8.1)*	27.4 (7.1)*	39.9 (12.3)*	35.8 (9.8)

Data are given as mean (SD). Group T-S, brain tumor resection under sevoflurane anesthesia; group T-P, brain tumor resection under propofol anesthesia; SE, state entropy; RE, response entropy; ET-CO$_2$, end-tidal CO$_2$; T, core temperature; SBP, systolic blood pressure; DBP, diastolic blood pressure; Vsyst, systolic blood flow velocity; Vdiast, diastolic blood flow velocity. [a]Value is PaCO$_2$. ND, not determined (measurements of end-tidal CO$_2$ [ET-CO$_2$] and core temperature [T] before anesthesia induction and just after extubation were not made; the depth of the anesthesia [SE, RE] was not measured after 2 h after extubation in the ICU).
 *$P<0.05$ compared to the baseline by paired t test (ET-CO$_2$ and T compared to the time point 2).
 #$P<0.05$ between the groups by paired t test.

42.8 cm/s (11.6 cm/s) in group T-P ($P>0.05$). This was by 16.6% below the baseline in the T–S versus 23.5% in the T–P group ($P<0.05$). After the extubation, Vmean increased by 18.3% in the group T-S and by 12.9% in the group T-P as compared to the baseline ($P>0.05$). Two hours after the extubation, Vmean was similar in both the groups: it was

by 10.0% and 6.7%, respectively, above the baseline ($P>0.05$).

Changes in RAP are shown in Fig. 3. During surgery (study points 3, 4, and 5), the mean (SD) RAP was significantly higher in the group T-P as compared to the group T-S (2.50 mm Hg·cm^{-1}·s^{-1}) [0.68 mm Hg·cm^{-1}·s^{-1}] versus 2.22 mm Hg·cm^{-1}·s^{-1}
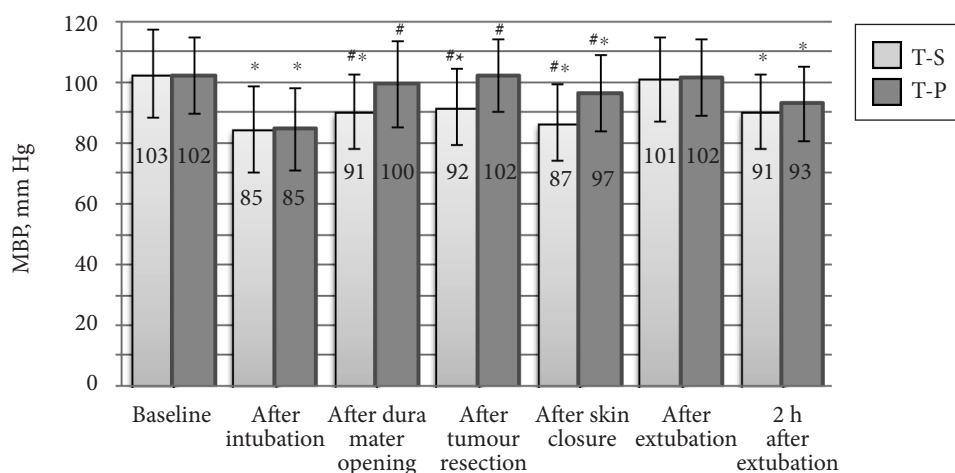

Fig. 1. Changes in the absolute values of the mean blood pressure (MBP) in the groups T-S and T-P throughout the study period
Group T-S, brain tumor resection under sevoflurane anesthesia (n=65); group T-P, brain tumor resection under propofol anesthesia (n=65). MBP (mm Hg) is shown as means (numbers) and standard deviation (error bars).
*$P<0.05$ compared to the baseline by paired t test. #$P<0.05$ between the groups by paired t test.
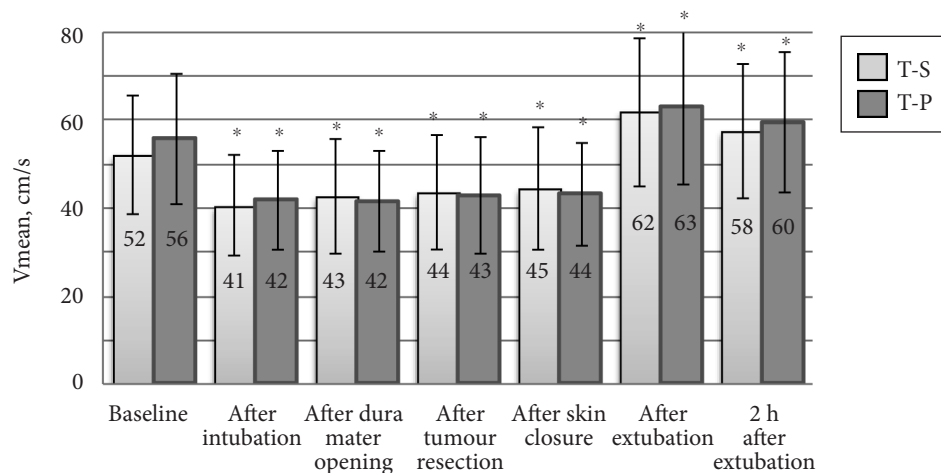
Fig. 2. Changes in the absolute values of the mean blood flow velocity (Vmean) in the groups T-S and T-P throughout the study period
Group T-S, brain tumor resection under sevoflurane anesthesia (n=65); group T-P, brain tumor resection under propofol anesthesia (n=65). Vmean (cm/s) in the middle cerebral artery is shown as means (number) and standard deviation (error bars).
*$P<0.05$ compared to baseline by paired *t* test.

[0.61 mm Hg·cm^{-1}·s^{-1}]; $P<0.05$) and was above the baseline by 28.9% in the group T–P versus 5.2% in the group T–S ($P<0.005$). After the extubation, RAP was by 10.3% below the baseline in the group T–P versus 15.6% below baseline in the group T–S ($P>0.05$). RAP was similar in both the groups also 2 hours after extubation: 19.4% and 13.4% below the baseline in the groups T–S and T–P, respectively ($P>0.05$).

The estimated cerebral perfusion pressure throughout the study is shown in Fig. 4. During surgery (study points, 3, 4, and 5), the mean (SD) eCPP was higher in the group T–P (58.8 mm Hg [14.0 mm Hg]) than the group T–S (50.7 mm Hg

[12.3 mm Hg]) ($P<0.005$) with a mean difference of 8.1 mm Hg (95% CI, 3.5–12.7 mm Hg). This was 3.2% below the baseline in the group T–P and 16.9% below the baseline in the group T–S ($P<0.005$). After the extubation, eCPP was 0.8% below the baseline in the sevoflurane group and 4.5% above the baseline in the propofol group ($P>0.05$). Two hours after the extubation, eCPP was 30.3% below the baseline in the group T–S and 23.1% in the group T–P ($P>0.05$).

Changes in CBFI are presented in Fig. 5. There were no overall differences between the groups. The mean (SD) CBFI within the middle cerebral artery territory decreased comparably in both the groups
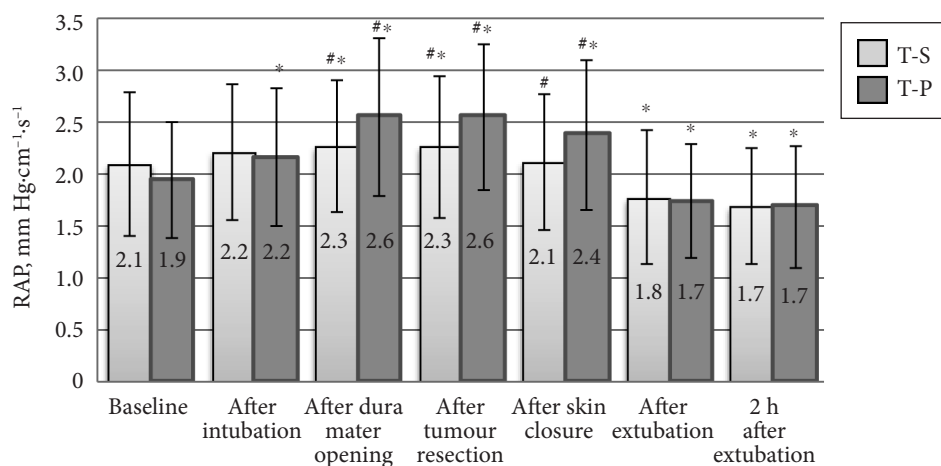

Fig. 3. Changes in the absolute values of the resistance area product (RAP)=MBP/Vmean in the groups T-S and T-P throughout the study period
Group T-S, brain tumor resection under sevoflurane anesthesia (n=65); group T-P, brain tumor resection under propofol anesthesia (n=65); MBP, mean blood pressure; Vmean, mean flow velocity in the middle cerebral artery.
RAP (mm Hg·cm^{-1}·s^{-1}) is shown as means (numbers) and standard deviation (error bars).
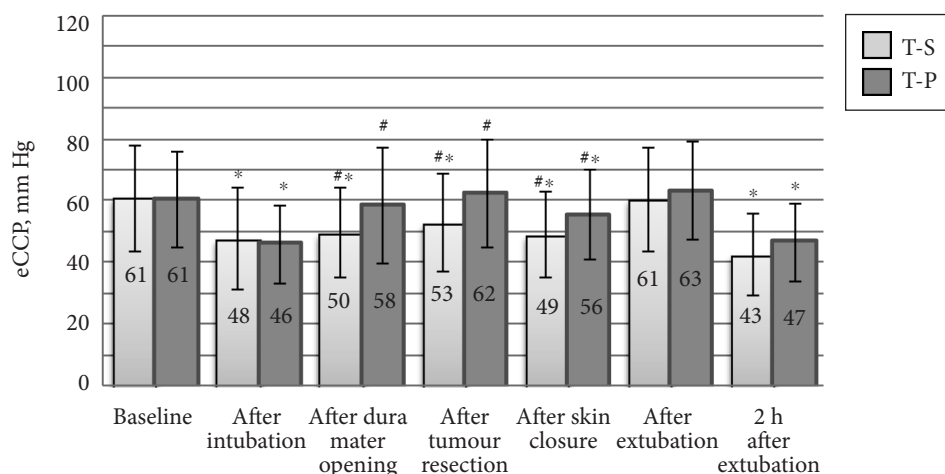*$P<0.05$ compared to the baseline by paired *t* test. #$P<0.05$ between the groups by paired *t* test.

Fig. 4. Changes in the absolute values of the estimated cerebral perfusion pressure (eCPP)=Vmean×(MBP–DBP)/(Vmean–Vdiast)
in the groups T-S and T-P throughout the study period

Group T-S, brain tumor resection under sevoflurane anesthesia (n=65); group T-P, brain tumor resection under propofol anesthesia (n=65). MBP, the mean blood pressure; DBP, diastolic blood pressure; Vmean, the mean blood flow velocity; Vdiast, diastolic blood flow velocity in the middle cerebral artery. eCPP (mm Hg) is shown as means (number) and standard deviation (error bars).
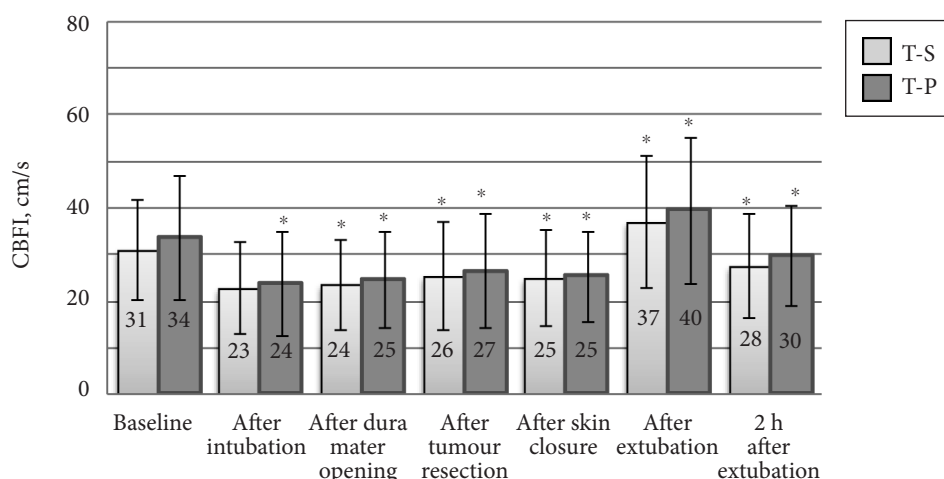*$P<0.05$ compared to the baseline by paired t test. #$P<0.05$ between the groups by paired t test.

Fig. 5. Changes in the absolute values of the cerebral blood flow index (CBFI)=eCPP/ RAP in the groups T-S and T-P
throughout the study period

Group T-S, brain tumor resection under sevoflurane anesthesia (n=65); group T-P, brain tumor resection under propofol anesthesia (n=65); eCPP, estimated cerebral perfusion pressure (mm Hg); RAP, resistance area product (mm Hg·cm^{-1}·s^{-1}).
CBFI (cm/s) is shown as means (number) and standard deviation (error bars).
*$P<0.05$ compared to the baseline by paired t test.

and remained similar throughout the maintenance of anesthesia (study points 3, 4, and 5): it was 20.1% and 24.0% below the baseline in the groups T–S and T-P, respectively (24.8 cm/s [9.5 cm/s] and 25.5 cm/s [9.8 cm/s], $P>0.05$). After the extubation, CBFI exceeded the baseline values by 19.6% in the sevoflurane group and by 18.3% in the propofol group ($P>0.05$). Two hours after the extubation, CBFI was below the baseline by 11.3% in the group T-S and by 11.6% in the group T–P ($P>0.05$).

Discussion

The maintenance of sufficient cerebral blood flow is important for oxygenation and function of the brain. During surgery, physiologic variables should be preserved within the normal range to maintain adequate cerebral oxygen supply. Hemodynamic properties, such as cerebrovascular reactivity for changing CO_2 concentration in blood (20, 21), and the influence of sevoflurane and propofol on autoregulation of cerebrovascular circulation have been widely analyzed (22–28). Comparative studies investigating the effect of these anesthetics on CBF velocity were also performed; however, they included only patients without intracranial pathology (3, 5, 6, 19, 22–25, 29–32). Thus, to our knowledge, this is the first study comparing effects of sevoflurane and propofol on the cerebral circula-

tion measured by means of TCD during craniotomy and tumor resection surgery.

The primary aim of the present randomized clinical investigation was to compare the cerebrovascular effects of sevoflurane and propofol by means of transcranial Doppler measurements under equipotent anesthesia. The aim was to compare the changes in cerebral hemodynamics at different stages of the operation, namely, after opening of the dura mater and intracranial tumor resection, when the influence of ICP was eliminated, and compare them to the baseline. Although early postoperative period does not reflect the effects of anesthetics, we were interested in the hemodynamic recovery profile following anesthesia with sevoflurane or propofol. Thus, our study extended up to 2 hours postoperatively.

The advantage of this study is represented by the effort to limit the impact of confounding factors between the groups as much as possible. Firstly, comparable level of the depth of anesthesia and consequently neuronal depression and cerebral metabolism were achieved using the indices derived from EEG signal. We used spectral entropy indices for continuous monitoring of the depth of anesthesia in both the groups. Spectral entropy of EEG correlated with individual cortical electrical activity and depression induced by sevoflurane and propofol suggesting that this measure can reflect changes in neuronal activity induced by these general anesthetics (16). The results presented by Maksimow et al. suggest good performance of spectral entropy in reflecting changes in neuronal activity at different surgical levels of anesthesia (33). In our study, electroencephalographic and frontal electromyographic monitoring was used to determine the level of consciousness in both the groups. The depth of anesthesia measured by entropy index in our study was negligibly deeper in the sevoflurane group versus the propofol group (mean SE of 40.6 [SD, 9.1] vs. 44.0 [SD, 8.4]). We think that the difference in SE between the groups by 3–4 points cannot be translated in significant differences in neuronal activity. In this way, we tried to keep neuronal activity similar between the study groups as much as possible. Secondly, physiologic parameters having an influence on cerebral circulation (T, SpO_2, $ET-CO_2$) were kept similar in both the groups during the study.

The disadvantage of transcranial Doppler sonography is the fact that it is not possible to measure cerebral blood flow directly. It can measure only the changes in cerebral blood flow velocity that is proportional to the changes in CBF in the corresponding vascular territory (34). Any change in the diameter of the insonated vessel would alter the relation between flow velocity and actual blood flow. However, it has been demonstrated by direct intraoperative measurements (35) and MRI measurements (36) of the middle cerebral artery that the diameter of the vessels does not change significantly during variations in MBP or CO_2, inducing vasodilation and vasoconstriction. The changes in cerebral blood flow under these circumstances are mainly related to the small resistance arterioles. In order to get better insight in the actual blood flow, cerebral perfusion pressure, and cerebrovascular resistance when blood flow velocity is measured, the use of indices has become widespread in recent years. We used CBFI, eCPP, and RAP, which all take into account systemic blood pressure.

Methodological drawback of our study is that propofol was used for induction of anesthesia in both the groups. However, due to a very short elimination half-life of propofol following bolus injection, we assumed that there were no residual effects of propofol starting with the study point 3 in the sevoflurane group.

The principal finding of the study is that cerebral blood flow velocity was decreased as compared to the baseline but without obvious differences between sevoflurane- and propofol-anesthetized patients during the surgery. In our study, the average decrease in cerebral blood flow velocity was 17% in the sevoflurane group and 24% in the propofol group. Cerebral blood flow velocity in the middle cerebral artery was found to be decreased by 20% to 32% in nonneurosurgical patients under sevoflurane anesthesia, whereas the decrease under the propofol anesthesia was reported to be from 31% to 52% (19, 22, 24, 25, 29, 30). In general, a decrease in cerebral blood flow velocity in our patients was somewhat smaller as compared to other studies. This might be explained by several factors. Higher doses of anesthetics and concomitant cardiac disease with a resultant greater decrease in MBP were reported in several studies. Underlying cerebral condition in our patients could have been associated with baseline changes in cerebrovascular hemodynamics, making the decrease during anesthesia less marked. The decrease in cerebral blood flow velocity within the middle cerebral artery can be explained by several mechanisms: vasodilatation of the large vessels or vasoconstriction of the small resistance arterioles (18). More expressed vasoconstriction of the small arterioles as reflected by considerably higher cerebrovascular resistance index (RAP) in our patients under propofol versus sevoflurane anesthesia may explain a similar decrease in cerebral flow velocity, regardless of significantly higher MBP in propofol-treated patients.

Cerebral perfusion pressure is usually calculated from the difference between MBP and ICP. Intracranial pressure is known to represent the effective downstream pressure (pressure at which blood flow through the cerebral circulation would cease) of the cerebral circulation in clinical practice. The cerebral

circulation will stop if the MBP equals the effective downstream pressure. Weyland et al. (26) and Hancock et al. (27) have suggested that cerebrovascular tone is the major determinant of effective downstream pressure in the absence of intracranial hypertension. The estimated cerebral perfusion pressure takes into account cerebral blood flow velocity and systemic arterial blood pressure. In our study, eCPP was higher in the propofol group and changed parallel to MBP for both anesthetics. Our results support the conclusions of a randomized prospective study by Petersen et al., examining patients before as well as during hyperventilation, who underwent craniotomy and cerebral tumors resection and were anesthetized with propofol, sevoflurane, and isoflurane (a target level of arterial carbon dioxide tension of 30–40 mm Hg). In this study, the mean arterial blood pressure and CPP were significantly higher in propofol-anesthetized patients compared with patients anesthetized with isoflurane or sevoflurane (37).

During the neurosurgical intervention, the mean arterial blood pressure was significantly lower in sevoflurane- than propofol-anesthetized patients (12.7% below the baseline and 2.7% below the baseline, respectively). Despite this, the change in the mean CBFI was similar in both the groups (20.1% and 25.7% below the baseline in the sevoflurane and propofol group, respectively). CBFI decreased by 24.0% when MBP decreased approximately by 10% from the baseline in patients who underwent elective lumbar discectomies under anesthesia with sevoflurane in a study by Molnar et al. (19). The cerebral autoregulation adjusts cerebrovascular resistance so that it can maintain CBF constant over a wide range of mean arterial pressure values. In healthy humans, cerebrovascular autoregulation remains intact at MBP values ranging from approximately 50 to 150 mm Hg, but the autoregulation can be influenced by various pathologic processes. It has been demonstrated that during anesthesia in patients without neurological disease, the cerebrovascular autoregulation is maintained with 0.5 and 1.0 minimum alveolar concentration (MAC) of sevoflurane, although the fast dynamic component of autoregulation is slightly impaired with 1.0 MAC (23). Other authors found that cerebral autoregulation was maintained during anesthesia with 1.2 and 1.5 MAC sevoflurane in patients who underwent nonintracranial neurosurgical procedures (28). Doses of sevoflurane used in our study were below 1 MAC. It was also shown that propofol did not impair cerebrovascular autoregulation regardless the concentration used (38). Thus, our study shows that cerebral autoregulation was preserved when cerebral neuronal activity was depressed to the same level (comparable level of anesthesia depth) with both anesthetics as cerebral blood flow index remained similar regardless a significant difference in the mean blood pressure.

Awakening after neurosurgery must be reasonably rapid and smooth. A 20%–30% increase in blood pressure above preoperative baseline values poses the risk of intracranial hemorrhage and brain swelling (11). An adequate range of blood pressure during and immediately after the emergence from anesthesia is difficult to predict and provide, and should be agreed between an anesthesiologist and a neurosurgeon. Magni et al. compared early postoperative recovery and hemodynamic events in patients who underwent craniotomy for supratentorial intracranial surgery and reported hypertension in 17% (sevoflurane group) and 40% (propofol group) of patients. Hypotension was present in 12% and 28% of patients, respectively (1). We preserved the mean blood pressure similar to the baseline after awakening in both the groups (1.7% below the baseline in the group T–S and 0.6% below the baseline in the group T–P). Immediately after the emergence from anesthesia and extubation of the patient, neuronal activity rises, cerebral metabolism increases, and consequently cerebral blood flow increases too. In our study, we documented the increased cerebral blood flow velocity to the similar values in both groups. At this stage, the cerebrovascular resistance index was decreased below the baseline in both the groups reflecting relaxation of the small resistance arterioles. Consequently, the cerebral blood flow index increased by about 19% compared to the baseline in both the groups. Estimated CPP was near the baseline (0.8% below) in the group T–S and exceeded the baseline by 4.5% in the group T–P providing sufficient brain oxygen supply at this stage. Two hours after the extubation, cerebral hemodynamic variables reflect continuing recovery following surgery and anesthesia, but may also reflect the influence of additional analgesic and antihypertensive therapy, which was used in a substantial number of patients.

Conclusions

There were no significant differences in cerebral hemodynamic changes measured by transcranial Doppler sonography at the comparable depth of anesthesia and awakening between sevoflurane- and propofol-anesthetized patients undergoing intracranial tumors resection surgery. Although cerebrovascular resistance and cerebral perfusion pressure (reflected by RAP and eCPP) were higher during anesthesia with propofol, cerebral blood flow velocity and cerebral blood flow index were comparable in both the groups, indicating that sevoflurane at the doses used in this study had no major effect on cerebral hemodynamics as compared with propofol.

Sevoflurano ir propofolio įtaka galvos smegenų hemodinamikai operuojant galvos smegenų navikus vienodo anestezijos gylio sąlygomis

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Raktažodžiai: galvos smegenų kraujotaka, transkranijinė ultragarsinė doplerografija, sevofluranas, propofolis, galvos smegenų navikai.

Santrauka. Galvos smegenų kraujotaka, operuojant galvos smegenų navikus vienodo anestezijos gylio sąlygomis bei ankstyvuoju pooperaciniu laikotarpiu ligoniams, kuriems anestezijai buvo vartojamas sevofluranas arba propofolis, nebuvo lyginta.

Tikslas. Palyginti galvos smegenų hemodinamiką transkranijinės ultragarsinės doplerografijos būdu, šalinant galvos smegenų navikus, stebint būklės entropiją (SE) sevoflurano arba propofolio anestezijos metu bei ankstyvuoju pooperaciniu laikotarpiu.

Medžiaga ir metodai. Atsitiktiniu būdu 130 pacientų pateko į sevoflurano (T–S grupė) arba propofolio (T–P grupė) grupę, palaikant anestezijos gylį 40–50 pagal SE. Galvos smegenų kraujo tėkmės greitis vidurinėje smegenų arterijoje (Vmean) matuotas transkranijiniu ultragarsiniu doplerografu, atvežus ligonį į operacinę (pradinis), atlikus endotrachėjinę intubaciją, atvėrus kietąjį dangalą, pašalinus naviką, užsiuvus operacinę žaizdą, ekstubavus ligonį bei praėjus dviem valandoms po ekstubacijos. Atsižvelgiant į sisteminį kraujospūdį, nustatytas galvos smegenų kraujagyslių pasipriešinimo indeksas (RAP), apskaičiuotas smegenų perfuzinis spaudimas (eCPP) ir galvos smegenų kraujotakos indeksas (CBFI).

Rezultatai. Sevoflurano anestezijos metu vidutinis (SD) SE buvo 40,6 (8,1), o propofolio – 44,0 (7,4). Vidurinis sisteminis kraujospūdis buvo patikimai didesnis T–P grupėje. Lyginant su pradiniu, Vmean vidutiniškai sumažėjo 16,6 proc. ir 23,5 proc. atitinkamai T–S ir T–P grupėse (p<0,05). Vidutiniai RAP ir eCPP buvo didesni T–P grupėje nei T–S grupėje (atitinkamai 28,9 proc. ir 5,2 proc. daugiau pradinio, p<0,005 bei 3,2 proc. ir 16,9 proc. mažiau pradinio, p<0,005). CBFI vidutiniškai sumažėjo nuo pradinio 20,1 proc. T–S grupėje ir 24,0 proc. T–P grupėje (p>0,05). Ekstubavus ligonį, po 2 valandų Vmean padidėjo panašiai abiejose grupėse, o RAP, eCPP ir CBFI reikšmės tarp grupių nesiskyrė.

Išvados. Šalinant galvos smegenų naviką, kai anestezijos gylis panašus, sevoflurano sukelti galvos smegenų kraujotakos pokyčiai nesiskyrė nuo propofolio sukeltų pokyčių. Mūsų atlikto tyrimo duomenys papildo žinias apie saugų sevoflurano vartojimą neuroanesteziologijoje.

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