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The Effect of Sevoflurane vs. TIVA on Cerebral Oxygen Saturation During Cardiopulmonary Bypass – Randomized Trial

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A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation;
D – writing the article; E – critical revision of the article; F – final approval of article; G – other

Abstract

Background. Neuropsychological and neurological deficits are still major causes of mortality and morbidity after cardiac surgery. These complications are thought to be caused by embolisms and cerebral hypoxia. Thus, continuous neuromonitoring is essential during cardiac surgery due to cerebral oxygen desaturation during different periods. Near-infrared spectrophotometry (NIRS), a non-invasive method, appears to offer many advantages for monitoring cerebral oxygenation and hemodynamics. Desaturation of cerebral oxygen may occur at the beginning of cardiopulmonary bypass (CPB) or during the low perfusion and rewarming stages if not corrected.

Objectives. This study was designed to assess the effects of sevoflurane on cerebral protection during CPB.

Material and Methods. Eighty patients were divided into two groups. Anesthesia was maintained either with fentanyl and midazolam (total intravenous anesthesia, TIVA) or with one minimum alveolar concentration of sevoflurane and fentanyl. Cerebral desaturation was defined as an absolute decrease in saturation of 20% from baseline cerebral saturation. When desaturation occurred, PaCO₂, hematocrit and PaO₂ levels were checked and corrected. If desaturation continued, anesthetic depth was increased to reserve saturation with 50–100 mg of propofol. NIRS values and hemodynamics were recorded at predetermined time intervals.

Results. Cerebral oxygen saturation values on the right side were higher in the sevoflurane group than in the TIVA group. The values on the left side were higher in the sevoflurane group than in the TIVA group, and meaningful differences were seen at the lowest temperature and at 36°C.

Conclusions. Oxygen saturation was higher in the sevoflurane group than in the TIVA group. Thus, the effect of sevoflurane was useful for maintaining cerebral oxygen saturation during CBP (*Adv Clin Exp Med* 2014, 23, 6, 919–924).

Key words: near-infrared spectrophotometry, cerebral oxygen saturation, cardiopulmonary bypass, sevoflurane.

Neuropsychological and neurological deficits are still major causes of mortality and morbidity after cardiac surgery. These complications are thought to be caused by embolisms and cerebral hypoxia [1–4]. Cerebral oxygen desaturation can occur during different periods of cardiac surgery; thus, continuous neuromonitoring is essential. Near-infrared spectrophotometry (NIRS) is a non-invasive method that appears to offer many advantages for monitoring cerebral oxygenation and hemodynamics [5–7]. Using NIRS to assess bifrontal regional cortical oxygen saturation (SRO₂) in patients undergoing cardiopulmonary bypass (CPB)

has revealed a correlation between low SRO₂ values and cognitive dysfunction, prolonged hospitalization and perioperative cerebrovascular accidents [8–11].

Desaturation of cerebral oxygen can occur at the beginning of CBP because of hemodilution or during the low perfusion and rewarming stages. The neurological outcomes of the patients are related to desaturation. Because volatile agents have a cerebroprotective effect, they are used as a maintenance method during CBP. Volatile agents decrease the cerebral metabolic rate (CMRO₂) in a dose-dependent manner in animals and humans [12]. One

minimum alveolar concentration (MAC) of sevoflurane anesthesia causes a decrease in global cerebral blood flow because of a pronounced reduction in CMRO_2 [13]. Opioids and benzodiazepines also decrease CMRO_2 , but not as much as volatile agents. Sevoflurane has a direct dose-dependent cerebral vasodilatory effect as well [14]. This study was designed to compare the effects of sevoflurane and total intravenous anesthesia (TIVA) on cerebral cortex oxygen saturation during CPB.

Material and Methods

Following approval by the local ethics and research committee and the receipt of written informed consent, 80 patients undergoing elective cardiac bypass surgery were included in the study. Exclusion criteria included a history of any neurological disease or neurosurgery, any carotid artery stenosis, left ventricular ejection fraction < 40%, re-operation and the need for concomitant valve surgery.

All the patients were premedicated with 0.1 mg/kg morphine administered intramuscularly 1 h before surgery. A randomization envelope was opened in the operating room, and patients were assigned to either the active treatment group or the control group. Standard monitoring was applied, including five-lead electrocardiography, digital pulse oximetry, capnography, radial arterial line and a triple-lumen catheter *via* the internal jugular vein.

Regional cerebral oxygen saturation was monitored using near-infrared spectroscopy (NIRS) (INVOS 3100; Somanetics, Troy, MI, USA). NIRS technology is based on the principle that all substances have a characteristic absorbance. The light source of the oximeter provides 2 continuous wavelengths of near-infrared light (730 and 810 nm) on the forehead, in the area corresponding to the junction between the anterior and middle cerebral arteries. Two detectors with a source detector spaced 3 and 4 cm apart distinguished the extra-cerebral tissue signals from the intra-cerebral tissue signals. The ratio of oxygenated hemoglobin to total hemoglobin was measured, and the superficial signal was subtracted from the deeper signal by the monitor to obtain the regional hemoglobin oxygen saturation in the frontal cortex [6].

Anesthesia was induced with 0.1 mg/kg intravenous midazolam, 10–15 µg/kg fentanyl and 0.6 mg/kg intravenous rocuronium. Anesthesia was maintained either with fentanyl and midazolam (TIVA) or with one MAC sevoflurane and fentanyl. All the patients were ventilated with 50% oxygen and 50% medical air. Minute ventilation was

adjusted to maintain partial carbon dioxide pressure (PaCO_2) at 35–45 mm Hg, as confirmed by serial arterial blood gas analysis. After the induction of anesthesia, a central catheter, a urinary catheter and a rectal temperature probe were placed. Intravenous fluids were administered according to the estimated insensible loss of 7 mL/kg/h during surgery and titrated according to the blood pressure and central venous pressure. A decrease in mean arterial pressure to < 60 mm Hg was treated with fluids in the presence of low central venous pressure or by use of vasopressors. If the hematocrit value was < 20%, a red blood cell transfusion was administered. When PaCO_2 was < 35 mm Hg during ventilation, ventilation was reduced to achieve PaCO_2 > 40 mm Hg. pH-stat management was used during CPB. CPB was instituted and maintained according to the standard protocol with standardized cannulation sites, pump flow, blood gas management, mean arterial pressure and temperature targets. Blood cardioplegia was used in all the patients. Pump flow was adjusted to obtain an adjusted output of 2.2 L/m² body surface area. Pump flow was reduced to 0.5 L/m² for aortic clamping and unclamping. The pumps for all the patients were roller pumps (Jostra, Hirrlingen, Germany) and oxygenators (Dideco, Mirandola, Italy).

Cerebral desaturation was defined as a negative change from the baseline cerebral saturation. If continued desaturation was observed, the patient's head position was checked to ensure that it had not been rotated. Anesthetic depth was increased with 50–100 mg of propofol after checking and correcting the PaCO_2 , hematocrit and PaO_2 levels.

Arterial blood gas samples were collected and NIRS values were recorded at various time intervals: baseline, intubation, after internal mammary artery dissection, after cross-clamping, at 34°C, at 32°C (lowest temperature), during warming at 36°C, post-bypass and after skin closure.

The data analysis was performed using Statistical Package for Social Sciences software (v. 11.5, SPSS Inc., Chicago, IL, USA). The Shapiro-Wilk test was used to check the normality of the continuous variable distributions. The data are expressed as mean ± standard deviation or median (range), where applicable. Means were compared using the unpaired *t*-test. The Mann-Whitney *U* test was used to compare median values. Repeated-measures analysis of variance was used to evaluate both hemodynamic and clinical measurements. The Bonferroni adjusted multiple comparison test was applied as a follow-up for statistically significant variance analyses. Nominal data were analyzed using Pearson's χ^2 or Fisher's exact test, where appropriate. Values of *p* < 0.05 were considered significant.

Results

The patient demographic data are shown in Table 1.

The changes in mean arterial pressure by time interval were similar ($p = 0.185$). No difference was detected in mean arterial pressure between the groups during any period ($p = 0.477$) (Fig. 1).

The changes in hematocrit level relative to the time interval were similar in the 2 groups ($p = 0.153$) (Fig. 2). There were no differences in oxygen saturation (SpO_2), $PaCO_2$, glucose or pH between the groups ($p = 0.829, 0.738, 0.150$ and 0.837 , respectively).

Cerebral oxygen saturation (SrO_2) values on the right side were higher in the sevoflurane group

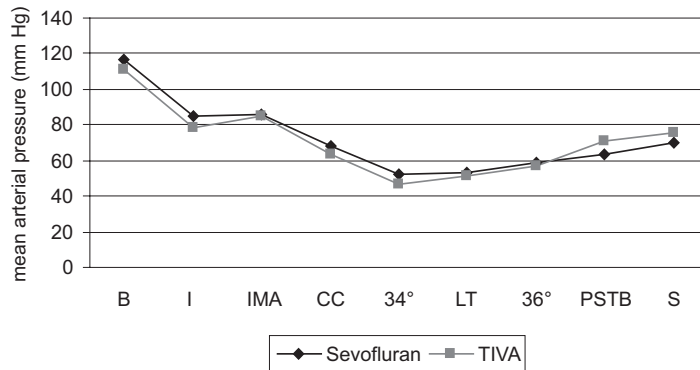


Fig. 1. Mean arterial pressure change during various time intervals (B – basal, I – intubation, IMA – internal mammary artery dissection, CC – after cross-clamping, at 34°C, LT – last temperature, PSTB – post-bypass, S – skin closure)

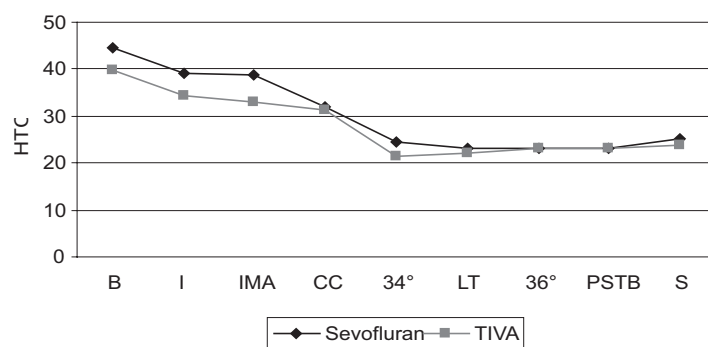


Fig. 2. Hematocrit (HTC) values during follow-up time periods (B – basal, I – intubation, IMA – internal mammary artery dissection, CC – after cross-clamping, at 34°C, LT – last temperature, PSTB – post-bypass, S – skin closure)

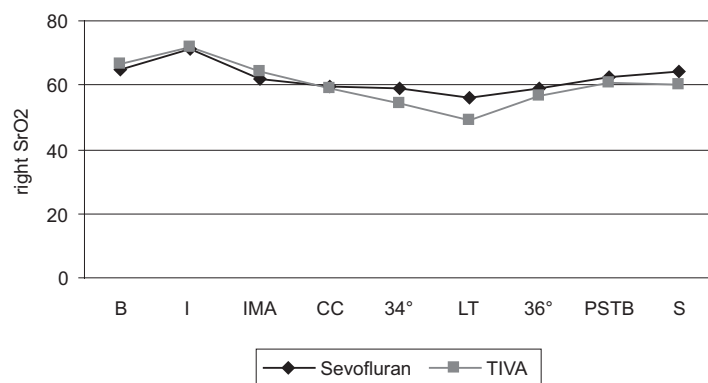


Fig. 3. Right SrO_2 values during follow-up time periods (B – basal, I – intubation, IMA – internal mammary artery dissection, CC – after cross-clamping, at 34°C, LT – last temperature, PSTB – post-bypass, S – skin closure) (* indicates a statistically significant difference)

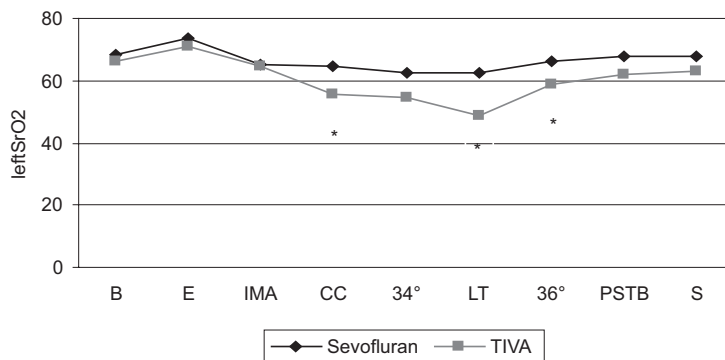
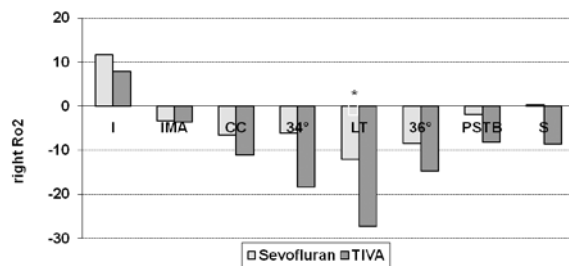
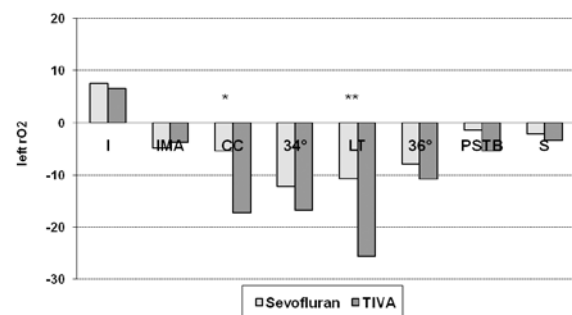
Table 1. Demographic variables

	Sevoflurane	TIVA	P value
Male/female	15/1	15/6	0.113
Age (years)	57.37 ± 9.8	57.33 ± 7.2	0.988
CPB time (min)	86.3 ± 20.2	90.0 ± 26.0	0.650
Cross-clamp time (min)	55.9 ± 14.3	58.6 ± 18.7	0.690
Other coexisting disease	4/16	5/21	1.0

Table 2. SrO₂ values according to measurement times. The values are presented as mean ± SD

	Right SrO ₂		Left SrO ₂	
	SEVO	TIVA	SEVO	TIVA
B	64.5 ± 7.1	66.5 ± 7.9	66.4 ± 7.7	66.4 ± 10
E	71.4 ± 7.8	71.7 ± 9.6	73.5 ± 10.1	70.7 ± 11.5
IMA	61.6 ± 7.6	64 ± 7.8	65 ± 9.9	64.5 ± 9.9
CC	59.8 ± 9.2	58.9 ± 8.6	64.6 ± 11.3	55.8 ± 7.2
34°	59.2 ± 7.8	54.5 ± 11.4	62.3 ± 11.9	54.7 ± 9.9
LT	56.3 ± 9	48.7 ± 7.6	62.4 ± 10.1	48.6 ± 9
36°	58.7 ± 8.9	56.8 ± 6.3	66 ± 10.2	58.6 ± 6.7
PSTB	62.5 ± 10	61 ± 6.6	67.8 ± 8.4	61.7 ± 6.5
S	64.4 ± 11	60.4 ± 8.7	67.8 ± 10.4	62.9 ± 11.2

B – basal, E – entubation, IMA – internal mammarian artery dissection, CC – after cross-clamping, at 34°C, LT – last temperature, PSTB – post-bypass, S – skin closure.

**Fig. 4.** Left SRO₂ values during follow-up time periods (B – basal, E – entubation, IMA –internal mammarian artery dissection, CC – after cross-clamping, at 34°C, LT – last temperature, PSTB – post-bypass, S – skin closure) (* indicates a statistically significant difference)**Fig. 5.** Right RO₂ values during follow-up time periods (I – intubation, IMA –internal mammarian artery dissection, CC – after cross-clamping, at 34°C, LT – last temperature, PSTB – post-bypass, S – skin closure) (* indicates a statistically significant difference)**Fig. 6.** Left RO₂ values during follow-up time periods (I – intubation, IMA – internal mammarian artery dissection, CC – after cross-clamping, at 34°C, LT – last temperature, PSTB – post-bypass, S – skin closure) (* indicates a statistically significant difference)

than in the TIVA group, but the only significant difference was determined at lowest temperature ($p = 0.012$). The values on the left side were also higher in the sevoflurane group than in the TIVA group, and significant differences were seen at cross clamping, at the lowest temperature and at

36°C ($p = 0.03$, 0.02 and 0.03 , respectively) (Table 2, Figs 3 and 4).

The change in SRO₂ on the right side compared with the baseline value, which is termed rO₂, was less in the sevoflurane group than in the TIVA group, with a significant difference at the lowest

temperature. On the left side, rO_2 differed significantly at the cross clamp and lowest temperature time intervals (Fig. 5 and 6).

The extubation and intensive care times were similar in both groups ($p = 0.212$ and 0.296).

Discussion

This study was designed to compare the effects of sevoflurane and TIVA on cerebral oxygen saturation in patients undergoing elective cardiac surgery. The success of cardiac surgery is related to the neurological outcome of the patients, which can be adversely affected by cerebral oxygen desaturation [9–11, 15]. During CPB, cerebral oxygen desaturation occurs at different time points, such as the beginning of bypass due to hemodilution, during low perfusion and during rewarming. Correcting the cause of desaturation is an important issue in anesthetic management, and preserving cerebral oxygen saturation is a major concern in cardiac surgery.

Many factors, including $PaCO_2$, pH and temperature, have been used to explain cerebral oxygen desaturation during cardiac surgery, and inflammatory activation has been reported as a main effect of CPB [16–19]. In this study, only the effect of sevoflurane on cerebral oxygen saturation was assessed, and no other regulatory parameters.

Hemodilution at the start of CPB causes a decline in regional cerebral oxygen saturation. Other critical times for desaturation are the low perfusion and early rewarming stages [20]. Cerebral cortical oxygen saturation reflects the dynamic balance between cerebral oxygen supply and consumption. When body temperature drops, the cerebral metabolic rate and oxygen consumption decrease, but the cerebral oxygen supply does not change significantly because the amount of arterial blood transported from the artificial pump to the aorta is steady. Thus, saturation can decrease during the initial part of the CPB procedure as well as the rewarming stage [16, 21].

In the current study desaturation was noted at the onset of CPB, which might have been due to blood-free prime-induced hemodilution.

According to the study findings, sevoflurane preserved cerebral oxygen saturation better than the fentanyl and midazolam combination, as saturation was higher in the sevoflurane group.

The effect of CPB temperature on the neurological outcome remains controversial. Regragui et al. reported a worse neurological outcome of normothermic bypass (37°C) compared with that of moderately hypothermic (32°C) perfusion [22]. Similar results were reported by Martin et al. [23]. In the present study, a moderately hypothermic bypass was used.

Piquette et al. administered intravenous nitroglycerin to prevent the decrease in NIRS associated with CPB during high-risk cardiac surgery and reported that nitroglycerin may also prevent a decrease in NIRS [24]. Although there are some conflicting results regarding NIRS and outcomes, NIRS monitoring is an easy, non-invasive and helpful technique for detecting cerebral oxygen saturation during cardiac surgery [25, 26].

The difference in oxygen saturation between the right and left sides was a confusing result of the present study. False-negative factors (e.g., skin, hair follicles, forehead shape, and A-V anatomic shunts) might have been responsible for the difference.

The results of this study indicate that the use of sevoflurane during CPB maintained cerebral oxygen saturation. Sevoflurane has a direct cerebral vasodilatory effect and plays a role in brain protection by reducing $CMRO_2$ [14]. Although there was desaturation in some patients, cerebral oxygen saturation was better in the sevoflurane group than in the TIVA group.

Several limitations of this study must be considered. Cerebral oximetry was not monitored in the critical care unit, and neurocognitive and neuropsychological tests must be used after surgery to identify neurological outcomes, as mentioned in other studies.

The present study demonstrated that cerebral oxygen saturation was higher in the sevoflurane group than in the TIVA group. This effect may be useful for preventing desaturation during perfusion, but more studies are needed to verify these results.

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