

Ph.D. Thesis

**Clinical assessment of some possibilities of peri-and intraoperative monitoring in
anesthesia**

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Introduction

The more and more sophisticated monitoring techniques are nowadays extremely important actors of the daily anesthesiological practice. The technical boom which has been experienced in the past two decades (depth of anesthesia monitors, relaxometry, hemodynamic monitoring possibilities in the intraoperative setting) contributed much to the safety of the anesthesiological work. Neurorobotic care is a special field of our discipline. Regarding anesthesia, drugs used during general anesthesia may influence cerebral blood flow, cerebral autoregulation and intracranial pressure. Therefore, intraoperative monitoring in this subspecialty has to be capable to meet these requirements. Besides this during neurointensive care the effect of the drugs used on intracranial pressure and level of consciousness is of critical importance.

From the jungle of the monitoring possibilities, this thesis intended to assess the usefulness of transcranial Doppler sonography in the intraoperative setting, the depth of anesthesia monitors and the importance of perioperative thermoregulation in sedated patients during intrahospital transport.

Parts of the thesis:

- Intraoperative studies:
 - Assessment of the effect of a routinely used anesthesiological regimen on cerebral blood flow at surgical level of anesthesia.
 - Assessment of the clinical usefulness of a depth of anesthesia monitor in a randomized, controlled study in order to show whether it is suitable to decrease intraoperative awareness and intraoperative dreams and therewith contributes to anesthesia safety.
- Postoperative study: The assessment of the incidence and prevention of hypothermia in patients under critical conditions treated at the ICU and transported to radiological investigations in a prospective, randomized study.

Patients and methods: According to the different methods used in the studies, they are shown in different chapters.

1. Assessment of the effect of sevoflurane on cerebral blood flow

Subjects were recruited from patients undergoing elective surgical procedures for lumbar disc herniation (lumbar discectomies). Further inclusion criteria were: ASA I-II physiological status, no hypertension, diabetes and stroke in previous history. Before the procedure, the whole study was explained for patients in detail, and all subjects gave written informed consent. The study was approved by the Local Medical Ethics Committee of the University of Debrecen Health and Medical Science Centre. *Anesthesia procedure:* All patients received 100 mg diclofenac and 7,5 mg midazolam (Dormicum, Egis, Budapest, Hungary) for premedication approximately 1,5-2 hours prior to induction per os. Anesthesia was induced with a bolus injection of 1-2,5 mg of propofol (Diprivan, AstraZeneca Pharmaceuticals, Wilmington, USA), depending on the clinical effect, followed by an intravenous administration of 4 µg/kgBW of fentanyl (Fentanyl, Richter Pharmaceuticals, Budapest, Hungary). Suxamethonium chloride (Midarine, GlaxoSmithKline, Switzerland) was used for intubation in the dose of 1 mg/kgBW. After the target level of BIS was reached (see below), sevoflurane (Sevorane, Abbott Pharmaceuticals) was introduced in a stepwise fashion to maintain the desired BIS level between 45 and 55. Patients were mechanically ventilated with FiO₂ 40% and the use of nitrous oxide was avoided.

Routine anesthesiological monitoring: ECG, pulse rate, non-invasive blood pressure measurement, end-tidal CO₂ measurement, and peripheral oxygen saturation (using pulseoxymetry) was measured throughout the study. After inhalational anesthesia was used, the expired sevoflurane was measured.

Transcranial Doppler measurements: All Doppler measurements were performed by the same experienced neurosonologist (GS). The middle cerebral artery was insonated at 50-55 mm depth through the temporal window by the 2 MHz probe of the Multidop- T transcranial Doppler device (DWL Elektronische Systeme GmbH, Sipplingen, Germany). A fixed probe was placed at the right temporal window in order to avoid misplacement during turning of the patients from supine to prone position after induction of anesthesia. In each case the most powerful signal of the middle cerebral artery was found and recorded for at least 10 cardiac cycles in order to

get stable blood flow velocity parameters. Systolic, diastolic and mean blood flow velocities, and pulsatility indices were recorded. The latter parameter was always controlled by an off-line calculation based on the Gosling-formula ($PI = (\text{Peak Systolic FV} - \text{Diastolic FV}) / \text{Mean FV}$).

Doppler measurements were performed before induction of anesthesia, in awake patients as well as after induction of anesthesia when a stable and appropriate level of depth of anesthesia was reached with sevoflurane. For sake of clarity, the decline of the induction dose of propofol was awaited. Administration of sevoflurane was started, when the BIS indicated the decline of the propofol effect. Doppler measurements were repeated only after a stable BIS level was reached with sevoflurane. Beside measured Doppler parameters, additional values were derived from blood flow velocity values as well as systemic arterial pressures at different time points of the measurements. According to the method first described by Aaslid et al., and later used for cerebral hemodynamic measurements by others we also calculated the following haemodynamic parameters off-line: *Estimated cerebral perfusion pressure (eCPP)* = $V_{\text{mean}} / [(V_{\text{mean}} - V_{\text{diast}}) * (BP_{\text{mean}} - BP_{\text{diast}})]$, *Resistance area product (RAP)* = $BP_{\text{mean}} / V_{\text{mean}}$ and *Cerebral blood flow index (CBFI)* = $\text{Estimated cerebral perfusion pressure} / \text{Resistance area product}$. V_{mean} and V_{diast} are the mean and diastolic blood flow velocities respectively in the middle cerebral artery. BP_{mean} and BP_{diast} are the systemic mean and diastolic blood pressures respectively. The logical background of using these indices is the fact that transcranial Doppler does not measure cerebral blood flow, only changes in mean blood flow velocities are proportional to changes in blood flow in the corresponding arterial territory. Furthermore, during transcranial Doppler measurements blood flow velocities are usually evaluated without the knowledge of the eventual change of the systemic blood pressure, which may also influence cerebral blood flow. These calculations were performed because we wanted to take into account the mean arterial pressure changes between the two examinations. Both the CPP and the RAP are derived from the systemic blood pressure while the CBFI, which reflects cerebral blood flow in the MCA territory, depends on the CPP and RAP changes.

Depth of anesthesia was measured by an A-1000 bispectral monitor (Aspect Medical Systems Inc., Natick, US). Electrodes were placed to the forehead and temple before induction of anesthesia in awake state of the patients. An average level of consciousness was recorded in patients before induction of anesthesia after asking

them to keep their eyes closed. After a stabilizing period, during which all sudden and additional light and acoustic stimuli were avoided, the numeric value of the bispectral indices were recorded as baseline values. After induction of anesthesia and introduction of sevoflurane, the minimal alveolar concentration of the inhalational agent was set stepwise on the anesthesia machine, which was needed for reaching the target level of depth of anesthesia (BIS 45-55). After the stabilisation of the bispectral index at the target level, patients were considered to reach the appropriate depth of anesthesia and all previously mentioned parameters (blood pressure, pulse rate, end tidal CO₂, expired sevoflurane concentration and Doppler velocities) were recorded again.

Means and standard deviations are reported for all values. Parameters with normal distribution were compared with the appropriate t-tests. A p-value of < 0.05 was considered to indicate statistical significant differences.

2. Assessment of the applicability of a depth of anesthesia monitor: Patients undergoing elective lumbar discectomies at the Department of Neurosurgery University of Debrecen, Health and Medical Science Centre were enrolled. Based on the preoperative risk stratification only patients with ASA I-II physiological status were included in the study. Before the procedure, the study was explained for all patients in detail, and they gave written informed consent. The study was approved by the Local Medical Ethics Committee of the University of Debrecen.

Randomisation procedure: After a random number generation (Statistica for Windows, Statsoft, Tulsa, USA) the patients were scheduled either to the group where the guidance of anesthesia was based on the routinely used clinical signs (Traditional group) or on the AAI index (AAI group). The grouping status of the patients was clarified in the operating theatre just before starting the anesthesiological procedure.

Anesthesiological methods: All patients received the same oral premedication one hour prior to surgery: 7,5 mg midazolam and 100 mg diclofenac were used. As a coinduction 5 mg midazolam and 1-2,5 mg/kgBW propofol was used, depending on the clinical effect, followed by a combination of sevoflurane-fentanyl and cisatracurium combination for maintenance. In the traditional group, the administration of anesthetic agents was based on the routinely used clinical signs, such as tendency of increasing pulse-rate and blood pressure, other vegetative signs

(sweating), level of consciousness, reflex signs (such as ciliary reflex) and eventual involuntary movements. In the AAI group, the administration of the anesthetic agents was based upon the AAI index: a target value of 15-25 was predetermined. We used routine anesthesiological monitoring throughout the procedure, including pulse rate, non-invasive blood pressure measurements, end-tidal CO₂ (EtCO₂), inhaled and exhaled concentration of the inhalational agent (in volume %) and FiO₂.

Monitoring anesthetic depth was performed by using ALARIS AEP monitor.

Electrode placement occurred in the standardized fashion as indicated by the supplier's description. AAI indices were recorded in both groups by the same person (B.Zs.).

While in the AAI group the anesthetist was aware of the AAI index, in the traditional group the display of the AEP device was turned apart from the anesthetist and only the helper person registered the AAI value. The monitor is capable of providing off-line information about the percentage amount of time the patient spent in superficial (AAI:25-100), appropriate (AAI:15-25) and deep (AAI: 0-15) level of sedation during the procedure. These data were also used for further analysis.

Right after finishing the anesthesia and four days later the patients were asked by a third, independent co-worker, who was unaware of the patients grouping status, about the following: „Did you experience dreams during surgery?“ „What was the last moment you remember before surgery?“ „What was the first moment you are able to recall after surgery?“. Recalls were classified according to the time of their occurrence as early (in the preoperative phase recalls from the patient rooms at the wards, in the postoperative phase recalls from the operating theatre) and late (preoperatively: recalls from the operating theatre, postoperatively: recalls from the recovery room).

Statistica for Windows programme was used for analysis. Means and standard deviations were calculated and are reported for all values. Analysis of variance was used for parametric statistics. For non-parametric analysis χ^2 -tests were used. A p value of <0.05 was considered as statistically significant.

3. Assessment of the incidence and prevention of hypothermia in patients under critical conditions treated at the ICU and transported to radiological investigations:

With the approval of the Ethics Committee and after obtaining verbal and written informed consent from patients or their relatives, we enrolled 30 adult patients being treated in an ICU and transported for routine follow-up CT and back again to the ICU.

All patients underwent an operation for abdominal trauma within the previous seven days. Before randomisation, all patients had to fulfill the following criteria in order to be included in the study population: abdominal trauma had to be the main underlying illness (additional minor injuries, such as simple fractures, hematomas or contusions were accepted), patients had to be between 20 and 50 years of age, 160 to 180 cm high, ASA score I-III before the operation, and have a systolic blood pressure of >90 mmHg, SpO₂ of >95%, heart rate ranging between 55 to 125/minutes, Htc >0,30, normothermic (core temperature between 36.0°C and 37.0 °C) and a standardized wound dressing secured with tape. Patients who underwent cardiac arrest and cardiopulmonary resuscitation, those with spinal cord or brain injury and patients with external fixation or open wound were not enrolled.

All patients underwent mechanical ventilation IPPV (frequency: 10-12/minutes, TV: 8ml/KGBW, PEEP: 5 cmH₂O) using Evita 4 mechanical ventilator (Dräger AG, Lübeck, Germany), inhaled gas was kept at constant temperature (32 °C). Trimax isokal (Fresenius- Kabi AG, Germany) was used for nutritional support. A combination of 15-20 mg/h midazolam (Dormicum, Roche) and 0.1 mg/h sufentanil (Janssen-Cilag, Beerse, Belgium) was used for sedation on the ICU.

During transport all patient received standard sedation regimen of 3-6 mg/kgBW/h propofol (Diprivan, Astra Zeneca, Planckstadt, Germany), 3 µg/kgBW/hour fentanyl (Fentanyl Janssen-Cilag, Beerse, Belgium) and 0.1 mg/kgBW vecuronium (Norcuron, Organon, The Netherlands).

Computer generated codes were used to assign the patients randomly into groups of active heating (Gr. A) and passive warming (Gr. B). In patients randomised into group A, active heating was provided using a carbon-fiber heating blanket (Therma Med GmbH, Bad Oeyenhausen, Germany) during the entire transport including the time spent in the CT. This carbon fiber blanket is an active warming blanket that can be used independently of mains power and ensures a constant distribution of surface warming to the patient during transport. The equipment includes a control unit and a battery pack. The total dimension of the blanket is 80x200 cm, the section which can be used for active heating is however 40x148 cm. Resistive heating is provided by passing a 7-8 ampere current through the carbon fiber. During transport, the blanket was set to provide 42 °C surface warming.

Patient randomized in group B were covered with the same carbon fiber blanket, but the actively heating section was not switched on throughout the study. In both groups

the patients were entirely covered with the carbon fiber blanket, except for the head. Additionally, the carbon fiber blanket was covered with a conventionally used wool blanket as well.

Before leaving the ICU, patients received standard transport monitoring for SAP, DAP, HR and SpO₂. In addition, a tympanic temperature probe was inserted. For the measurement of temperature, a Mon-a-Therm digital thermometer (Mallinckrodt Anesthesiology Products, St. Louis, USA) were used, with a measuring accuracy and precision of near 0.1 °C. The aural probe was inserted followed by occluding the aural canal with cotton and fixing the probe to the external ear. The first reading was taken at least five minutes after inserting the tympanic probe.

Intrahospital transport occurred within the hospital building, where the ambient temperature is kept centrally at 21±1°C. In the CT Lab, the ambient temperature was kept at 16.0°C because of technical reasons.

An investigator, blinded to treatment assignments recorded parameters (SAP, DAP, HR, SpO₂, tympanic temperature) before transport was started, during transport, before starting the CT, during CT, after CT, during transporting the patient back to ICU. In order to ensure the blindness, the treating physician covered the patient with carbon fiber blanket and opened the randomisation envelope. According to the randomisation he was the one who either switched on the blanket or let it turn off, and thereafter covered the heating blanket with wool blanket. The blinded investigator was allowed to deal with the patients only after this.

Our a-priori planning predicted a 1.5°C difference with a common standard deviation of 1°C at the end of the study period, with a power of 0.85. To achieve a minimum power of 0.85 at a significance level of 0.05, a total sample size of 30 was calculated, when comparing parameters with Mann-Whitney test. Our post-hoc analysis resulted in a power of >0.95.

Results

1. Assessment of the effect of sevoflurane on cerebral blood flow

Twenty persons (12 males and 8 females) entered the study. The mean age of the patients was 42,3±5,2 years. Fourteen among them belonged to ASA I, whereas six to ASA II categories based upon the preoperative risk assessment. The most important

parameters recorded before and after induction of anesthesia are summarized in Table 1.

We found that induction of anesthesia resulted in a significant decrease of the mean arterial blood pressure by approximately 10%, whereas pulse rate remained relatively stable during the procedure. Parameters of respiration, such as end-tidal CO₂ and oxygen saturation did not change at the desired level of anesthesia as compared to the initial values. As the decrease of the bispectral index indicates, at the time point of the Doppler measurements the proper depth of anesthesia was reached.

Absolute blood flow velocities within the middle cerebral artery all significantly decreased along with reduction of the mean arterial pressure. The decrease in absolute blood flow velocities was approximately 20% for mean, 16% for systolic and 22% for diastolic blood flow velocities respectively. A statistically significant decrease in pulsatility index could be observed after induction of anesthesia.

When when we took changes in systemic blood pressure levels into account during the procedure, a statistically significant decrease in cerebral perfusion pressure of 18,3% was found, which was somewhat higher than it could be awaited from the reduction of the systemic mean arterial pressure (Figure 1.). The calculated index of cerebral blood flow within the middle cerebral artery territory decreased from 38.8 ± 11.4 to 28.9 ± 14.3 indicating a significant reduction by 25,5% (Figure 2.). If one takes into consideration that the corresponding decrease in middle cerebral artery mean blood flow velocity (which is supposed to reflect changes in the blood flow within the corresponding arterial territory) was approximately 20%, despite the obvious differences, the values are still comparable. As shown in Figure 3, induction of anesthesia resulted in a statistically significant, 15% increase of the resistance area product (RAP), indicating an elevation of the cerebrovascular resistance within the middle cerebral artery territory.

2. Assessment of the applicability of a depth of anesthesia monitor:

One hundred and four patients were included, 53 patients were randomized into the AAI group and 51 into the conventional group.

Comparison of the AAI values in the two groups: The table below demonstrates the percentage amount of time the patients spent above the zone of surgical anesthesia, within this zone and below this zone. Obviously, patients who underwent

conventionally guided anesthetics spent less time both above the target zone, and within it, while they were deeper sedated for a longer period of time in average.

	AAI	Traditional	P-values
Above zone (superficial)	27.2±15.9%	16.8±16.1%	p<0.001
Within zone (proper)	55.1±15,7%	44.6±20.3%	p<0.001
Below zone (deep)	18.1±11.6%	38.5±24.3%	p<0.001

Analysis of the questionnaire:

- Right after surgery and four days after the procedure the patients were asked whether they experienced dreams during the anesthesia. The amount of dreams was comparable in the two groups right after surgery. The number of recalled dreams decreased later on in a similar fashion in both groups. Thus, the incidence of intraoperative dreams was similar in the conventional and AAI groups.
- The last events the patients could recall, when we asked them right after surgery, events from the ward and events from the OR were of similar amount. However, asking our patients 4 days after the surgery resulted almost exclusively in recalls from the operating theatre only. The difference between the two groups was not statistically significant.
- Four days after surgery patients were asked to recall their first event after surgery. There were no statistical differences between recalls from the ward or from the OR between the two groups.

Anesthetic and analgesic agent consumption:

- When comparing the consumption of fentanyl between the two groups, no significant differences could be found. It was 4.79±1.31 µg/kgBW/h in the conventional, and 4,6±1,7µg/kgBW/h in the AAI group. In contrast to this, more sevoflurane was used for anesthetics in the conventional group (1.38±0.41 vol%), than in the AAI group (1.16±0.4 vol%). The difference was statistically significant (p<0.001), it made up approximately 18% in average.

3. Assessment of the incidence and prevention of hypothermia in patients under critical conditions treated at the ICU and transported to radiological investigations:

An overall number of 30, (fifteen patients in each groups) were randomized.

- The most important parameters regarding transport

	Active warming (A)	Passive warming (B)	p-value
Duration of transport to the CT-lab (min)	19,9±2,2	20,6±1,7	0,44
Duration of CT (min)	19,7±2,0	20,1±2,7	0,9
Duration of transport from CT-lab to ICU (min)	20,0±1,7	21,3±3,4	0,29

- Normothermia (defined as a tympanic membrane temperature of 36.0-37.0 °C) was observed in all patients before leaving the ICU.
- Morphometric and demographic characteristics of the patients in each treatment group were similar. None of the potential confounding factors differed significantly in the two groups.
- Except for tympanic temperature, vital parameters (SAP, DAP, HR, SpO2) did not differ significantly among the two groups throughout the study.
- Patients assigned to group A remained normothermic during the whole procedure.
- Patients of group B showed a statistically significant decrease of core temperature during transport to CT, as compared with the actively warmed group.
- After CT, the difference between the core temperatures of the two groups increased, passively warmed patients became hypothermic during the CT scan and remained hypothermic until arriving back to the ICU.

Discussion

1. Assessment of the effect of sevoflurane on cerebral blood flow

In our study we demonstrated a decrease in systemic blood pressure after reaching the proper level of anesthesia with sevoflurane, which resulted in a decrease in cerebral blood flow and a decrease in cerebrovascular resistance. This is the first study which assessed the impact of sevoflurane on cerebral blood flow velocity along with taking blood pressure changes into account by calculating estimated cerebral perfusion pressure, cerebral blood flow index and cerebrovascular resistance index. The use of these indices became widespread in the recent years especially in studies assessing changes in cerebral blood flow and cerebral perfusion pressure of preeclamptic patients and of those suffering from head injury. A fairly good correlation was found between TCD-derived indices and changes in cerebral blood flow during autoregulatory tests in humans.

There are only few studies available in the literature which used BIS or AAI guided induction and maintenance and measured cerebral blood flow or cerebral blood flow velocity during sevoflurane anesthesia. Similar to our results, these authors also found a decreased cerebral blood flow velocity at surgical level of anesthesia. In their study, Kaisti et al. demonstrated that cerebral blood flow during sevoflurane anesthesia is dose-dependent: the drug induces a decrease in cerebral blood flow in all regions of the brain at minimal alveolar concentration (MAC) of 0-1, whereas CBF gradually increases in the frontal cortex at MAC 1-1,5. A further increase of MAC results in a decrease in regional CBF at the territory of the frontal cortex along with an increase in the cerebellum. It has to be noted, that at the most widely used concentrations of sevoflurane results can be classified into three sets: no change, increase and decrease in cerebral blood flow or cerebral blood flow velocity. The reasons for these discrepancies may be methodological (different techniques used for measuring cerebral blood flow or cerebral blood flow velocity at different concentration of the anesthetics), different induction regimens used (eventual potentiation of the effect of sevoflurane on hemodynamics) as well as individual variations of the drug effect on cerebral circulation at the same MAC level. At present, the most widely accepted explanation for the different effects of sevoflurane on cerebral blood flow is that at low concentrations sevoflurane possesses an indirect vasoactive action secondary to flow-metabolism

coupling. With higher concentrations the direct vasodilatory effects of sevoflurane are more important leading to increases in cerebral blood flow.

The most important methodological limitation of the most frequently used transcranial Doppler sonography is the fact that it is unable to measure cerebral blood flow directly, only changes in cerebral blood flow velocity as measured in the vessel is proportional to the change of CBF in the corresponding vascular territory. The prerequisite of the measurements is to accept, that blood flow changes during transcranial Doppler measurements may reflect changes in CBF only in case the diameter of the large vessels remains constant. Additionally, changes in systemic blood pressure may influence cerebral blood flow and thus cerebral blood flow velocities. To avoid these bias, we introduced estimated cerebral perfusion pressure, cerebral blood flow and cerebral resistance indices, which also take changes in systemic blood pressure into account. Although informations gathered from these indices (decreased cerebral blood flow index, increased cerebrovascular resistance index) showed similar trends as absolute blood flow velocity parameters (decrease in mean blood flow velocity and increased pulsatility indices), they also served with additional information. The systemic mean arterial pressure decreased by approximately 10% in our study after reaching the surgical level of anesthesia. Theoretically, a decrease in systemic blood pressure should evoke a vasodilation of the cerebral arterioles for keeping cerebral blood flow constant, if cerebral autoregulation is maintained and no additional vasoactive effect is present. Taking into consideration that at clinically used doses cerebral autoregulation is preserved during sevoflurane anesthesia the magnitude of decrease in the mean arterial pressure (10%) alone should have not evoke changes in cerebral blood flow index or at least not in the magnitude we observed (25%). Theoretically, a decrease in cerebral blood flow velocity within the middle cerebral artery may be explained by two mechanisms: either vasodilation of the large vessels (e.g. middle cerebral artery) or vasoconstriction of the small resistance arterioles. If latter is the case, pulsatility index and cerebrovascular resistance index should increase, which in fact was observed in our study. Putting our results in a logical order with these previous observations, the major vasodilatative effect of sevoflurane should take place at the level of the large vessels. Although cerebrovascular resistance and pulsatility index both increased during administration of the agent, the observed a decrease in cerebral blood flow velocity was larger in magnitude (25,5%), as it could be awaited from the magnitude of decrease in peripheral resistance (15%). This observation may be explained with the combination of

the constrictor effect of the slight decrease in end-tidal CO₂ and the vasodilatory effect of sevoflurane on the large basal cerebral arteries. The vasodilative effect of sevoflurane was observed by previous authors in human studies. From animal experiments we also know that this inhalational agent exerts a dilatative effect on both large and small cerebral vessels via ATP-sensitive potassium-channel activation. So far human observations proving the large vessel-dilatative effect of sevoflurane has not been published.

On the other hand: MRI measurements of the middle cerebral artery showed that the diameters of the vessel do not change during vasodilatory and vasoconstrictor stimuli and changes in cerebral blood flow are mainly related to the small resistance arterioles. In view of this, another explanation for the present results might be that sevoflurane at low concentrations as used in the present study decreases cerebral metabolism (as reflected by bispectral index) and thereby leads to vasoconstriction of the resistance vessels. This presumably counteracts the autoregulatory vasodilation of the resistance vessels evoked by the decreased cerebral perfusion pressure. According to the presently available data this explanation should be considered as more probable.

In conclusion: we found a decreased systemic blood pressure, cerebral blood flow velocity and an increase in cerebrovascular resistance at surgical level of sevoflurane anesthesia. Our results may indicate either a direct vasodilative effect of the agent on the cerebral arteries or a vasoconstriction of the resistance arterioles caused by decreased metabolism of the brain tissue. Further human clinical investigations are needed to clarify the cerebrovascular effects of sevoflurane at clinically used doses.

2. Assessment of the applicability of a depth of anesthesia monitor:

In the present study we demonstrated that an experienced anesthetist is capable of providing appropriate depth of anesthesia to his patients. This is supported by our observation that there were no differences between intraoperative dreams and recalls between the AAI and conventional groups. Our results are conflicting with some previous observations, which reported on decreased occurrence of intraoperative awareness when using depth of anesthesia monitors. It has to be noted, however, that the previous studies enrolled high risk patients, such as posttraumatic surgical patients, cardiac surgery patients and cesarean section patients. It is widely accepted, that those are the patient groups, where a higher incidence of intraoperative awareness can be observed. Beside this, the most important risk factors for intraoperative awareness are

ASA III-V physiological status, the anesthetic technique (avoidance of the use of inhalational agents), whereas gender and age of the patients are not or not too decisive factors. In view of this, our study population cannot be considered as high risk for intraoperative awareness, because it consisted of patients with ASA I-II physiological status and we used inhalational agents during the anesthetics for a low risk procedure. Conceivably this is the explanation for our observation, that neither in the AAI, nor in the conventional group any intraoperative awareness cases could be recorded. After recalling the reported low incidence of the intraoperative awareness -0.1-0.2%, thus, 1-2 cases for anesthetics - and taking into consideration that the use of awareness monitors decreased the incidence only slightly even among high risk patients, our results are not surprising.

The incidence of intraoperative dreams is not exactly known, but there are reports on very frequent occurrence of them. In our study population approximately half of the patients reported on intraoperative dreams when we asked them right after surgery. It has to be noted that the incidence of recalling the intraoperative dreams gradually decreased until the 4th postoperative day. This observation is in agreement with the previous report, which stated that intraoperative dreams may be observed more frequently in younger patients with lower ASA physiological status and the number of recalled dreams decreases with time in the postoperative period.

An important finding in our study is related to the postoperative recovery. When asking patients on the 4th postoperative day about their first postoperative events that they were able to recall, 1/3 of the patients in the AAI group reported on events from the operating theatre, and this ratio was only 1/4 in the conventional group. Although these values did not reach the level of statistical significance, it may show a tendency, which may be assessed in further, larger study populations. The findings may indicate a faster postoperative recovery in the AAI group, which is in agreement with the previous reports. The longer recovery period of the non-AAI group may be explained by our other observation that in the conventional group, the patients spent more time in the zone of the deeper sedation than those patients, who's anesthetics were AAI-guided.

Beside providing an appropriate level of sedation, the other argument for using depth of anesthesia monitors so far was decrease of the anesthetic agent consumption. It has to be noted, that the results are somewhat conflicting, there are reports which could not prove that with the use of awareness monitors anesthetics can be spared. In the

present study, the amount of fentanyl was comparable in the two groups and the sevoflurane consumption was also only slightly decreased (18% in average) in the AAI group, which corresponds to the previous observations.

To analyse our methods and results critically, it is clear that in anesthetics for low-risk, elective surgical procedures in patients with ASA I-II physiological status, the use of the AAI monitor did not serve with additional decrease in intraoperative awareness and dreams when compared it to the conventional work of an experienced anesthetist. Although an advantage of the AAI monitoring is the slight decrease in anesthetic consumption, this is counterbalanced by the cost of the single-use electrodes. Therefore, there are already reports questioning necessity of the routine use of awareness monitors.

What is than the future of the awareness monitors in low-risk patients? They might be helpful for less experienced anesthetists and residents or for those who are using an unusual anesthesiological technique. The other future prospect may be related to the previous observation stating that the long-term mortality is higher in patients who spent longer time under deeper sedation as assessed electrophysiologically. This „cumulative deep hypnosis”, if it will become an independent predictor of postoperative long-term mortality may underline the importance of the routine use of depth of anesthesia monitors.

3. Assessment of the incidence and prevention of hypothermia in patients under critical conditions treated at the ICU and transported to radiological investigations:

Previously it has been shown that hypothermia is frequently observed phenomenon in trauma victims during rescue, at the emergency department in the OR as well as in the ICU. However, data on intrahospital transfer have been lacking so far. We found that hypothermia occurred in all patients who were passively insulated during intrahospital transport. Our finding that major heat loss was associated with CT scanning, may be explained by the low ambient temperature in the CT Lab (16°C) as compared to the ambient temperature in the other parts of the hospital. We demonstrated that active warming using a carbon fiber blanket is capable of preventing hypothermia during transport of ICU patients to different diagnostic procedures. Previously it has been already proven that resistive heating is far more effective for maintaining normothermia than passive insulation with aluminized or wool blankets. Therefore, it

is hardly surprising that core temperature increased in actively warmed patients, whereas it continued to decrease in those who were passively insulated. As a result, core temperature was higher in the actively warmed group at arrival to the ICU by 1.5 °C, when they returned to the ICU. This difference is of clinical importance, since temperature differences of this magnitude are associated with numerous complications. The cutaneous contribution to the autonomic thermoregulatory cold defenses is about 20%. This indicates that every four degrees of skin warming compensates for one degree of core hypothermia with respect to initiation of arterio-venous shunt vasoconstriction. Numerous previous clinical studies proved that hypothermia is associated with major and minor complications. The minor complications are slowing of the metabolism of different medications, shivering, thermal discomfort and increased sensitivity to pain stimuli. In the critical care setting, the major complications, such as danger of myocardial ischemia, decreased activity of the coagulation system, increased incidence of surgical wound infections and longer ICU and hospital stay may be of high importance. With respect to this, more attention has to be paid for diagnosis and prevention of thermoregulatory disturbances in the critical care setting.

Summary

In the thesis we summarize the results of three studies which used newer anesthesiological monitoring systems. The main conclusions of the results were:

1. At the proper level of anesthesia, sevoflurane decreases mean arterial pressure and therewith cerebral blood flow. In the international anesthesiological literature we were the first to use derived indices for the assessment of cerebral blood flow which take changes of the systemic blood pressure into account.
2. We have shown that sevoflurane evokes direct dilation of the larges vessels of the brain. Beside this, decreased cerebral blood flow is caused by decreasing of the systemic blood pressure.
3. We proved, that in patients with ASA I-II severity grading, an experienced anesthetist is able to provide proper level of anesthesia, intraoperative awareness and dreams are not more freqeunt than with the use of a depth of anesthesia monitor.
4. We also demonstrated that if anesthetics are guided based routine clinical signs patients spend longer time periods in the zone of deeper sedation as assessed by depth of anesthesia monitors.
5. We were the first showing that there is a high incidence of hypothermia in patients transported from ICU to radiological investigations under sedation.
6. In our study we have shown that this hypothermia may be effectively prevented by active warming systems during transport.

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