SHORT THESIS FOR THE DEGREE OF DOCTOR OF PHILOSOPHY (PhD)

The Relative Exposure of the Operating Room Staff to Sevoflurane During Intracerebral Surgery and Identification of the Source of Exposure

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The Relative Exposure of the Operating Room Staff to Sevoflurane During Intracerebral Surgery and Identification of the Source of Leakage

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The Examination takes place at Department of Anesthesiology and Intensive Care, Faculty of Medicine, University of Debrecen, April 15th, 2016, at 11 AM.

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The PhD Defense takes place at the Lecture Hall of Building A, Department of Internal Medicine, Faculty of Medicine, University of Debrecen, april 15, 2016, at 1 PM.

Background

The potential adverse effects of volatile anesthetics on operating room staff has been the subject of numerous investigations since 1967. Among the possible long-term consequences of chronic exposure, investigators described hepatotoxicity and nephrotoxicity, carcinogenesis, decreased immunity, impaired fertility, and adverse effects on fetal development. Although the development of such events may take years of cumulative exposure, headaches, somatic and mental fatigue, and reduced cognitive ability are more likely to develop, and hence deserve increased attention. In the last decades simultaneously with the publication of studies on the harmful effects of subclinical doses of halogens, investigations have emerged to determine the treshold levels of exposure. The most appropriate unit of measurement in this case was the airborn concentration in parts per million (ppm) averaged to an 8 hours period. The NIOSH (National Institute for Occupational Safety and Health) is the most categorical if it comes to threshold determination. This limits the acceptable atmospheric concentration of all inhalational anesthetics to 2 ppm. However, no standards have been set based on unified consensus in the European Union to the present days. It should be noted that the limits have remained only recommendations so far, and none of the countries has integrated them in the category of safety conditions or requirements.

To minimize this potential environmental risk, identification of surgical procedures that are associated with increased release of volatile anesthetics is imperative. In this context, several investigators have documented that mask induction of anesthesia, the use of uncuffed tracheal tubes, or the use of laryngeal mask airways, refilling the vaporizer could increase environmental exposure However, there is limited information on whether release of volatile anesthetics from the surgical field may pose an additional risk to the surgeon.

This question seems particularly relevant during neurosurgical operations in which the craniotomy exposes the brain to the operating room environment. The brain has high blood perfusion, extensive capillary network, and high fat content, all promoting a relatively rapid and marked tissue accumulation of a lipophylic drug such as sevoflurane, which has a brain-blood partition coefficient of 1.7. However, sevoflurane has a low blood-gas partition coefficient (0.69), which may result in significant escape from the blood when the circulation is open for exchange with air. Along these lines, we speculated that exposure of a large surface area of the brain and capillaries during craniotomy for tumor resection might give rise to enhanced release of sevoflurane, which in turn may lead to an increased exposure of the surgeon, whose breathing zone is in close proximity to the craniotomy window.

Objectives

Our primary aim in this study was to investigate whether escape of the volatile anesthetic sevoflurane from the surgical site during craniotomy for tumor resection increases the exposure of the neurosurgeon to the anesthetic when compared with the anesthesiologist. To test our primary hypothesis, we sought answers to the following specific questions.

Are the concentrations of sevoflurane close to the craniotomy window and hence the surgeon's breathing zone different from those in the breathing zone of the anesthetist's and at remote sites in the operating room Is there a correlation between the sevoflurane concentration near the surgical site and the size of the craniotomy window?

In our second investigation we wanted to test the hypothesis that different isolation techniques during intracranial surgeries pose different exposure levels of the anesthetist to sevoflurane. To test our hypothesis we compared the

exposure level of the anesthetist positionig at the end of the operating table with that when located on the side of the table.

The main objective of our third study was to answer the question whether the concentration of sevoflurane at the patient's mouth differed depending on whether the balloon was inflated under controlled conditions to recommended pressure using a pressure gauge or empirically, that is under manual control of the pilot balloon only.

Methods

Patients (*n*=103) undergoing craniotomy for the removal of intracerebral tumors were both women and men aged 51.5 ±14 yr. All patients signed an informed consent approved by the local Medical Ethics Committee, and the study was performed in accordance with the Helsinki Declaration II and Good Clinical Practice protocols. For induction of anesthesia, we used propofol (1–2.5 mg/kg), whereas for maintenance of anesthesia we used the combination of fentanyl-rocuronium-sevoflurane. The sevoflurane-air mixture was administered via an anesthesia machine (Zeus, Draeger Medical AG & Co. KG, Lübeck, Germany) using a low-flow technique (2 L/min fresh gas flow). Tracheal tubes were armored RüschFlex tracheal tubes made of polyvinyl chloride with a low-pressure cuff. All endotracheal balloons were inflated to pressures slightly above 30 mm Hg. During the full course of the operation, we monitored the following variables: arterial blood pressure, heart rate, O2 saturation using pulse oxymetry, end-tidal CO2 concentration, and end-tidal sevoflurane concentration. Craniotomy and the opening of the dura were always initiated after the tissue saturation of sevoflurane. The surface area of the craniotomy window was measured in square centimeters. Subsequently, we applied low-flow anesthesia technique at a sevoflurane concentration ranging from 0.7 to 2.3 V% (mean 1.4

V%), as required to maintain adequate anesthesia. All operations were performed in recently built operating rooms with modern ventilation and air-conditioning systems. The operating room was also equipped with a scavenging system compliant with international standards. Air was continuously circulated in the operating room and changed or refilled (e.g., upon pressure decrease evoked by opening of the doors of the OR) at a rate of approximately 50 m3/min

Sample Collection and Quantification

For the detection of airborne anesthetics, we used a detection setup that consisted of a portable air sampling pump (224-51MTX Air Sampling Pump, SKC, Dorset, England), an integrated tube system, and an absorber ampule coupled to the tube system. During the, the distal part of the tube containing the absorber was placed in one of the following three locations: 1) the surgeon's breathing zone; 2) the anesthesiologist's breathing zone; or 3) the farthest corner of the operating room. In the second series of our first study, the third air sampling site was changed from the corner of the operating room to the close proximity of the patient's mouth (within 5 cm of the tracheal tube). A suction pump attached to the sample collector ensured that air samples flowed through the absorber where the anesthetic was collected for later quantification. Because our intention was to estimate evaporation from the craniotomy site, the sample collection was restricted to the period from opening to complete closure of the dura mater. After the termination of sample collection, the ampule containing the absorber was hermetically sealed and sent for quantification by chromatography. The quantifications were performed by an independent chemist, who was blinded to the origin of the sample and other key variables of the study.

Statistics

Because the samples did not show normal distribution, comparative statistics were performed by nonparametric tests. Data sets were initially evaluated by Kruskal–Wallis analysis of variance, which, if significant, was followed by pairwise comparison of selected subgroups using Mann–Whitney *U*-test. The relationship between the quantity of sevoflurane in the absorbers and the area of the craniotomy window was assessed by Spearman rank correlation analysis. Median sevoflurane concentrations and balloon pressure were compared using Mann–Whitney U-test and Student's unpaired t-test, respectively. Differences were considered statistically significant if $P < 0.05$. Calculations were carried out using Statistica for Windows software (StatSoft, Tulsa, Oklahoma, USA).

Results

Absorbers in the surgeon's breathing zone (0.24 ± 0.04 ppm) captured a significantly lower amount of sevoflurane compared with absorbers in the anesthesiologist's breathing zone (1.40 ±0.37 ppm) and comparable with that in the farthest corner of the operation room (0.25 ± 0.07 ppm). There was no correlation between the amount of absorbed sevoflurane and the size of craniotomy window, even when adjusting for the variation in duration of surgery. In the second series of sampling, absorbers in the proximity of the patient's mouth captured the highest amount of sevoflurane (1.54 ± 0.55 ppm), followed by the anesthesiologist's (1.14 ±0.43 ppm) and the surgeon's (0.15 ± 0.05 ppm) breathing zones.

When comparing the exposure of the anaesthetists at different locations depending on the isolation technique, we found that there was a significant difference among the two groups. If the anaesthesia team is located at the

patient's feet the concentration of airborn sevoflurane in the anesthesiologost's breathing zone was significantly lower (0.19±0.15 ppm) compared to the that at the bedside position (1.34±1.09 ppm).

Under controlled conditions intracuff pressures were successfully inflated to a pressure between 25 and 30cmH2O; mean [SD], 27.7 [1.9] cmH2O. In contrast, when cuffs were inflated under manual control, intra-cuff pressures were found to be higher; 53.0 [17.0] cmH2O (P <0.001). Median (IQR) concentration of sevoflurane after inflating the endotracheal cuffs under manometer control was 1.0±2.6 ppm, whereas under manual control was 0.79±1.49 ppm (p=0.78). Concentration of sevoflurane detectable at the patients' mouth showed no association with sevoflurane concentration at plateau pressure (Spearman's rank correlation coefficient -0.08 p=0.63), but did show a significant association with the end-tidal concentration and the minute volume of sevoflurane (Spearman's rank correlation coefficient to 0.55, p= 0.003)

Discussion

The main findings of the first study were as follows: 1) during intracerebral surgery, the surgeon's exposure to sevoflurane does not exceed magnitudes measurable in the farthest corner of the operating room. 2) the surgeon's sevoflurane exposure appears to be independent of the size of the craniotomy window; 3) the anesthesiologist's exposure was about sixfold higher than the surgeon's exposure; and 4) the increased exposure of the anesthesiologist can be, at least in part, associated with "escape" of the anesthetic from around the tracheal cuff. This report addresses the possible contribution of direct release of a volatile anesthetic from the incised brain tissue during intracerebral tumor surgery. The rationale for addressing this issue was that the brain is a site of high accumulation of anesthetics, and when incised, brain tissue and open capillaries

may theoretically become sources of sevoflurane release. The first to receive additional exposure from these sources would be the surgeon, whose breathing zone is in the closest proximity to the craniotomy window. Our measurements, however, did not corroborate this hypothesis and indicated no signs of increased sevoflurane concentrations at this detection site. In fact, sevoflurane in absorbers placed in the surgeon's breathing zone was not different from that in absorbers placed at the farthest corner of the operating room. Furthermore, despite a fairly large variation in the size of the craniotomy window (3–70 cm2), we found no significant correlation with the amount of sevoflurane captured by absorbers in the surgeon's breathing zone. Collectively, these observations suggest that intracerebral surgery does not pose additional environmental risks for the operating neurosurgeon. The other significant finding of our study is the increased exposure of the anesthesiologist that exceeded the surgeon's exposure by about sixfold. Our finding is consistent with several previous reports that underscored the increased exposure of the anesthesiologist to volatile anesthetic during various types of surgeries. In attempting to identify the source of the anesthesiologist's increased exposure, we considered the possibility that it may be related to the anesthesiologist's position during surgery and their proximity to the patient. During intracerebral surgery, the anesthesiologist and the anesthesia machine are at the patient's right or left side, not at the head as with other surgery types. Furthermore, the isolation of the patient's head is such that the tracheal tube is always within the reach of the anesthesiologist for necessary adjustments. If there is any significant escape of sevoflurane from the patient's mouth, it could easily lead to a higher exposure of the anesthesiologist who is sitting close by. To test this hypothesis, we placed absorbers in the proximity of the tracheal tube at the patient's mouth and compared the absorbed sevoflurane concentration with the concentrations at the surgeon's and the anesthesiologist's breathing zones. The highest sevoflurane values were indeed revealed by absorbers placed in the proximity of the patient's mouth. This finding is also

supported by previous observations by several independent groups describing “escape”of volatile anesthetics around the tracheal tube, despite adequate inflation of the tracheal cuff. Having identified the source, we speculate that the surgeon’s lower exposure can be ascribed to the fact that passive diffusion of the volatile anesthetic is diminished with increasing distance from the source (tracheal tube) and further decreased by the barrier posed by the surgical drapes that separate the surgeon from the patient’s airway and the anesthesiologist.

A word of caution should be made regarding the role of the ventilation system in the context of our observations. The findings that sevoflurane in the absorbers placed in the surgeon’s breathing zone and in the corner of the operating room showed about sixfold lower concentrations compared with absorbers placed in the anesthesiologist’s breathing zone seem to eliminate concerns regarding the contribution of poor ventilation (otherwise all three detectors would have showed comparable values). Another issue worth mentioning is that during more demanding operations, when an assistant has to leave the room for additional tools or supplies, opening of the operating room door produces an atmospheric pressure decrease. This in turn accelerates airflow and air clearance and facilitates the restoration of the internal atmospheric pressure in the operating room. In our second investigation, we have demonstrated that the location of the team does influence the amount of sevoflurane measured at the anaesthetist’s breathing zone. When comparing the exposure of the anaesthetists at different locations depending on the isolation technique, we found that there was a significant difference among the two groups: the exposure of the anaesthetists to sevoflurane is lower if the anaesthesia team is located at the patient’s feet (0.19±0.15 ppm) compared to that at the bedside (1.34±1.09 ppm) position. Our third investigation highlights that empirically inflated cuffs may result in intracuff pressures that frequently exceed the recommended limits of 25 to 30 cmH2O. To avoid the unwanted impact of high cuff pressures on the tracheal

tissue cuff inflation should be performed under guidance of a manometer to ensure an ideal cuff pressure.

Moreover, higher cuff pressures do not seem to promote a more complete sealing of the trachea or decrease of environmental pollution and exposure of staff. Our observations are in line with previous in-vitro observations in bench-top models revealing fluid leakage across the endotracheal cuff even at intraballoon pressure of 60 cmH2O.4 This leakage can be ascribed to the presence of longitudinal folds within the cuff wall and this is particularly common in cuffs made of PVC. Major discrepancies between tracheal diameter and balloon size in the individual patient may increase the likelihood and number of longitudinal folds in the balloon wall. In further exploring the source of sevoflurane causing the apparent local increase in its concentration at the patient's mouth, we also assessed associations with various key parameters of the actual ventilation. The only parameters that could be related to the sevoflurane concentration at the patient's mouth was the end-tidal sevoflurane concentration and the minute volume, suggesting that the locally increased concentration of the volatile anaesthetic may be linked to the ventilated lung.

It should be emphasized, however, that sevoflurane values meassured in this study did not exceed the safe limits (2 ppm) defined by international guidelines and were also comparable with values previously reported by independent groups. Nevertheless, even these values may gain clinical significance if evaluating the personnel's cumulative exposure over many years. For instance, studies have demonstrated significant alterations in exploratory behavior, lower scores in learning and memory tests, and an overall increase in anxiety in rats chronically exposed to subanesthetic doses of sevoflurane, desflurane, or halothane.

Summary

Although exposure levels to inhalation anesthetics in operating rooms have been reduced substantially during the last decades, it cannot be completely eliminated even when well-maintained anesthesia systems equipped with gas-scavenging units are used in well-ventilated rooms. The possible health hazards from exposure to trace concentrations of inhalational anaesthetics cannot yet be definitively excluded.

In our investigation we assessed the exposure of the operating room staff members to anesthetics during craniotomy surgery and tried to find the possible causes of differences. In summary, our study does not corroborate the notion that significant release of sevoflurane from the craniotomy window poses an additional source of exposure for the operating neurosurgeon and underscores the need to focus on improving the working conditions for the anesthesiologist, who is the subject of much higher exposure during these types of surgical operations. The increased exposure is related to the anesthesiologist's position during surgery, isolation technique and his proximity to the patient's airway. The much lower exposure of the anaesthesia team to sevoflurane performed with the team positioned at the end of the operating table in contrast to bedside position may be of importance for occupational safety of the anaesthesia staff.

The present study highlights that empirically inflated cuffs may result in intracuff pressures that frequently exceed the recommended limits of 25 to 30cmH2O. However the higher cuff pressures do not seem to promote a more complete sealing of the trachea or decrease environmental pollution and exposure of the operating room staff. Therefore to avoid the unwanted impact of

high cuff pressures on the tracheal tissue, cuff inflation should be performed under guidance of a manometer to ensure an ideal cuff pressure.

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Candidate: Béla Tankó
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List of publications related to the dissertation

1. **Tankó, B.**, Fülesdi, B., Novák, L., Pető, C., Molnár, C.: Endotracheal tube cuff inflation with and without a pressure gauge to minimise sevoflurane pollution during intermittent positive pressure ventilation.
   Eur. J. Anaesth. 31 (3), 172-173, 2014.
   DOI: http://dx.doi.org/10.1097/EJA.0000000000000018
   IF:2.942

2. **Tankó, B.**, Molnár, L., Fülesdi, B., Molnár, C.: Occupational Hazards of Halogenated Volatile Anesthetics and their Prevention: Review of the Literature.
   J. Anesth. Clin. Res. 5 (7), 1-7, 2014.
   DOI: http://dx.doi.org/10.4172/2155-6148.1000426

3. Szelei, E., Molnár, C., Büdi, T., **Tankó, B.**, Mikos, B., Novák, L., Fülesdi, B.: Does isolation technique have any impact on inhalational exposure of neuroanaesthetists to sevoflurane during craniotomies?
   Eur. J. Anaesth. 27 (11), 994-996, 2010.
   DOI: http://dx.doi.org/10.1097/EJA.0b013e32833cad40
   IF:1.679

4. **Tankó, B.**, Molnár, C., Büdi, T., Pető, C., Novák, L., Fülesdi, B.: The relative exposure of the operating room staff to sevoflurane during intracerebral surgery.
   Anesth. Analg. 109 (4), 1187-1192, 2009.
   DOI: http://dx.doi.org/10.1213/ane.0b013e3181b0cbea
   IF:3.083

List of other publications

5. **Tankó B.**: Anesztézia epilepszia-sebészeti beavatkozásokhoz és éber kraniotómiákhoz. In: Neuroanesztézia és neurointenzív terápia. Szerk.: Fülesdi Béla, Tassonyi Edömér, Molnár Csilla, Medicina Könyvkiadó Zrt., Budapest, 141-144, 2013.

6. **Tankó B.**, Kovács G., Szelei E., Fülesdi B., Molnár C.: A halogénezett volatilis anesztetikumok által okozott munkahelyi ártalmak és megelőzésük: irodalmi áttekintés. *Anaesthesiol. Intenziv Ther. 41* (2), 74-81, 2011.

7. Molnár C., Büdi T., Pető C., **Tankó B.**, Bognár L., Fülesdi B.: Inhalációs anesztetikumok mütéti területből történő párolgásának vizsgálata intracerebralis tumormütétek során: Előzetes eredmények. *Anaesthesiol. Intenziv Ther. 38* (1), 18-21, 2008.

8. Molnár C., Kovács Z., **Tankó B.**, Fülep Z., Vitális E., Sárkány P., Fülesdi B.: Különböző elven müködő anesztézia mélység mérő monitorok klinikai alkalmazásának összehasonlítása idegsebészeti beavatkozások során =Comparison of two different indices used in anaesthesia depth monitors during neurosurgical operations. *Anaesthesiol. Intenziv Ther. 37* (3), 115-120, 2007.

Total IF of journals (all publications): 7,704
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