

The Personnel's Sevoflurane Exposure in the Postanesthesia Care Unit Measured by Photoacoustic Gas Monitoring and Hexafluoroisopropanol Biomonitoring

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Purpose: Room ventilation in the postanesthesia care unit (PACU) is often poor, although patients exhale anesthetic gases. We investigated the PACU personnel's environmental and biological sevoflurane (SEVO) burden during patient care.

Design: Prospective, observational study.

Methods: Air pollution was measured by photoacoustic gas monitoring in the middle of the PACU, above the patient's face, and on the PACU corridor. Urinary SEVO and hexafluoroisopropanol concentrations were determined.

Findings: Mean air pollution was 0.34 ± 0.07 ppm in the middle of the PACU, 0.56 ± 0.17 ppm above the patient's face, and 0.47 ± 0.06 ppm on the corridor. Biological preshift exposure levels were 0.13 ± 0.03 mcg/L (SEVO) and 4.72 ± 5.41 mcg/L (hexafluoroisopropanol). Postshift concentrations increased significantly to 0.20 ± 0.06 mcg/L ($P = .004$) and 42.18 ± 27.82 mcg/L ($P < .001$).

Conclusions: PACU personnel were environmentally and biologically exposed to SEVO, but exposure levels were minimal according to current recommendations.

Keywords: sevoflurane, biomonitoring, postanesthesia care unit, occupational anesthetic gas exposure.

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MODERN VOLATILE ANESTHETICS such as sevoflurane (SEVO) are frequently used, but the concomitant chronic gas exposure of health care professionals is problematic. Although organ dysfunctions, infertility, teratogenicity, and structural chromosomal aberrations have not

been observed after chronic low-dose SEVO exposure (less than 2 ppm), genomic instability, expressed as an increase in micronucleus frequencies in peripheral blood lymphocytes as well as in DNA strand breaks and sister chromatid exchanges, has been proven.

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Furthermore, rare cases of contact dermatitis and allergic asthma have been reported.¹⁻⁴

Protection of health care professionals against exposure to waste anesthetic gases has markedly improved over the past decades. Specifically, technical advancements such as laminar flow air conditionings and gas scavenging systems can reduce air pollution significantly. However, they are almost always used in operating rooms only and not in postanesthesia care units (PACUs), although patients exhale anesthetic gases after surgery.⁵ Thus, personnel in the PACU are often particularly concerned about potential hazardous side effects.

Interestingly, few studies have investigated gas pollution levels in the air of PACUs. A recently published study summarized the results of five investigations, the first conducted in 1972, stating that concentrations in the air may exceed recommended exposure levels, especially if the volume flow rate in the PACU is low.⁶ Biological SEVO monitoring in PACU personnel, which most directly reflects SEVO absorption, metabolism, and excretion, was evaluated once by measuring urinary postshift SEVO concentrations and inorganic fluoride levels.³ However, inorganic fluoride is not specific to SEVO biotransformation and SEVO itself has a short half-life of 2.8 hours. Thus, postshift urinary SEVO levels alone may not represent the actual biological SEVO burden. An alternative is the determination of urinary hexafluoroisopropanol (HFIP), a stable metabolite of SEVO with a half-life of 19 hours, which has been proven useful for SEVO biomonitoring, but has not yet been determined in PACU personnel.⁷

Therefore, this study aimed to assess the biological SEVO burden in PACU personnel by monitoring urinary preshift and postshift SEVO and HFIP concentrations. Air pollution levels in the PACU and on the corridor around the PACU were additionally measured. Moreover, factors that potentially influence the personnel's SEVO burden (eg, number of patients in the PACU, personnel's sex) were analyzed.

Methods

Ethical approval for this prospective observational study, which was conducted between October

2017 and January 2018 in a German University Hospital, was granted by the Local Research Ethics Committee (5184-14, Ruhr-University Bochum, Germany; December 2015). All participants provided written informed consent. Measurements were conducted in accordance with the Declaration of Helsinki.

Setting—PACU and Corridor

The personnel's environmental and biological exposure to SEVO was measured in a PACU sized 78.25 m² with a room volume of 227 m³. It was equipped with a ventilation system with a three-staged filter, which achieved an air exchange rate of 11.5 per hour without recirculation. Other gas scavenging systems were not used. The PACU had two doors leading to the surrounding corridor, which were kept closed (except for patient transfer), and no windows. The temperature ranged between 20°C and 25°C, the relative humidity was 25% to 60%. The PACU was designed for nine patients after ear, nose, and throat surgery, orthopaedic surgery, or gynecologic surgery, but it was also used as a preoperative holding area.

The corridor around the PACU had an area of 65 m² with a room volume of 195 m³ and was edged by two closed doors at each side. The PACU and the operating theater could be reached by the corridor, but the doors were kept closed. Neither a special ventilation system nor a gas scavenging system was used.

The PACU was operational Monday to Friday from 8:30 a.m. to 17:30 p.m. Personnel did not leave the PACU during the work shift, except for a half-hour break. None of them had a known liver or kidney disease. The personnel's sex and their workspace on the previous day were recorded, as well as the number of patients in the PACU (preoperative and postoperative) and the type of anesthesia (intravenous anesthesia vs balanced anesthesia).

Method of Air Pollution Measurement

Photoacoustic gas monitoring (Innova 1412; Innova AirTech Instruments, LumaSense, Denmark) was used to determine SEVO concentrations in the air at three different positions:

- In the middle of the PACU at a height of 150 cm (the personnel's anticipated breathing zone).
- At a distance of 25 cm above the patient's nose and mouth within the first hour after PACU arrival (patient's breathing zone); the airway device was always removed in the operating room and patients could open their eyes at PACU arrival.
- In the corridor around the PACU at a height of 150 cm.

The gas monitor measured mean (\bar{c}_{mean}) and maximum (\bar{c}_{max}) SEVO concentrations in real-time with a lower detection limit of 0.01 ppm and a reproducibility of $\pm 1\%$. The measuring interval was 35 seconds. Current threshold limit concentrations for SEVO in the air are shown in Table 1.⁴

Method of SEVO and HFIP Biomonitoring

PACU personnel were asked to empty their bladder directly before and after the work shift. Urine samples were immediately stored at -20°C and thereafter transferred to an external laboratory. A blinded environmental toxicologist determined SEVO and HFIP concentrations by using the headspace gas chromatography-mass spectrometry method, which had a lower detection limit of 0.5 mcg/L for both substances.

Statistical Analysis

The programs Excel 2007 (Microsoft Corp, Redmond, WA) and IBM SPSS version 20 (IBM Corp, Armonk, NY) were used for analysis. After testing data for normal distribution by use of Kolmogorov-Smirnov tests and Lilliefors significance corrections, significance was calculated with an error probability less than 5% (P value $< .05$) with Freeman-Halton extension of Fisher's exact tests, Students t tests, or the one-way analysis of variance as appropriate. Pearson's coefficients were used for correlations.

Because of the study's observational character, the sample size was not calculated (pilot study), but the number of measurements orientated toward comparable previous studies.

Table 1. Current Threshold Limit Concentrations for SEVO (Sevoflurane) in the United States, Canada, and Some European Countries

Country	Threshold Limit Concentration for SEVO (ppm)
USA	2
Canada	—
Austria	10
Denmark	5
England	—
Finland	10
France	—
Germany	—
Italy	—
Netherlands	—
Norway	20
Spain	—
Sweden	10
Switzerland	—

Values are given as time-weighted exposure limit in parts per million (ppm) for an 8-hour working day (1 ppm is equal to 0.001 mL SEVO per liter or 1 mL SEVO per cubic meter). In the United States, the exposure limit of 2 ppm refers to a SEVO limit concentration, which should not be exceeded during a procedure, which is a 1-hour working period.⁴

Results

During the study period, 28 ± 5 patients were daily monitored in the PACU and 15 ± 3 of them had received SEVO in the operating room (Table 2).

Air Pollution Measurements in the Middle of the PACU

SEVO pollution in the middle of the PACU at a height of 150 cm was measured 10 times for 9 hours each. The mean SEVO concentration was 0.34 ± 0.07 ppm and the daily maximum SEVO concentration was 4.43 ± 2.37 ppm. Figure 1 shows the exemplary SEVO pollution level over time during a normal working day. Incoming patients, who were exposed to SEVO in the operating room, caused measurable gas peaks and increased the baseline SEVO concentration significantly (Table 2). Furthermore, the mean SEVO concentration in the PACU depended significantly on the number of exposed patients (\bar{c}_{mean} [ppm]): 1 patient, 0.30 ± 0.14 ; 2 patients, 0.36 ± 0.14 ; 3 patients, 0.54 ± 0.20 ; 4 patients, 0.69 ± 0.21 ; $P < .001$).

Table 2. SEVO Concentration in the Middle of the PACU at a Height of 150 cm

Study Day	Number of Patients [n (Total/After SEVO exposure)]	SEVO Baseline (ppm)	SEVO Maximum (ppm)	SEVO After Arrival; First 15 min (ppm)	P Value (SEVO Baseline Versus SEVO After Arrival)
1	31/20	0.40 ± 0.21 (n = 987)	1.52	0.50 ± 0.13	< .001
2	21/9	0.26 ± 0.25 (n = 969)	4.18	0.32 ± 0.04	< .001
3	23/16	0.41 ± 0.28 (n = 948)	3.88	0.46 ± 0.21	.016
4	30/18	0.43 ± 0.25 (n = 986)	2.41	0.57 ± 0.14	< .001
5	27/14	0.32 ± 0.30 (n = 903)	2.63	0.51 ± 0.24	< .001
6	28/17	0.34 ± 0.27 (n = 943)	8.12	0.40 ± 0.14	< .001
7	31/19	0.39 ± 0.36 (n = 857)	6.63	0.54 ± 0.18	< .001
8	26/11	0.24 ± 0.38 (n = 948)	8.67	0.44 ± 0.35	< .001
9	29/12	0.27 ± 0.22 (n = 901)	3.54	0.34 ± 0.12	< .001
10	29/16	0.28 ± 0.19 (n = 924)	2.75	0.40 ± 0.11	< .001

PACU, postanesthesia care unit; SEVO, sevoflurane.

The total number of patients (all patients monitored in the PACU regardless of the used anesthetics) and the number of patients, who underwent SEVO anesthesia are given. Baseline SEVO pollution was continuously measured on 10 different days for 9 hours each (SEVO baseline; n = number of measurements per day). The SEVO maximum represents the highest concentration measured within the 9 hours period. Incoming patients after SEVO exposure caused measurable peaks within the first 15 minutes after PACU arrival, which differed significantly from baseline concentrations (15 minutes measurements: approximately 25 measurements).

Air Pollution Measurements in the Patients' Breathing Zones

SEVO concentrations within the patients' breathing zones were measured 25 times for 1 hour each at

different days and when no other patient after SEVO anesthesia was in the PACU. The mean SEVO concentration was 0.44 ± 0.10 ppm and the maximum concentration was 1.74 ± 1.54 ppm. Detailed analysis revealed that highest SEVO

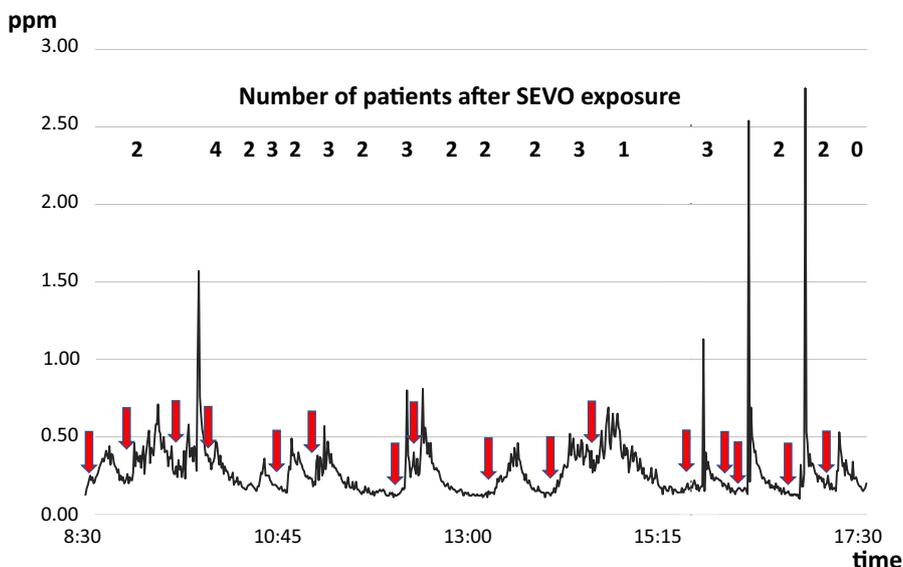


Figure 1. SEVO concentration in the PACU. Example of an air pollution measurement in the middle of the room at a height of 150 cm. A total of 924 measurements were performed. Sixteen patients obtained SEVO in the operating room. A mean SEVO concentration of 0.28 ± 0.19 ppm was detected. Peaks rose up to 2.75 ppm. Arrows demonstrate incoming patients. The number of patients, who exhale SEVO in the PACU over time is shown at the top. PACU, postanesthesia care unit; SEVO, sevoflurane. This image is available in color online at www.jopan.org.

concentrations were always detected within the first 15 minutes after arrival ($\bar{c}_{\text{mean}} = 0.56 \pm 0.17$ ppm), before air pollution levels kept stable for a longer period (second and third quarter of an hour: $\bar{c}_{\text{mean}} = 0.42 \pm 0.09$ ppm and 0.36 ± 0.09 ppm). After 1 hour in the PACU, SEVO was still exhaled by the patients, although to a lesser extent ($\bar{c}_{\text{mean}} = 0.34 \pm 0.13$ ppm) (first quarter vs remaining three quarters: $P < .001$). A characteristic decay curve is demonstrated in Figure 2.

Air Pollution Measurements on the Corridor

SEVO pollution on the corridor in front of the closed PACU door was measured on three different days from 11 a.m. to 4 p.m. with the sampling probe fixed at a height of 150 cm. The mean SEVO concentration was 0.47 ± 0.06 ppm and significantly higher than in the PACU ($P = .015$). The transfer of exposed postoperative patients through the corridor to the PACU always caused measurable peaks (Figure 3). The maximum concentration was 1.53 ± 0.27 ppm.

Urinary SEVO and HFIP Biomonitoring

Preshift and postshift urinary concentrations of SEVO and HFIP were determined in PACU health care professionals on 10 different days ($n = 5$ women, $n = 5$ men).

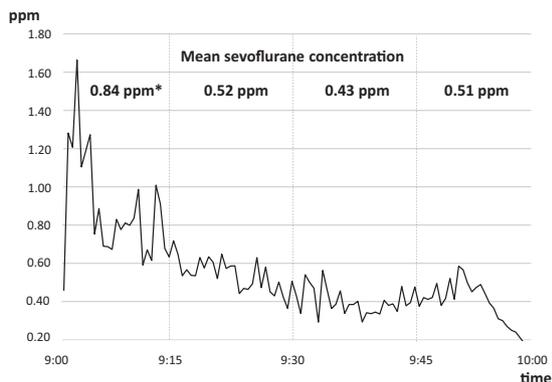


Figure 2. Concentration of exhaled sevoflurane in the patient's breathing zone. Sevoflurane pollution was measured within the first hour after the patient's transfer to the PACU. The sampling line was placed at a distance of 25 cm above the nose and mouth. Highest pollution levels were detected within the first 15 minutes (approximately 25 measurements) after the patient's arrival. *Significant difference. PACU, postanesthesia care unit.

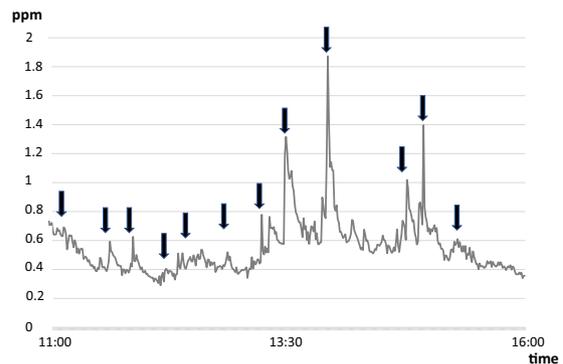


Figure 3. SEVO pollution on the corridor in front of the PACU door. Pollution levels resulted from exposed postoperative patients, who were transferred from the operating room to the PACU, the latter locked by a door with numerical code. Its opening lasted at least 1 minute, in which the patient exhaled SEVO in the air of the corridor (black arrows). PACU, postanesthesia care unit; SEVO, sevoflurane. This image is available in color online at www.jopan.org.

SEVO was detected in 80% of the preshift samples in a concentration of 0.13 ± 0.03 mcg/L. The metabolite HFIP was detected in all preshift samples in a concentration of 4.72 ± 5.41 mcg/L. Biological postshift exposure levels were 0.20 ± 0.06 mcg/L (SEVO) and 42.18 ± 27.82 mcg/L (HFIP). Both postshift concentrations increased significantly compared with preshift baseline concentrations (SEVO, $P = .004$; HFIP, $P < .001$). The concentration of SEVO in the air and in urinary postshift SEVO samples showed a weak linear correlation ($R^2 = 0.473$), but no statistical significance ($P = .167$) (Figure 4A). The metabolite HFIP did not correlate to SEVO air pollution levels, neither in its actually measured concentration ($R^2 = 0.261$; $P = .126$), nor in its corrected form (postshift minus preshift concentration; $R^2 = 0.196$; $P = .587$) (Figure 4B).

Influencing Factors and Interindividual Differences

The personnel's workspaces on the day before biomonitoring were as follows: three had at least 1 day off (preshift SEVO, 0.12 ± 0.04 mcg/L; preshift HFIP, 1.00 ± 1.57 mcg/L), three had worked in the PACU (preshift SEVO, 0.12 ± 0.02 mcg/L; preshift HFIP, 7.13 ± 7.68 mcg/L), and four had worked in the operating room (preshift

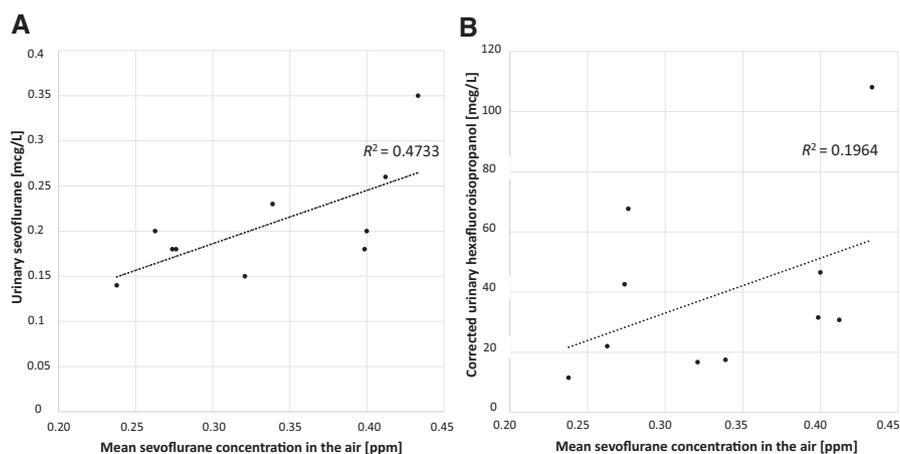


Figure 4. Correlations between SEVO pollution in the air and urinary SEVO or HFIP, respectively. A weak linear correlation is seen between SEVO pollution and SEVO biomonitoring, but no statistical significance ($P = .167$) (A). HFIP biomonitoring revealed no linear correlation, neither in its actually measured form (data not shown) nor in its corrected form (postshift HFIP minus preshift HFIP) ($P = .587$) (B). HFIP, hexafluoroisopropanol; SEVO, sevoflurane.

SEVO, 0.13 ± 0.04 mcg/L; preshift HFIP, 3.16 ± 3.12 mcg/L). Neither preshift SEVO nor preshift HFIP concentrations were significantly influenced by the personnel’s workplace on the previous day (SEVO, $P = .855$; HFIP, $P = .349$).

The personnel’s sex did not affect preshift and postshift SEVO and HFIP concentrations significantly (SEVO preshift, women 0.11 ± 0.03 mcg/L vs men 0.14 ± 0.03 mcg/L, $P = .153$; HFIP preshift, women 4.68 ± 6.48 mcg/L vs men 2.01 ± 1.32 mcg/L, $P = .393$; SEVO postshift, women 0.23 ± 0.06 mcg/L vs men 0.18 ± 0.04 mcg/L, $P = .159$; HFIP postshift, women 50.57 ± 33.87 mcg/L vs men 35.20 ± 18.84 mcg/L, $P = .401$). The interindividual differing biotransformation of SEVO is shown in Table 3.

Discussion

This study demonstrates that PACU health care professionals are biologically exposed to SEVO during routine work, although our PACU exceeds all current standards of room ventilation (at least six air changes per hour are recommended) and the average SEVO burden in the air was low.⁸

In 1977, the National Institute for Occupational Safety and Health introduced the first exposure limits for halogenated agents, which was 2 ppm for SEVO when used without nitrous oxide.⁹ Since then, other countries established time-weighted exposure limits for SEVO as well, ranging from 2 to 20 ppm, whereas some have not defined any exposure limit yet.⁴

Table 3. Biological SEVO Burden and Interindividual Differences

Personnel’s Sex	SEVO Baseline (ppm)	SEVO Maximum (ppm)	Preshift SEVO (mcg/L)	Preshift HFIP (mcg/L)	Postshift SEVO (mcg/L)	Postshift HFIP (mcg/L)
Female	0.40 ± 0.21	1.52	0.09	0.5	0.20	22.04
Female	0.40 ± 0.21	1.52	0.17	0.61	0.20	64.53
Male	0.32 ± 0.30	2.63	0.15	3.24	0.15	19.98
Male	0.32 ± 0.30	2.63	0.12	0.5	0.14	31.22

HFIP, hexafluoroisopropanol; SEVO, sevoflurane.

Two same-sex health care professionals worked together for 8.5 hours in the PACU. The concentration of SEVO in the air was obviously identical, and the inhaled mass must have been comparable, because postshift urinary SEVO concentrations were very similar. However, postshift HFIP concentrations varied considerably, showing that individual factors must affect the biotransformation of SEVO.

In this study, SEVO pollution in the middle of the PACU was 0.34 ppm with little fluctuation over time, which is considered minimal and comparable to previous studies (0.11 to 0.43 ppm; prescribed higher SEVO levels of 0.92 and 1.12 ppm resulted from a shorter measuring distance to the patient).^{3,5,6,10} Moreover, we showed that incoming patients after SEVO exposure increased the baseline significantly. This is interesting, because the airway device was always removed in the operating room (it is known that the airway device *in situ* increases PACU pollution levels significantly) and patients could open their eyes at the time of PACU arrival, which indicates that the residual gas concentration must have been low.¹¹ However, expiratory SEVO concentrations of 0.1% to 0.2% still correspond to 1,000 to 2,000 ppm, which are exhaled in the PACU air and might explain the baseline's increase. The fact that the SEVO concentration in the PACU depended significantly on the number of exposed patients fits in well with this result.

Decay curves after anesthetic gas exposure in the PACU had once been described, but in patients after anesthesia with a mixture of nitrous oxide and SEVO only and at a shorter measuring distance to the patient's mouth and nose (15 vs 25 cm in this study). The authors reported SEVO peak concentrations of greater than 12 ppm after PACU arrival, followed by a subsequent decline, which appears similar to our results, although pollution levels were 10 times lower in our study.¹⁰ This can be explained by the greater distance between the measuring probe and the patient's breathing zone, as well as by a more powerful air conditioning. However, the personnel's risk for gas exposure was highest within the first 15 minutes, at a time, in which patients usually need the most intensive care. Here, an oxygen-scavenging mask may be useful.⁵

A biological exposure limit for urinary SEVO, which represents, because of its short half-life, very recent gas exposure only, does not exist. Some investigators calculated biological equivalent concentrations (BECs), which correspond to 2 ppm SEVO in the air, but results are not uniform and vary between 1.9 and 3.9 mcg/L.^{7,12,13} However, a postshift concentration of 0.20 mcg/L as measured in this study is less than any prescribed BEC, which

matches with the low SEVO pollution and thus must be considered minimal.

In the literature, there is another study only investigating urinary SEVO concentrations in PACU personnel. The authors reported a concentration of 4 mcg/L, which is 20 times higher than that observed in this study, although air pollution was comparable (0.43 vs 0.34 ppm). Interestingly, even genotoxicity increased in exposed personnel.³

Urinary HFIP, used to estimate the personnel's all-day SEVO burden in the PACU, was detectable in all preshift samples, although in 30% the last SEVO exposure was 36 to 60 hours ago. This matches with the results from two other studies, pointing out that HFIP has a long half-life of at least 19 hours and that its elimination may need approximately 2 days.^{7,14} However, it also indicates that daily SEVO exposure may increase preshift HFIP concentrations over time. Thus, the preshift concentration must be known to assess postshift HFIP levels correctly, especially because HFIP accumulation is supposed by some authors.¹⁵

In the literature, there is no information about HFIP concentrations in PACU workers, but few measurements were performed in operating room personnel. Concentrations were 62.5 to 85.5 mcg/L, which is two times higher than in this study (corrected HFIP 37 mcg/L), although air pollution was higher.¹² Comparable to urinary SEVO, biological limit concentrations are not defined for HFIP, but BECs corresponding to 2 ppm SEVO in the air have been calculated. Results are inconsistent as well and vary between 318 and 2,773 mcg/L. However, it should be noted that—in contrast to previous studies—no positive linear correlation was observed between SEVO concentrations in the air and urinary SEVO or HFIP levels, respectively.^{7,12,13} A reason could be that the personnel's inhalational SEVO exposure was underestimated, as measurements were performed in the middle of the room and not in their individual breathing zone. Nevertheless, a biological exposure of 37 mcg/L is obviously low.

Furthermore, we demonstrated that the biotransformation of SEVO and, accordingly, the biological SEVO burden are interindividually different and must be influenced by other factors than air

pollution levels alone. Data revealed that neither the personnel's sex nor the workspace on the previous day had a significant impact on urinary SEVO and HFIP concentrations. However, it is known that a genetic polymorphism of the enzyme CYP2E1, which is involved in HFIP production, as well as smoking and alcohol consumption can influence SEVO biotransformation.¹²

This study has a few limitations. First, it is difficult to generalize our results, because the measurements were conducted in our unique PACU, which is not necessarily comparable to other PACUs. Furthermore, patients obtained SEVO as inhalational anesthetic only, which might differ from other clinical standards. Specifically the potential use of nitrous oxide is of importance, as it decreases the recommended exposure limit concentration in the air from 2 to 0.5 ppm. Second, the all-day SEVO concentration in the air was determined in the middle of the PACU and not in the worker's individual breathing zone, because the sampling probe, which has a length of 8 m, could be a hindrance in critical situations. Moreover, PACU personnel work in the middle of the room

most of the time and not that close to the patient's breathing zone. However, SEVO concentrations in the personnel's breathing zone might have been higher. Finally, the sample size was small, which is because of the study's design (pilot study).

Conclusions

PACU personnel are environmentally and biologically exposed to SEVO during patient care, but the overall gas burden is minimal in relation to current environmental recommendations. Urinary SEVO, as well as urinary HFIP concentrations were consistent with air pollution measurements, although a linear correlation could not be observed. Specifically HFIP might be useful to assess all-day and long-term exposure, but pre-shift concentrations should be known to evaluate postshift concentrations correctly. Efforts are needed to further minimize occupational anesthetic gas exposure.

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