Exposure to Sevoflurane and Nitrous Oxide During Four Different Methods of Anesthetic Induction

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The National Institute for Occupational Safety and Health-recommended exposure levels for nitrous oxide exposure are 25 ppm as a time-weighted average over the time of exposure. The exposure limit for halogenated anesthetics (without concomitant nitrous oxide exposure) is 2 ppm. Inhaled sevoflurane provides an alternative to IV induction of anesthesia. However, the inadvertent release of anesthetic gases into the room is likely to be greater than that with induction involving IV anesthetics. We therefore evaluated anesthesiologist exposure during four different induction techniques. Eighty patients were assigned to one of the induction groups to receive: 1) sevoflurane and nitrous oxide from a rebreathing bag, 2) sevoflurane and nitrous oxide from a circle circuit, 3) propofol 3 mg/kg, and 4) thiopental sodium 5 mg/kg. Anesthesia was maintained with sevoflurane and nitrous oxide via a laryngeal mask. Trace concentrations were measured directly from the breathing zone of the anesthesiologist.

During induction, peak concentrations of sevoflurane and nitrous oxide with the two IV methods rarely exceeded 2 ppm sevoflurane and 50 ppm nitrous oxide. Concentrations during the two inhalation methods were generally <20 ppm sevoflurane and 100 ppm nitrous oxide. During maintenance, median values were near 2 ppm sevoflurane and 50 ppm nitrous oxide in all groups. Sevoflurane concentrations during inhaled induction frequently exceeded the National Institute for Occupational Safety and Health-recommended exposure ceiling of 2 ppm but mostly remained <20 ppm. Exposure during the maintenance phase of anesthesia also frequently exceeded the 2-ppm ceiling. We conclude that operating room anesthetic vapor concentrations are increased during inhaled inductions and remain increased with laryngeal mask ventilation.

Implications: We compared waste gas concentrations to sevoflurane and nitrous oxide during four different induction methods. During inhaled induction with a rebreathing bag or a circle circuit system, waste gas concentrations frequently exceed National Institute for Occupational Safety and Health limits of 2 ppm sevoflurane and 50 ppm nitrous oxide. Therefore, we recommend that people at risk (e.g., women of childbearing age) should pay great attention when using this technique.

(Anesth Analg 1999;88:925–9)

Some contamination of the operating rooms by waste anesthetic gases is unavoidable when anesthetic gases are used. The amount of contamination increases when unsealed airway devices and/or high concentrations of inhaled anesthetics are used; inhaled induction of anesthesia, for example, is especially problematic (1,2). The health consequences of environmental exposure to operating room anesthetic vapor concentrations are controversial (3). However, there is considerable epidemiological evidence that trace concentrations of anesthetics are associated with spontaneous abortion and infertility (4,5).

European and United States health authorities recommend exposure limits for volatile anesthetics (Table 1). Although an occupational exposure standard for sevoflurane has not been established by regulatory agencies, a maximal level of 20 ppm has been set by the manufacturer without a detailed justification (data provided by manufacturer). This is higher than the European recommended exposure limits for other volatile anesthetics (6). In contrast, the United States National
Institute of Environmental Health and Safety (NIOSH) recommends a time-weighted average of 25 ppm for nitrous oxide and a ceiling of 2 ppm for volatile anesthetics, although these levels were set long before the introduction of sevoflurane (7,8).

The aim of our study was to evaluate time-dependent changes in air contamination by waste anesthetic gases during four different anesthetic induction techniques.

**Methods**

We measured trace concentrations of sevoflurane and nitrous oxide during the induction, maintenance, and recovery from anesthesia in 80 patients scheduled for gynecological procedures. The details of induction and maintenance are described in an accompanying article (9). Briefly, four different methods of induction were performed: 1) sevoflurane and nitrous oxide from a rebreathing bag (Sevo/Bag), 2) sevoflurane and nitrous oxide from a circle system on a conventional anesthesia machine (Sevo/Circle), 3) propofol 3 mg/kg (propofol), and 4) thiopental sodium 5 mg/kg (thiopental).

A laryngeal mask was used to secure the airway during anesthesia. Anesthesia was then maintained with clinically necessary amounts of sevoflurane in 60% nitrous oxide in oxygen. Great care was taken throughout induction and anesthesia to maintain the best possible mask seal, to avoid excessive peak inspiratory pressure, and to minimize occupational exposure to operating room anesthetic vapor concentrations. The study was conducted in an operating room that had 17 air exchanges/h, with all ventilation being fresh air. The anesthesia machine was connected to a scavenging system, which, in turn, was connected to the hospital vacuum system, which aspirated at a rate of 45 L/min.

Ambient gas was sampled continuously from a Teflon tube (Merck, Vienna, Austria) fixed to the shoulder of the anesthesiologist (breathing zone). As in previous studies (10), operating room anesthetic vapor concentrations of sevoflurane and nitrous oxide samples were determined at 1-min intervals with a Brüel & Kjaer 1301 (Naerum, Denmark) photoacoustic infrared spectrometer. The lower detection limit with this system is 0.09 ppm for sevoflurane and 0.1 ppm for nitrous oxide. Before the study, the system was calibrated for each gas, e.g., with 20.8 ppm sevoflurane in pure nitrogen to provide an accuracy of ±2% over the entire relevant range. Appropriate compensations were included to neutralize the potential confounding effects of humidity, air pressure, and temperature. We similarly compensated for potential interactions among sevoflurane, nitrous oxide, water, and carbon dioxide.

The time course of each anesthetic procedure was divided into four periods: preinduction, induction, maintenance, and recovery. Cumulative values were calculated for 5 min for preinduction and induction, whereas a 10-min cumulative value was calculated for the maintenance and recovery periods. Results are presented as medians with 10th, 25th, 75th, 90th, and outliers ranging within the 95th percentiles. Values were compared using nonparametric tests (Mann-Whitney U-test); P < 0.05 was considered statistically significant.

**Results**

Typical time courses of the waste gas concentrations during preinduction, induction, maintenance, and recovery of anesthesia are presented in Figures 1 and 2. Cumulative data during the different parts of anesthesia and for each group are presented as box plots in Figures 3 and 4. Violations of different threshold values of 0.5, 2, 20, and >20 ppm sevoflurane, and of 25, 50, 100, and >100 ppm nitrous oxide according to the different international occupational standards (Table 1) as a percentage of time are presented in Table 2.

During induction, peak concentrations of sevoflurane and nitrous oxide with the two IV methods rarely
exceeded 2 ppm sevoflurane and 50 ppm nitrous oxide. Peak concentrations of sevoflurane during the two inhalation methods rarely exceeded 20 ppm (Table 2). Overall, the concentrations of sevoflurane and nitrous oxide during induction were significantly lower in the IV groups (thiopental and propofol) than the inhalation groups (Sevo/Bag and Sevo/Circle). The range of the waste gases during induction was greater in the Sevo/Circle than in the Sevo/Bag group, but the difference was not statistically significant.

Median waste gas concentrations during maintenance were approximately 2 ppm sevoflurane and approximately 50 ppm nitrous oxide in all groups. During the recovery period, median waste gas concentrations were similar in all groups, near 1 ppm sevoflurane and approximately 25 ppm nitrous oxide (Figs. 3 and 4).

Discussion

Nine major studies of anesthetic vapor concentrations between 1971 and 1985 indicated that occupational exposure to unscavenged waste anesthetic gases is associated with adverse effects in healthcare workers (11–19). In contrast, seven other studies failed to identify a statistically significant correlation (20–26). Although these studies were criticized for design limitations, meta-analyses identified substantial basis for
concern, even when analysis was restricted to the best available data (27–29). The major identified toxicities were spontaneous abortion (relative risk roughly 1.3–1.9) and infertility. When assessing the value of these epidemiological studies, however, it should be taken into consideration that it had been impossible to draw a direct connection between the level of exposure and untoward health response because most studies lacked exposure measurement. This may be important because universal adoption of scavenging systems did not occur until 1980.

Nevertheless, most international health authorities have set occupational standards ranging from a low to a relatively high level, demonstrating the lack of consensus in this field. For example, NIOSH has specified that it is unable to identify a safe level of exposure for waste anesthetic gases. It therefore recommends that the risk be minimized by “reducing exposures to the greatest extent possible” (8). The NIOSH recommendations for nitrous oxide exposure are now 25 ppm, as a time-weighted average. Interestingly, the recommended exposure level for nitrous oxide in Europe is considerably higher: 25–50 ppm as a time-weighted average over an 8-h working day. Nitrous oxide concentrations were relatively high during maintenance anesthesia (40–57 ppm) in all groups. These high values are presumably from leakage from laryngeal mask airways (30). Because median values were near the 2-ppm NIOSH limit, it is apparent that half the values exceeded this value. However, most measurements were well within the European recommendations.

Operating room anesthetic vapor concentrations would presumably be higher with lower air turnover and a smaller fraction of fresh air. For example, relatively high concentrations have even been observed in poorly ventilated postanesthesia care units (34). In this respect, it is worth noting that air exchange in the operating room we studied far exceeds current recommendations by the American Institute of Architects and the United States Department of Health and Human Services, which specify six air exchanges per hour, with only two being fresh (35).

In summary, we conclude that inhaled induction techniques with sevoflurane and nitrous oxide in adults violate NIOSH-recommended exposure limits (31), whereas gas concentrations in properly scavenged operating rooms reportedly comply with NIOSH-recommended exposure limits (32,33). The operating room anesthetic vapor concentrations we observed during mask induction in adults were considerably lower than the levels reported during pediatric anesthesia (31) and were comparable to values obtained during triple vital-capacity inhaled inductions (2).

Concentrations were averaged over the relevant study period in each case. Sevoflurane concentrations can be directly compared with the relevant recommended ceiling exposure limits. Nitrous oxide concentrations cannot be directly compared with recommended exposure limits because the limits for this agent are expressed in terms of a time-weighted average over an 8-h work day.

### Table 2. Percentage of Time Exceeding Recommended Exposure Limits

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<tr>
<th></th>
<th>Thiopental</th>
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| Sevoflurane |            |          |            |          |            |          |            |          |
|------------|------------|----------|-------------|----------|
| Preinduction | 46        | 50       | 4           | 0        |
| Induction   | 48        | 42       | 10          | 0        |
| Maintenance | 22        | 56       | 21          | 1        |
| Recovery    | 32        | 58       | 10          | 0        |

| N₂O         |            |          |            |          |            |          |            |          |
|------------|------------|----------|-------------|----------|
| Preinduction | 97        | 3        | 0           | 0        |
| Induction   | 79        | 15       | 1           | 5        |
| Maintenance | 26        | 28       | 17          | 17       |
| Recovery    | 59        | 26       | 11          | 4        |

Concentrations were averaged over the relevant study period in each case. Sevoflurane concentrations can be directly compared with the relevant recommended ceiling exposure limits. Nitrous oxide concentrations cannot be directed compared with recommended exposure limits because the limits for this agent are expressed in terms of a time-weighted average over an 8-h work day.
The authors gratefully acknowledge the support and generous assistance of the gynecological anesthesia and surgical nurses in Operation Group SC.

References