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Effect of total flow rate on the concentration of degradation products generated by reaction between sevoflurane and soda lime

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Summary

We have compared concentrations of degradation products in the circle system during sevoflurane anaesthesia at different fresh gas flows. Twenty-four patients underwent sevoflurane anaesthesia with fresh gas flows of 1 litre min^{-1} (1L group), 3 litre min^{-1} (3L group), or 6 litre min^{-1} (6L group) ($n = 8$ in each group). During anaesthesia, the concentrations of degradation products were measured every hour, and the temperature of soda lime, end-tidal carbon dioxide concentration, inspired and end-tidal sevoflurane concentrations, and carbon dioxide elimination were measured. $CF_2{=}C(CF_3){-}O{-}CH_2F$ (compound A) was the only degradation product detected. The mean maximum concentration of compound A was 19.7 (SD 4.3) ppm in the 1L group, 8.1 (2.7) ppm in the 3L group and 2.1 (1.0) ppm in the 6L group ($P < 0.05$). The maximum temperature of soda lime was 44.6 (1.5) °C in the 1L group, 37.0 (4.4) °C in the 3L group and 29.1 (5.1) °C in the 6L group ($P < 0.05$). There were no significant differences in end-tidal sevoflurane concentration or mean carbon dioxide elimination between the groups. Only compound A was detected following anaesthesia, with higher concentrations observed at lower flow rates. (*Br. J. Anaesth.* 1995; **74**: 667–669)

Key words

Anaesthetics volatile, sevoflurane. Complications, inhalation anaesthesia. Carbon dioxide, absorption. Ventilation, fresh gas flow.

Sevoflurane is known to react with soda lime producing several degradation products [1, 2]. These products differ according to the concentration of sevoflurane in the circle system [3, 4], temperature [5–7] and type [3, 8, 9] of carbon dioxide absorbent, and its freshness [9] and water content [10, 11]. However, there have been no reports on concentrations of degradation products in the circle system induced by differences in fresh gas flow used in clinical practice. In this study, patients underwent sevoflurane anaesthesia at fresh gas flows of 1, 3 or 6 litre min^{-1}, and the concentrations of degradation products in the circle system at each flow rate were compared. As the generation of degradation products is affected by the temperature of the carbon dioxide absorbent [5–7] and the temperature of the carbon dioxide absorbent is affected by the patient's carbon dioxide elimination and also fresh gas flow, we measured the temperature of the carbon dioxide absorbent and carbon dioxide elimination.

Patients and methods

This study was approved by the institution's Committee on Human Research, and informed consent was obtained from all subjects.

We studied 24 patients undergoing tympanoplasty; all were ASA I or II. Exclusions included patients with liver or renal dysfunction or severe cardiovascular disease based on history, laboratory findings or physical examination.

Premedication comprised hydroxyzine 50 mg i.m. and atropine 0.5 mg i.m., 45 min before induction of anaesthesia, with thiopentone 4–5 mg kg^{-1} followed by vecuronium 0.12–0.15 mg kg^{-1}. In the first eight patients a fresh-gas flow of 1 litre min^{-1} was used for maintenance of anaesthesia after tracheal intubation (1L group). The fresh-gas flow was increased to 3 litre min^{-1} for the next eight patients (3L group) and to 6 litre min^{-1} for the final eight patients (6L group). In each group the ratio of oxygen flow to nitrous oxide flow was adjusted to maintain the oxygen concentration in the inspiratory limb greater than 30%. The sevoflurane concentration was adjusted to maintain systolic arterial pressure within $\pm 25\%$ of the baseline value. Ventilation was controlled by setting the tidal volume of the ventilator to 10–12 ml kg^{-1}, and ventilatory frequency was adjusted to maintain end-tidal carbon dioxide partial pressure at 4.8–5.3 kPa.

Soda lime (Sodasorb II, W. R. Grace and Co., Lexington, MA, USA) was used as the carbon dioxide absorbent. Fresh carbon dioxide absorbent was used for each patient. The anaesthesia machine used was a Modulas II Anesthesia System (Ohmeda, Madison, WI, USA). The circle system hoses were made of polyester elastomer, and fittings were made of silicone rubber. The Y-piece was made of polypropylene. The other components of the circle system (valves, fresh gas inlet, canister, etc) were the standard used with the Modulas II Anesthesia System.

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In order to monitor the temperature of the soda lime, two temperature probes (temperature probe model 9182, Hioki Electric Co., Nagano, Japan) were inserted into the centre of the top and bottom of the upper canister. The temperature was recorded every 15 min.

During anaesthesia, end-tidal carbon dioxide concentration and inspired and end-tidal sevoflurane concentrations were monitored using a mass spectrometer (Medical Gas Analyzer 1100, Perkin Elmer, Pomona, CA, USA). The patient's carbon dioxide elimination during anaesthesia was calculated as minute expired volume times mean expired carbon dioxide concentration. Minute expired volume was measured using a linearized electronic Wright respirometer (BOC Medishield Essex, UK). Mean expired carbon dioxide concentration was obtained using a bypassed minimixing chamber, and then measured by mass spectrometry [12]. Hourly mean values were calculated from the values measured every 1 min.

Gas samples for measurement of degradation products were obtained from the inspiratory limb of the circle system. The concentrations of the degradation products were measured hourly using a gas chromatograph (model GC-9A, Shimadzu, Kyoto, Japan) equipped with a gas analyser (model MGS-5, Shimadzu, Kyoto, Japan).

The analysis conditions for gas chromatography were a column temperature maintained at 100 °C and an injection inlet temperature maintained at 140 °C. Nitrogen was used as the carrier gas at a flow rate of 50 ml min^{-1}. The detector was a hydrogen flame ion detector (FID). The column was a glass column 5 m in length and 3 mm in internal diameter filled with 20% DOP Chromosorb WAW (Technolab S.C. Corp., Osaka, Japan) 80/100 mesh. The sample volume was 1 ml. The gas chromatograph was calibrated with standard calibration gas prepared from stock solutions of $CF_2{=}C(CF_3){-}O{-}CH_2F$ (compound A) and $CH_3OCF_2CH(CF_3)OCH_2F$ (compound B) (Maruishi Pharmaceutical Co., Ltd, Osaka, Japan).

Table 1. Patient characteristics (mean (SD) [range])

Group	Age (yr)	Height (cm)	Body weight (kg)
1 litre min^{-1}	51.6 [24–69]	159.8 (7.3) [146–169]	61.7 (8.2) [49–78]
3 litre min^{-1}	50.9 [21–68]	158.7 (12.6) [146–184]	56.6 (10 4) [48–80]
6 litre min^{-1}	49.9 [20–63]	156.3 (12.1) [137–170]	53.9 (10.8) [40–66]

All results are expressed as mean (SD). The concentration of compound A, temperature of the soda lime, end-tidal sevoflurane concentration and carbon dioxide elimination were compared by one-way analysis of variance (ANOVA) followed by Scheffe's test to evaluate statistical significance between any two groups. A P value of 0.05 or less was considered statistically significant.

Results

There were no significant differences in age, height or body weight between the groups (table 1). The only degradation product of sevoflurane detected was $CF_2{=}C(CF_3){-}O{-}CH_2F$ (compound A). The individual maximum concentration of compound A was 19.7 (4.3) (14.1–27.4) ppm in the 1L group, 8.1 (2.7) (4.6–11.5) ppm in the 3L group and 2.1 (1.0) (1.1–3.9) ppm in the 6L group ($P < 0.05$) (table 2). There were no differences between groups in end-tidal sevoflurane concentration when individual maximum concentrations of compound A were observed (table 2).

The individual maximum temperature of the soda lime was 44.6 (1.5) °C in the 1L group, 37.0 (4.4) °C in the 3L group and 29.1 (5.1) °C in the 6L group ($P < 0.05$) (table 2). The concentration of compound A in the circle system at each measurement point was highest in the 1L group, followed by the 3L group and then the 6L group ($P < 0.05$) (fig. 1).

End-tidal sevoflurane concentration ranged from 1.0% to 2.4% for the three groups, with no significant difference between the groups. The mean volume of carbon dioxide eliminated by the patient varied from 88.3 to 217.0 ml min^{-1} between the three groups; the differences were not statistically significant.

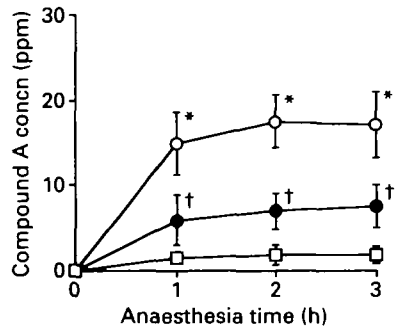

Figure 1. Comparison of concentrations of compound A at fresh gas flows of 1 (○), 3 (●) and 6 (□) litre min^{-1} (mean, SD). * $P < 0.05$ *vs* 3 litre min^{-1} and 6 litre min^{-1}; † $P < 0.05$ *vs* 6 litre min^{-1}. $n = 8$ in each group.

Table 2. Maximum compound A concentration, corresponding end-tidal sevoflurane concentration and maximum temperature of soda lime (mean (SD)). Corresponding end-tidal sevoflurane concentration = end-tidal sevoflurane concentration when individual maximum compound A concentrations were observed. Significant differences ($P < 0.05$): * compared with 3-litre min^{-1} and 6-litre min^{-1} groups; † compared with 6-litre min^{-1} group.

	Maximum compound A concn (ppm)	Corresponding end-tidal sevoflurane concn (%)	Maximum temperature of soda lime (°C)
1 litre min^{-1}	19.7 (4.3)*	2.0 (0.3)	44.6 (1.5)*
3 litre min^{-1}	8.1 (2.7)†	1.9 (0 3)	37.0 (4.4)†
6 litre min^{-1}	2 1 (1.0)	1.8 (0.3)	29.1 (5.1)

Discussion

The concentration of compound A was highest in the 1L group and lowest in the 6L group. It is known that the generation of degradation products is increased at high temperatures of soda lime [5–7]. In this study, the concentration of compound A was increased at low flow rates, which are associated with higher temperatures of soda lime. In addition, it can be assumed that compound A accumulates in the circle system at low flow rates.

The following factors have been shown to affect concentrations of degradation products. (1) The temperature of soda lime [5–7], (2) fresh gas flow, (3) the patient's carbon dioxide elimination, (4) concentration of sevoflurane in the circle system [3, 4], (5) type of carbon dioxide absorbent used [3, 8, 9], (6) freshness of the absorbent [9] and (7) water content of absorbent [10, 11]. In the present study, (5)–(7) were deliberately kept constant; there was no significant difference between groups for (3) and (4). Therefore the only variable was fresh gas flow and the consequent change in soda lime temperature. However, the reduction in concentration of degradation product, as the flow increased, would be caused partly by reduced carbon dioxide absorption/lower temperature of soda lime and partly by greater washout of the degradation product.

The LC_{50} value of compound A in rats is 331 (7) ppm with inhalation for 3 h, 203 (4) ppm with inhalation for 6 h and 127 (9) ppm with inhalation for 12 h [13, 14]. The concentrations of compound A measured in the present study were lower than the LC_{50} for rats at all flow rates. Sevoflurane anaesthesia has been administered to more than 1 million patients in Japan, and no organic disorders thought to result from anaesthesia have been reported. However, as anaesthesia is generally performed at a flow rate of 6 litre min^{-1} in Japan, the safety of sevoflurane anaesthesia at low flow rates has yet to be confirmed. It has been reported that no abnormalities are seen in laboratory tests of renal and hepatic function after sevoflurane anaesthesia at low flow rates [9, 15] or closed circuit [16]. However, further studies on the safety of sevoflurane anaesthesia at low fresh gas flows are warranted.

References

1. Wallin RF, Regan BM, Napoli MD, Stern IJ. Sevoflurane: A new inhalational anesthetic agent. *Anesthesia and Analgesia* 1975; **54**: 758–765.
2. Hanaki C, Fujii K, Morio M, Tashima T. Decomposition of sevoflurane by sodalime. *Hiroshima Journal of Medical Sciences* 1987; **36**: 61–67.
3. Bito H, Ikeda K. Long-duration, low-flow sevoflurane anesthesia using two carbon dioxide absorbents. *Anesthesiology* 1994; **81**: 340–345.
4. Morio M, Fujii K, Satoh N, Imai M, Kawakami U, Mizuno, T, Kawai Y, Ogasawara Y, Tamura T, Negishi A, Kumagai Y, Kawai T. Reaction of sevoflurane and its degradation products with soda lime. *Anesthesiology* 1992; **77**: 1155–1164.
5. Strum DP, Johnson BH, Eger EI II. Stability of sevoflurane in soda lime. *Anesthesiology* 1987; **67**: 779–781.
6. Kudo M, Kudo T, Oyama T, Matsuki A. Reaction products of sevoflurane wih components of sodalime under various conditions. *Masui* 1990; **39**: 39–44.
7. Ruzicka JA, Hidalgo JC, Tinker JH, Baker MT. Inhibition of volatile sevoflurane degradation product formation in an anesthesia circuit by a reduction in soda lime temperature. *Anesthesiology* 1994; **81**: 238–244.
8. Liu J, Laster MJ, Eger EI II, Taheri S. Absorption and degradation of sevoflurane and isoflurane in a conventional anesthetic circuit. *Anesthesia and Analgesia* 1991; **72**: 785–789.
9. Frink EJ, Malan TP, Morgan SE, Brown EA, Malcomson M, Brown BR Jr. Quantification of the degradation products of sevoflurane in the two CO_2 absorbants during low-flow anesthesia in surgical patients. *Anesthesiology* 1992; **77**: 1064–1069.
10. Wong, DT, Lerman J. Factors affecting the rate of disappearance of sevoflurane in Baralyme. *Canadian Journal of Anaesthesia* 1992; **39**: 366–369.
11. Strum DP, Eger EI II. The degradation, absorption, and solubility of volatile anesthetics in soda lime depend on water content. *Anesthesia and Analgesia* 1994; **78**: 340–348.
12. Sanjo Y, Ikeda K. A small bypass mixing chamber for monitoring metabolic rate and anesthetic uptake: The bymixer. *Journal of Clinical Monitoring* 1987; **3**: 235–243.
13. Gonsowski CT, Laster MJ, Eger EI II, Ferrell LD, Kerschmann RL. Toxicity of compound A in rats: Effect of 3-hour administration. *Anesthesiology* 1994; **80**: 556–565.
14. Gonsowski CT, Laster MJ, Eger EI II, Ferrell LD, Kerschmann RL. Toxicity of compound A in rats: Effect of increasing duration of administration. *Anesthesiology* 1994; **80**: 566–573.
15. Bito H, Ikeda K. Plasma inorganic fluoride and intracircuit degradation product concentrations in long-duration, low-flow sevoflurane anesthesia. *Anesthesia and Analgesia* 1994; **79**: 946–951.
16. Bito H, Ikeda K. Closed circuit anesthesia with sevoflurane in humans. *Anesthesiology* 1994; **80**: 71–76.