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Quantification of the degradation products of sevoflurane using four brands of CO_2 absorbent in a standard anesthetic circuit

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Abstract

Purpose. CO_2 absorbents convert sevoflurane to fluoromethyl-2,2-difluoro-1-(trifluoromethyl) vinyl ether (compound A), whose toxicity in rats raises concern regarding the safety of sevoflurane in a low-flow system. The type of CO_2 absorbent is one of factors that affect compound A concentration in the anesthetic circuit. The aim of the present study was to investigate the concentration of compound A in an anesthetic model circuit following the use of different brands of soda lime and Baralyme.

Methods. We measured the concentrations of compound A in four different brands of CO_2 absorbent using a low-flow ($1\,l \cdot min^{-1}$ fresh gas) model circuit in which 2% sevoflurane was circulated. Sodasorb II, Baralyme, Sofnolime and Wakolime-A were used as CO_2 absorbents. The concentration of compound A was measured hourly, and the temperature of the CO_2 absorbent was monitored.

Results. The maximum concentration of compound A in the circuit was highest for Baralyme (25.5 ± 0.6 ppm) (mean ± SD), followed by Sodasorb II (18.9 ± 1.6 ppm), Wakolime-A (16.1 ± 0.7 ppm), and Sofnolime (15.8 ± 1.4 ppm). The maximum temperature was 50.8 ± 1.3°C for Baralyme, 48.8 ± 1.3°C for Wakolime-A, 47.0 ± 1.4°C for Sodasorb II, and 43.5 ± 3.9°C for Sofnolime.

Conclusion. The relative concentrations of compound A in the low-flow circuit were Baralyme > Sodasorb II > Wakolime-A = Sofnolime.

Key words Anesthetic system · Low-flow anesthesia · Anesthetics · volatile · Sevoflurane · CO_2 absorbent · Compound A

Introduction

Sevoflurane reacts with the CO_2 absorbent used in anesthesia, resulting in the generation of fluoromethyl-2,2-difluoro-1-(trifluoromethyl) vinyl ether (compound A) [1], which has been reported to be toxic in rats [2–6]. Since the concentration of compound A in the anesthesia circuit is higher in low-flow sevoflurane anesthesia than in relatively high-flow anesthesia (flow rates of 3 to $6\,l \cdot min^{-1}$ [7,8]), there has been some controversy regarding the safety of low-flow sevoflurane anesthesia.

Factors that affect compound A concentration in the anesthetic circuit may include the sevoflurane concentration [2,8–11], CO_2 production by the patient [8], ventilation [8], the fresh gas flow rate [7,8], the temperature of the CO_2 absorbent [11–13], the type of CO_2 absorbent [2,9,10,13–17], the freshness of the CO_2 absorbent [16,18,19], and the water content of the CO_2 absorbent [10,18–21]. In particular, in vitro and in vivo studies looking at different types of CO_2 absorbent have reported that the concentration of compound A formed was greater when Baralyme was used than when soda lime was used [9,15–17]. Soda lime, however, is commercially available under several brand names. Although Sodasorb has been investigated extensively, little is known about the other brands. In the present study we investigated the formation of compound A in an anesthetic model circuit after the use of different brands of soda lime (Sofnolime, Wakolime-A, and Sodasorb II) and Baralyme. Both the concentration of compound A in the circuit and the CO_2 absorbent temperature were measured.

Materials and methods

The anesthesia machine used was a Modulus CD Anesthesia System (Ohmeda, Madison, WI, USA). The four brands of CO_2 absorbent used were Sodasorb II (W.R. Grace & Co., Lexington, MA, USA), Baralyme (Allied Healthcare Products, St. Louis, MO, USA), Sofnolime (Molecular Products, Essex, England), and Wakolime-A (Wako Pure Chemical Industries, Osaka, Japan). One kilogram of each fresh CO_2 absorbent was placed in the upper canister, and glass balls were placed in

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the lower canister as filler. Temperature was monitored in the center of the upper canister. A 3-l latex bag connected to the Y-piece of the circuit acted as a compliant "lung," and CO_2 was delivered at a flow rate of 150 ml·min^{-1} into the distal portion of the bag. The "lung" was ventilated 10 times·min^{-1} with a measured expired tidal volume of 500 ml. The anesthesia system was loaded for 5 min with an initial fresh gas (100% oxygen) flow rate of 6 l·min^{-1} containing 2% sevoflurane. Subsequently the fresh gas flow rate was reduced to 1 l·min^{-1}, and the tidal volume setting was readjusted to maintain the volume of 500 ml. The sevoflurane vaporizer setting was adjusted to maintain 2% sevoflurane in the circuit. Each experiment was performed for 4 h and repeated four times with each absorbent.

Gas samples were obtained from the inspiratory limb just beyond the inspiratory valve. Analysis of sevoflurane was performed with a Capnomac (Datex, Helsinki, Finland). The concentration of compound A was measured every hour in each experiment with a gas chromatograph (model GC-9A, Shimadzu, Kyoto, Japan) equipped with a gas sampler (model MGS-5, Shimadzu, Kyoto, Japan). For gas chromatography, the column temperature was maintained at 100°C and the injection inlet temperature was 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), and 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) with a 80/100 mesh. The gas chromatograph was calibrated with standard calibration gas prepared from stock solutions of compound A (Maruishi Pharmaceutical, Osaka, Japan).

Measured values are expressed as means ± SD. Intergroup comparisons were performed by one-way analysis variance with Fisher's protected least significant difference. A P value of less than 0.05 was considered statistically significant.

Results

The maximum concentration of compound A in the circuit was highest with the use of Baralyme (25.5 ± 0.6 ppm), followed by Sodasorb II (18.9 ± 1.6 ppm), Wakolime-A (16.1 ± 0.7 ppm), and Sofnolime (15.8 ± 1.4 ppm) ($P < 0.05$). The same CO_2 absorbent ranking was obtained at 1-h intervals (Fig. 1). For all absorbents, the maximum concentration of compound A was observed 2 h after the start of the study.

The maximum temperature of the CO_2 absorbent was 50.8 ± 1.3°C for Baralyme, 48.8 ± 1.3°C for Wakolime-A, 47.0 ± 1.4°C for Sodasorb II, and 43.5 ± 3.9°C for Sofnolime. There were significant differences in the maximum temperature between Baralyme and Sodasorb II ($P < 0.05$), Baralyme and Sofnolime ($P < 0.01$), and Wakolime-A and Sofnolime ($P < 0.01$). There were no significant differences between Baralyme and Wakolime-A, Wakolime-A and Sodasorb II, or Sodasorb II and Sofnolime.

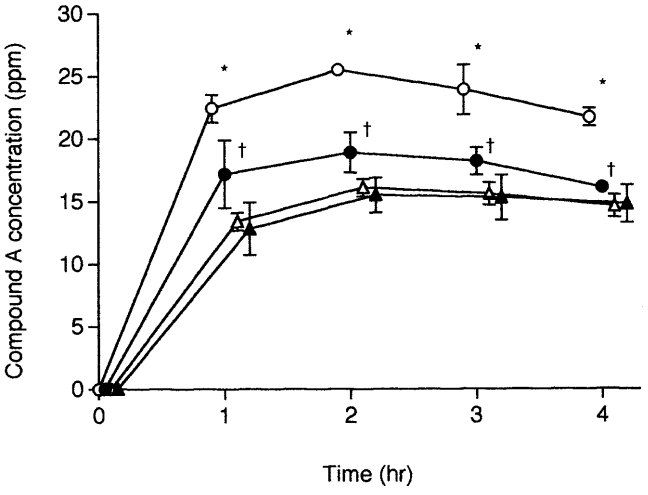

Fig. 1. Comparison of compound A concentrations in the anesthesia circuit with four CO_2 absorbents. *Open circles* indicate Baralyme. *$P < 0.05$ vs Sodasorb II (*closed circles*), Wakolime-A (*open triangles*), and Sofnolime (*closed triangles*). †$P < 0.05$ vs Wakolime-A and Sofnolime. Values shown are means ± SD

Discussion

Both the interaction of sevoflurane and the formation of compound A with different types of CO_2 absorbents have been reported in several in vitro studies [2,10,13–15,17]. In the studies on the interaction of sevoflurane with the CO_2 absorbent, reactivity was assessed by the reduction in sevoflurane concentration [2,15,22]. However, since the concentration of compound A was not measured, the precise amount of sevoflurane that reacted with the absorbent, compared with that simply absorbed to the absorbent, could not be accurately determined. Even when the total amount of compound A formed in vitro was measured [10,14], the results obtained in a test tube or a flask may not always represent those obtained in clinical anesthesia, since the compound A contained in the recirculating gas is partially absorbed to the CO_2 absorbent or degraded to compound B. In the present study, therefore, we used a standard anesthesia machine and circuit, including a sevoflurane vaporizer, to measure the concentration of compound A.

Table 1. Composition of CO_2 absorbents (% weight)

Ingredient	Baralyme	Sodasorb II	Wakolime-A	Sofnolime
$Ca(OH)_2$	74	76.5	79.2	>75
KOH	5	2.25	0.1	—
NaOH	—	2.25	4.2	<3
$Ba(OH)_2$	11	—	—	—
Sodium silicate	—	—	0.4	—
H_2O	10	18.9	13.6	12~19
$Mg(OH)_2$	—	—	0.5	—
$Al(OH)_3$	—	—	0.3	—

To reduce the effect of the other parameters mentioned previously that may affect the formation of compound A, particularly those that are dependent on the patient, an in vitro system that mirrored the human lung was utilized. In this system, a 3-l latex bag was connected to a model circuit, and CO_2 gas was delivered at 150 ml·min^{-1}. This rate of CO_2 gas delivery was determined to be appropriate on the basis of our previous measurements of CO_2 elimination by the patient during anesthesia [9].

Our study demonstrated that the concentration of compound A in the circuit was higher for Baralyme, followed by Sodasorb II, Wakolime-A, and Sofnolime in descending order. The finding that Baralyme produced greater amounts of compound A than Sodasorb II is in agreement with previous studies [9,15–17]. Cunningham et al. [13] also found that the concentration of compound A was lower when Sofnolime was used than when Baralyme or Sodasorb II was used, but the data were not statistically analyzed. The lower concentration of compound A produced with the use of Sofnolime or Wakolime-A was expected, since both of these absorbents contain little (Wakolime-A) or no (Sofnolime) KOH, and sevoflurane is most reactive with the KOH alkaline component in CO_2 absorbents (Table 1) [13,23]. However, contrasting results have been reported in two studies. Osawa et al. [17] reported that the production of compound A was greater when Wakolime-A was used than when Baralyme or Sodasorb II was used. The differences between this and our study may be a reflection of the absorbents used [13], since they were from different batches, or the fact that their study was carried out in surgical patients where the results would be affected by CO_2 production by the patient. Kudo et al. [14] also obtained findings contrary to ours, however, their experiments were not performed in a circuit system, which may explain the different results obtained.

Heat generated by the CO_2 absorbent is the result of the reaction between the CO_2 absorbent and CO_2 or sevoflurane. In our experiments, although a constant volume of CO_2 was delivered into the model circuit, the temperature of the CO_2 absorbent differed among the four samples. Therefore, the differences in temperature among the four groups can be attributed to the differences in the heat generated by the reaction between the CO_2 absorbent and CO_2 or sevoflurane. In our experiments, there was agreement between the production of compound A and the temperature of the CO_2 absorbent, except for Wakolime-A. The temperature of Wakolime-A is considered to be affected by its formulation or water content.

The difference between the circle system in clinical anesthesia and the model circuit used in the present study consists in the presence or absence of the water expired by the patient. However, in the present study Sodasorb II and Baralyme produced concentrations of compound A similar to those measured in previous clinical studies, supporting the notion that there is no significant difference between the data obtained in the model circuit and in clinical anesthesia. In addition, the change in the concentration of compound A over time was similar to that seen in clinical anesthesia studies [9,24,25]; the concentration of compound A reached a peak 2 h after the start of anesthesia.

In conclusion, we found that the concentration of compound A in the anesthetic circuit varied depending on the type of CO_2 absorbent used. The following descending order of production of compound A was obtained: Baralyme > Sodasorb II > Wakolime-A = Sofnolime. The differences in compound A production among the different CO_2 absorbent brands are probably due to the differences in their formulations. In particular, the amount of KOH within the CO_2 absorbent is considered to have a strong influence on compound A production.

References

1. Wallin RF, Regan BM, Napoli MD, Stern IJ (1975) Sevoflurane: a new inhalational anesthetic agent. Anesth Analg 54:758–765
2. Morio M, Fujii K, Satoh N, Imai M, Kawakami U, Mizuno T, Kawai Y, Ogasawara Y, Tamura T, Negishi A, Kumagai Y, Kawai T (1992) Reaction of sevoflurane and its degradation products with soda lime: toxicity of the byproducts. Anesthesiology 77: 1155–1164

3. Gonsowski CT, Laster MJ, Eger EI II, Ferrell LD, Kerschmann RL (1994) Toxicity of compound A in rats: effect of a 3-hour administration. Anesthesiology 80:556–565
4. Gonsowski CT, Laster MJ, Eger EI II, Ferrell LD, Kerschmann RL (1994) Toxicity of compound A in rats: effect of increasing duration of administration. Anesthesiology 80:566–573
5. Kandel L, Laster MJ, Eger EI II, Kerschmann RL, Martin J (1995) Nephrotoxicity in rats undergoing a one-hour exposure to compound A. Anesth Analg 81:559–563
6. Keller KA, Callan C, Prokocimer P, Delgado-Herrera L, Friedman MB, Hoffman GM, Wooding WL, Cusick PK, Krasula RW (1995) Inhalation toxicity study of a haloalkene degradant of sevoflurane, compound A (PIFE), in Sprague-Dawley rats. Anesthesiology 83:1220–1232
7. Bito H, Ikeda K (1995) Effect of total flow rate on the concentration of degradation products generated by reaction between sevoflurane and soda lime. Br J Anaesth 74:667–669
8. Fang ZX, Eger EI II (1995) Factors affecting the concentration of compound A resulting from the degradation of sevoflurane by soda lime and Baralyme® in a standard anesthetic circuit. Anesth Analg 81:564–568
9. Bito H, Ikeda K (1994) Long-duration, low-flow sevoflurane anesthesia using two carbon dioxide absorbents: quantification of degradation products in the circuit. Anesthesiology 81:340–345
10. Fang ZX, Kandel L, Laster MJ, Ionescu P, Eger EI II (1996) Factors affecting production of compound A from the interaction of sevoflurane with Baralyme® and soda lime. Anesth Analg 82:775–781
11. Munday IT, Ward PM, Foden ND, Jones RM, Van Pelt FNAM, Kenna JG (1996) Sevoflurane degradation by soda lime in a circle breathing system. Anaesthesia 51:622–626
12. Ruzicka JA, Hidalgo JC, Tinker JH, Baker MT (1994) Inhibition of volatile sevoflurane degradation product formation in an anesthesia circuit by a reduction in soda lime temperature. Anesthesiology 81:238–244
13. Cunningham DD, Huang S, Webster J, Mayoral J, Grabenkort RW (1996) Sevoflurane degradation to compound A in anaesthesia breathing systems. Br J Anaesth 77:537–543
14. Kudo M, Kudo T, Matsuki A (1990) Reaction products of sevoflurane with new Sodalime-A under various conditions (in Japanese with English abstract). Masui (Jpn J Anesthesiol) 39: 626–631
15. Liu J, Laster MJ, Eger EI II, Taheri S (1991) Absorption and degradation of sevoflurane and isoflurane in a conventional anesthetic circuit. Anesth Analg 72:785–789
16. Frink EJ, Malan TP, Morgan SE, Brown EA, Malcomson M, Brown BR Jr (1992) Quantification of the degradation products of sevoflurane in two CO_2 absorbents during low-flow anesthesia in surgical patients. Anesthesiology 77:1064–1069
17. Osawa M, Shinomura T, Murakawa M, Mori K (1995) Compound A concentration and the temperature of CO_2 absorbents during low-flow sevoflurane anesthesia in surgical patients. J Anesth 9:1–5
18. Wong DT, Lerman J (1992) Factors affecting the rate of disappearance of sevoflurane in Baralyme. Can J Anaesth 39:366–369
19. Bito H, Ikeuchi Y, Ikeda K (1998) Effects of water content of soda lime on compound A concentration in the anesthesia circuit in sevoflurane anesthesia. Anesthesiology 88:66–71
20. Strum DP, Eger EI II (1994) The degradation, absorption, and solubility of volatile anesthetics in soda lime depend on water content. Anesth Analg 78:340–348
21. Steffey EP, Laster MJ, Ionescu P, Eger EI II, Gong D, Weiskopf RB (1997) Dehydration of Baralyme® increases compound A resulting from sevoflurane degradation in a standard anesthetic circuit used to anesthetize swine. Anesth Analg 85:1382–1386
22. Strum DP, Johnson BH, Eger EI II (1987) Stability of sevoflurane in soda lime. Anesth Analg 67:779–781
23. Kudo M, Kudo T, Oyama T, Matsuki A (1990) Reaction products of sevoflurane with components of soda lime under various conditions (in Japanese with English abstract). Masui (Jpn J Anesthesiol) 39:39–44
24. Bito H, Ikeda K (1994) Plasma inorganic fluoride and intracircuit degradation product concentrations in long-duration, low-flow sevoflurane anesthesia. Anesth Analg 79:946–951
25. Bito H, Ikeda K (1996) Renal and hepatic function in surgical patients after low-flow sevoflurane or isoflurane anesthesia. Anesth Analg 82:173–176