Laboratory Investigations

Factors affecting the rate of disappearance of sevoflurane in Baralyme

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The effects of temperature, water and Baralyme exhaustion on the rate of disappearance of sevoflurane in Baralyme were studied in an in vitro model. We found that the rate of disappearance of sevoflurane in Baralyme increased as the temperature increased and decreased as the concentration of water increased. The disappearance of sevoflurane also decreased in the presence of exhausted Baralyme compared with fresh Baralyme. The slower rate of disappearance of sevoflurane in Baralyme in the presence of water and Baralyme exhaustion suggests that the disappearance of sevoflurane may be self-limiting in the clinical setting.

Les effets de la température de l'eau et de l'épuisement de l'absorbant sur le taux de disparition du sévoflurane dans le Baralyme ont été étudiés sur un modèle in vitro. Nous avons trouvé que la vitesse de disparition du sévoflurane dans le

Baralyme augmentait avec la température et diminuait en proportion inverse de la concentration hydrique. En présence de Baralyme épuisé, la disparition du sévoflurane diminuait comparativement au Baralyme frais. Le fait que la vitesse de disparition du sévoflurane soit plus lente en présence d'eau et de Baralyme épuisé suggère que la disparition du sévoflurane pourrait se limiter d'elle-même dans un contexte clinique.

Key words

ANAESTHETICS, VOLATILE: isoflurane, sevoflurane;
CARBON DIOXIDE: absorption, soda lime, Baralyme;
EQUIPMENT: absorbers;
MEASUREMENT TECHNIQUES: chromatography, gas.

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Supported, in part, with a grant from Maruishi Pharmaceutical Inc., Osaka, Japan.

Presented, in part, at the annual meeting of the Canadian Anaesthetists' Society, June 1988.

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Accepted for publication 16th December 1991.

Sevoflurane is a polyfluorinated ether inhalational anaesthetic agent with a minimum alveolar concentration of 2.05% in human adults¹ and a blood/gas partition coefficient of 0.60.² This low blood/gas partition coefficient together with its pleasant odour should provide a rapid induction and emergence from anaesthesia.³ Strum *et al.* studied the disappearance of sevoflurane in soda lime in an *in vitro* setting.⁴ They found that the rate of disappearance of sevoflurane was very rapid and directly proportional to temperature. Grodin *et al.* studied the change in halothane vapour concentration with addition of liquid halothane to soda lime contained in flasks.⁵ They found that the rate of increase of halothane vapour concentration was significantly greater with fresh soda lime compared to dried soda lime. The purpose of this study was to identify factors that may affect the rate of disappearance of sevoflurane in Baralyme and explore possible mechanisms for this disappearance.

Methods

This *in vitro* study was conducted in two parts.

Part I

To compare the rate of disappearance of sevoflurane in Baralyme (Chemetron Medical Division, Allied Healthcare Products, Inc., St Louis, Missouri, U.S.A.) and soda lime (Mallinckrodt Inc., Glens Falls, New York, U.S.A.),

TABLE I

Study conditions (37° C)	Sevoflurane half-lives (h)
Control*	105.00
Soda lime	3.85
Baralyme	0.75
Baralyme, exhausted	23.00

*Contained no Baralyme or soda lime.

6 μ l (1 vols%) of liquid sevoflurane and 12 μ l (2 vols%) of liquid isoflurane were added to three 125 ml flasks that contained 20 g of either fresh Baralyme, dried exhausted Baralyme or fresh soda lime. Exhausted Baralyme was prepared by circulating 10 L $\cdot$ min⁻¹ of 100% carbon dioxide through fresh Baralyme for 60 min. The exhausted Baralyme was then dried passively by flushing dry air at a flow rate of 5 L $\cdot$ min⁻¹ for 24 hr. The flasks that contained Baralyme or soda lime and the liquid anaesthetics were sealed and immersed in a 37° C waterbath for three hours. Gas samples (0.5 ml) were withdrawn from the flasks at 5, 15, 30, 60, 120, 180 and 330 min and the concentrations of sevoflurane and isoflurane were analyzed by gas chromatography. The gas chromatograph used in this study consisted of a column containing 10% SF-96 on chromosorb WHP 60/80 mesh, 0.32 cm $\times$ 360 cm, and a flame ionization detector supplied with an air/hydrogen gas mixture (flow rates of 280 and 40 ml $\cdot$ min⁻¹, respectively). The carrier gas used was nitrogen, flowing at a rate of 40 ml $\cdot$ min⁻¹.

The natural logarithm of the concentrations of sevoflurane and isoflurane in the gas phase were plotted against time. Data were fitted using least squares linear regression analysis. The slope (b) of the best fit line was determined and the half-life ($t_{1/2}$) was calculated according to: $t_{1/2} = -0.693/b$. The rates of disappearance of sevoflurane and isoflurane in Baralyme and soda lime were compared using their respective half-lives.

Part 2

To determine the effects of water and temperature on the rate of disappearance of sevoflurane in Baralyme, 6 μ l (1 vols%) of liquid sevoflurane and 12 μ l (2 vols%) of liquid isoflurane were added to eleven 125 ml flasks. Distilled water (0, 0.2, 0.4, 0.6 or 1.0 ml) was added to ten of the flasks each containing 20 g of fresh Baralyme. Five were incubated at 37° C and five at 22° C in a waterbath. Liquid sevoflurane and isoflurane were added to one flask that contained no Baralyme to serve as a control (37° C). Gas samples were withdrawn and analyzed as described in part one. The natural logarithm of the anaesthetic concentrations were plotted against time for each volume of water. The slopes of the regression lines for zero and 0.2 ml of water at 37° C were compared using Student's t test. To

FIGURE 1 Effect of water on the rate of disappearance of sevoflurane in 20 g Baralyme at 37° C. Percent sevoflurane remaining in the flask were plotted against time in the presence of various amounts of water (0.0–1.0 ml). The time zero sevoflurane and isoflurane concentrations sampled were used as the baseline value of 100%. The anaesthetic concentrations sampled at later times were expressed as a percentage of the initial anaesthetic concentration at time zero. Isoflurane was incubated with Baralyme without water.

TABLE II

Volume of water (ml)*	Sevoflurane half-life (h)	
	22° C	37° C
0.0	5.25	0.8
0.2	8.25	1.8
0.4	9.6	1.83
0.6	11.5	3.1
1.0	19.3	4.5

*Added to 20 g of Baralyme.

investigate the effect of temperature on the rate of disappearance of sevoflurane in the presence of various amounts of water, the relationship between the half-lives of sevoflurane and the volume of water was determined for both 37° C and 22° C. The slopes of the two regression lines for 37° C and 22° C were compared using the Student's t test. Statistical significance was accepted as $P \leq 0.05$.

Results

The disappearance half-lives of sevoflurane in soda lime, Baralyme, exhausted Baralyme and the control are shown in Table I. The half-life of sevoflurane in Baralyme was only one-fifth that of its half-life in soda lime. The half-life of isoflurane in soda lime was 71 hr. The effect of water on the rate of disappearance of sevoflurane in Baralyme at 37° C and 22° C are shown in Figure 1 and Table II. The r^2 for all regressions was ≥ 0.978 . The half-life of sevoflurane in Baralyme at 37° C with 0.2 ml of water was greater

FIGURE 2 Effect of temperature and water on the rate of disappearance of sevoflurane in Baralyme. Sevoflurane half-lives were plotted against increasing amounts of water from 0 to 1 ml at 37 and 22° C. Sevoflurane half-life increased with increasing amounts of water and decreasing temperature.

($P < 0.001$) than that with no water. The half-life of sevoflurane in Baralyme increased directly with increasing volumes of water at both temperatures. At 22° C, the half-life in Baralyme was six times that at 37° C (Table II). Sevoflurane half-lives were plotted against increasing amounts of water from 0 to 1 ml at 37° and 22° C (Figure 2). The half-lives were greater ($P < 0.001$) at 22° C than at 37° C.

Discussion

We found four factors affected the rate of disappearance of sevoflurane: first, the type of carbon dioxide absorber, Baralyme or soda lime; second, the degree of exhaustion of the carbon dioxide absorber; third, the amount of water in the preparation; and fourth, the temperature.

Our results indicate that the rate of disappearance of sevoflurane is five times greater in Baralyme than in soda lime. This is consistent with the finding of Liu *et al.*⁶ where sevoflurane was degraded four times more rapidly in Baralyme than in soda lime in an *in vivo* model with a circle anaesthetic circuit. Baralyme is comprised of barium hydroxide and calcium hydroxide whereas soda lime is comprised of sodium hydroxide, calcium hydroxide and potassium hydroxide. In Baralyme, water is incorporated into the structure of barium hydroxide as an octahydrate ($\text{Baralyme}(\text{OH})_2 \cdot 8 \text{H}_2\text{O}$) whereas in soda lime, water is present as a thin film on the granule surface. Furthermore, the composition of trace components such as silicone hydroxide, magnesium hydroxide and aluminum hydroxide varies amongst manufacturers (Morio M: unpublished data). This difference in chemical composition and water content can account in part for the difference in rate of

disappearance of sevoflurane in Baralyme compared to soda lime.

The disappearance of sevoflurane in exhausted Baralyme is thirty times slower than that of fresh Baralyme. This striking difference may be attributed to the presence of barium carbonate instead of barium hydroxide in the former preparation. In addition, water that is generated as the Baralyme becomes exhausted may also be important. As discussed below, the disappearance of sevoflurane is decreased with the presence of water in the preparation.

We found in our *in vitro* model that the disappearance half-life of sevoflurane in Baralyme was directly proportional to the amount of water present. In other words, the rate of disappearance of sevoflurane in Baralyme was inversely proportional to the amount of water. At 37° C, a 0.8% mixture of water in Baralyme decreased the rate of disappearance of sevoflurane in Baralyme by a factor of five. Grodin *et al.*⁵ had previously suggested the role of water in reducing halothane adsorption in an *in vitro* model with soda lime. They studied the vapour concentration of halothane when fresh and dried soda lime was incubated with liquid halothane in flasks at room temperature. With fresh soda lime, the vapour concentration increased linearly as the volume of liquid halothane increased. However, with dried soda lime, the vapour concentration was undetectable until large volumes of liquid halothane were added. Further addition of liquid halothane caused a linear increase in vapour concentration. The authors postulated that dried soda lime can adsorb large quantities of halothane by a molecule sieve-like mechanism. Only after saturation of this reservoir does the vapour concentration increase. Ma *et al.*⁷ found that molecular adsorption by a naturally occurring molecular sieve was dependent on temperature and the amount of presorbed water. He postulated changes in intracrystalline diffusion caused by blockage of pores by water molecules was the major factor in slowing the adsorptive process. This hypothesis is consistent with the effect of water on the rate of disappearance of sevoflurane in Baralyme in the present study.

We found that the rate of disappearance of sevoflurane in Baralyme was six to seven times greater at 37° C than at 22° C ($P < 0.001$). This finding is consistent with the effect of temperature on the disappearance of sevoflurane in soda lime reported by Strum *et al.*⁴ Using an *in vitro* model with flasks that contained 1.9% sevoflurane in the presence of 100 g of fresh soda lime, they found that the rates of disappearance of sevoflurane were 6.46, 31.04 and 57.36% per hour at 22, 37 and 54° C respectively. There was a linear relationship between the rate of sevoflurane disappearance and temperature.

Strum *et al.*⁴ cautioned against the use of sevoflurane in the presence of soda lime because of trace concentration of

degradation products. Wallin *et al.*² identified two sevoflurane degradation products, compounds A and B, following exposure to soda lime. Hanaki *et al.*⁸ studied sevoflurane degradation using a semi-closed anaesthetic circuit with soda lime absorber, fresh gas flow of six litres per minute and a sevoflurane concentration of 2.7%. Compound A reached a maximum concentration of 4 parts per million while Compound B was undetectable. This concentration of Compound A was far below threshold levels for toxicity in animal studies. We did not observe any unexplained gas chromatographic peaks during the analysis of the vapour phase even at high sensitivities. This may be explained by the lower temperature, lower initial sevoflurane concentration, shorter duration of sampling and different amounts of water used in our model.

Is the loss of sevoflurane in Baralyme due to degradation or adsorption a clinically important problem? This question was addressed by Liu *et al.*⁶ using a circle anaesthetic circuit with Baralyme or soda lime absorbers and a carbon dioxide inflow of 200 ml·min⁻¹. Liquid sevoflurane was injected intermittently into the inspiratory limb of the circuit to maintain a sevoflurane concentration of 2%. The volume of sevoflurane required, which was equated to the loss due to absorption and degradation, was small. The authors concluded that except for a slight delay at induction of anaesthesia, the loss of sevoflurane due to degradation and absorption should not affect adequate anaesthetic delivery in a clinical practice.

In summary, we found that the rate of disappearance of sevoflurane in fresh Baralyme was more rapid than in exhausted Baralyme, increased as the temperature increased and decreased as the volume of water present in the flask increased. We also found that the rate of disappearance of sevoflurane was more rapid in Baralyme than in soda lime. The clinical importance of these findings remains to be established.

Acknowledgements

The authors wish to thank Mr. G.A. Volgyesi for his technical assistance and Dr. R.E. Creighton for his editorial assistance.

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