Partly exhausted soda lime or soda lime with water added, inhibits the increase in compound A concentration in the circle system during low-flow sevoflurane anaesthesia

G. MORIWAKI, H. BITO AND K. IKEDA

Summary
We performed low-flow sevoflurane anaesthesia at a flow rate of 1 litre min⁻¹ in three groups (n=8 each) using 600 g of fresh soda lime (control group), 600 g of soda lime with 60 ml of water added (water group) or 600 g of soda lime saturated with carbon dioxide, that is partly exhausted soda lime (carbon dioxide group). Degradation products in the system were measured hourly. Inspired and end-tidal carbon dioxide and sevoflurane concentrations, carbon dioxide and temperature of the soda lime were monitored. CF₂=CF(CF₃)-O-CH₂F (compound A) was the only sevoflurane degradation product detected. The mean maximum concentration of compound A was significantly higher in the control group (mean 16.0 (SD 5.0) ppm) than in the water (1.4 (1.0) ppm) or carbon dioxide (4.0 (1.8) ppm) group, and the maximum temperature of the soda lime was significantly lower in the carbon dioxide group (30.7 (3.5) °C) than in the control (43.4 (1.8) °C) or water (40.8 (1.8) °C) group (P<0.05). The use of partly exhausted soda lime or soda lime with water added reduced compound A concentrations in the system during low-flow sevoflurane anaesthesia. (Br. J. Anaesth. 1997; 79: 782–786).

Key words

Sevoflurane is known to react with carbon dioxide absorbents, resulting in generation of five degradation products. Among these degradation products, CF₂=CF(CF₃)-O-CH₂F (compound A) has been reported to be nephrotoxic in rats, suggesting that it may be desirable in clinical practice to minimize its production. It has been reported that compound A concentrations in the circle system tend to decrease over time during closed or low-flow sevoflurane anaesthesia and that fresh soda lime tends to produce higher concentrations of compound A than partly exhausted soda lime. Therefore, we felt that the use of partly exhausted soda lime (prepared by exposing soda lime to carbon dioxide) rather than fresh soda lime might inhibit the production of degradation products during low-flow sevoflurane anaesthesia. It has also been reported that decreasing the water content of soda lime increases the production of sevoflurane degradation products in vitro. However, there have been no clinical studies on the effects of soda lime with water added on the generation of degradation products during sevoflurane anaesthesia. In this study, we performed low-flow sevoflurane anaesthesia using fresh soda lime, soda lime with water added and soda lime saturated with carbon dioxide to investigate the effects of these differences in soda lime on the concentration of degradation products in the system.

Patients and methods
This study was approved by the Institutional Committee on Human Research and informed consent was obtained from all patients.

We studied 24 patients, ASA I or II, undergoing tympanoplasty. Patients were allocated randomly to one of three groups (n=8 each) to undergo low-flow sevoflurane anaesthesia with three different carbon dioxide absorbents. In the control group, anaesthesia was performed using 600 g of fresh soda lime (Sodasorb II, WR Grace, Lexington, MA, USA). In the water group, anaesthesia was performed using 600 g of fresh soda lime to which 60 ml of distilled water at 25 °C was added immediately before use. In the carbon dioxide group, 600 g of partly exhausted soda lime was used. The partly exhausted soda lime was prepared by placing 600 g of fresh soda lime in an anaesthesia system equipped with a 1-litre test lung, with the oxygen flow rate set to 1 litre min⁻¹ and a carbon dioxide flow rate of 200 ml min⁻¹, ventilating the test lung with a tidal volume of 500 ml at a rate of 12 cycles min⁻¹ for 6 h, and then removing the soda lime and leaving it at room temperature for 6 h.

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Patients were premedicated with hydroxyzine 50 mg and atropine 0.5 mg i.m., 30 min before entering the operating room. Anaesthesia was induced with thiopentone 4–5 mg kg\(^{-1}\) and vecuronium 0.12–0.15 mg kg\(^{-1}\). After intubation of the trachea and connection to the anaesthesia system, the fresh gas flow rate was set to nitrous oxide 0.6 litre min\(^{-1}\) and oxygen 0.4 litre min\(^{-1}\). The lungs were ventilated mechanically with a tidal volume of 10 ml kg\(^{-1}\), and ventilation rate was adjusted to maintain an end-tidal carbon dioxide partial pressure of 4.0–5.3 kPa. The concentration of sevoflurane was adjusted to maintain systolic arterial pressure within ±20% of baseline. The anaesthesia machine used was a Modulas II Anaesthesia System (Ohmeda, Madison, WI, USA). The operating room was maintained at a temperature of 25 °C and 50% relative humidity.

The following variables were measured after the start of mechanical ventilation. The temperature of the soda lime was recorded every 15 min using a temperature probe (temperature probe model 9182, Hioki Electric Co., Nagano, Japan) inserted into the centre of the canister. Inspired and end-tidal carbon dioxide concentrations and inspired and end-tidal sevoflurane concentrations were monitored by mass spectrometry (Medical Gas Analyzer 1100, Perkin Elmer, Pomona, CA, USA). Minute carbon dioxide production by the patient was calculated based on minute expired volume and mean expired carbon dioxide concentration. Minute expired volume and mean expired carbon dioxide concentrations were measured using a linearized electric Wright respirometer (BOC Medishield, Essex, UK) and a bypassed mini-mixing chamber for mass spectrometry, respectively. Gas samples for measurement of degradation products were obtained from the inspiratory limb of the anaesthesia system every hour until 3 h after termination of anaesthesia.

Sample gas for measurement of degradation products was collected from the inspiratory limb of the anaesthesia system using a gas-tight syringe (20 ml). Concentrations of degradation products were measured using a gas chromatograph (model GC-9A, Shimadzu, Kyoto, Japan) equipped with a gas sampler (model MGS-5, Shimadzu, Kyoto, Japan) and a bypassed mini-mixing chamber for mass spectrometry, respectively. Gas samples for measurement of degradation products were obtained from the inspiratory limb of the anaesthesia system every hour until 3 h after termination of anaesthesia.

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In order to determine the water content of the soda lime, samples of fresh soda lime were treated in the same way as in each group and the water content was then measured. In addition, three 600-g samples of fresh soda lime and three 600-g samples of fresh soda lime with water added were processed in the same way as the soda lime used in the carbon dioxide group, and the time at which carbon dioxide was no longer absorbed in the inspiratory limb of the circle system was measured.

All values are expressed as mean (sd). The concentration of compound A, temperature of the soda lime, end-tidal sevoflurane concentration and carbon dioxide production were compared by one-way analysis of variance (ANOVA) followed by Bonferroni/Dunn. \(P<0.05\) was considered statistically significant.

**Results**

There were no significant differences in age, height or body weight between the three groups (table 1). The only degradation product of sevoflurane detected was CF\(_2\)=C(CF\(_3\))-O-CH\(_2\)F (compound A). The maximum concentration of compound A was higher in the control group than in the water or carbon dioxide group (\(P<0.05\)) (table 2). There were no significant differences between the groups in end-tidal sevoflurane concentration at the time of measurement of the individual maximum concentration of compound A (table 2).

The individual maximum temperature of the soda lime was significantly lower in the carbon dioxide group than in the two other groups (\(P<0.05\)) (table 2). The concentration of compound A in the circle system at each measurement point decreased 60 min after the start of measurement in the following order:

**Table 1** Patient characteristics (mean (sd) or range)

<table>
<thead>
<tr>
<th></th>
<th>Age (yr)</th>
<th>Height (cm)</th>
<th>Body weight (kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>59.3 (36–76)</td>
<td>154.9 (8.5)</td>
<td>53.6 (8.3)</td>
</tr>
<tr>
<td>Carbon dioxide group</td>
<td>54.6 (32–68)</td>
<td>155.9 (4.2)</td>
<td>56.0 (8.1)</td>
</tr>
<tr>
<td>Water group</td>
<td>59.0 (43–72)</td>
<td>157.4 (7.6)</td>
<td>49.8 (6.5)</td>
</tr>
</tbody>
</table>

**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 were observed. \(*P<0.05\) compared with carbon dioxide group and water group; †\(P<0.05\) compared with control group and water group

<table>
<thead>
<tr>
<th></th>
<th>Maximum compound A concn (ppm)</th>
<th>Corresponding end-tidal sevoflurane concn (%)</th>
<th>Maximum temperature of soda lime (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>16.0 (5.0)†</td>
<td>1.9 (0.4)</td>
<td>43.4 (1.8)</td>
</tr>
<tr>
<td>Carbon dioxide group</td>
<td>4.0 (1.8)</td>
<td>1.7 (0.3)</td>
<td>37.0 (3.3)†</td>
</tr>
<tr>
<td>Water group</td>
<td>1.4 (1.0)</td>
<td>1.8 (0.4)</td>
<td>40.8 (1.8)</td>
</tr>
</tbody>
</table>
control group > carbon dioxide group > water group (i.e. the lowest concentration of compound A was seen in the water group). The differences between the three groups were significant. However, significant differences were observed only between the control and water groups and between the control and carbon dioxide groups at 120 and 180 min ($P < 0.05$) (fig. 1).

There were no differences in mean carbon dioxide production per hour between the groups (fig. 2). End-tidal sevoflurane concentrations also did not differ significantly between the groups (fig. 3). In the carbon dioxide group, rebreathing was observed in three of the eight patients, but end-tidal carbon dioxide partial pressure was maintained at 4.0–5.3 kPa until the end of the experiment in these three patients. The water content in the soda lime was 18% in the control group, 8% in the carbon dioxide group and 27% in the water group. Under the conditions used in our study, the soda lime with water added lost its ability to absorb carbon dioxide approximately 1–2 h sooner than fresh soda lime (fig. 4).

**Figure 1** Concentrations of compound A in the anaesthesia system with fresh soda lime (○), partly exhausted soda lime (●) and soda lime with water added (□) (mean, SD). *$P < 0.05$ compared with partly exhausted soda lime and soda lime with water added; †$P < 0.05$ compared with soda lime with water added.

**Figure 2** Hourly mean carbon dioxide eliminated by the patient with fresh soda lime (○), partly exhausted soda lime (●) and soda lime with water added (□) (mean, SD).

**Figure 3** Concentrations of end-tidal sevoflurane with fresh soda lime (○), partly exhausted soda lime (●) and soda lime with water added (□) (mean, SD).

**Figure 4** Concentrations of carbon dioxide in the inspiratory limb of the anaesthesia system with fresh soda lime (●) and soda lime with water added (○) (mean, SD).

**Discussion**

The results of our study indicated that concentrations of compound A in the circle system were reduced significantly during low-flow sevoflurane anaesthesia when partly exhausted soda lime or soda lime with water added, rather than fresh soda lime, was used as the carbon dioxide absorbent. It is unclear if low-flow sevoflurane anaesthesia can lead to renal injury in humans. Some reports indicated that low-flow sevoflurane anaesthesia had no effect on renal function in patients, however, at least one study suggested that low-flow sevoflurane anaesthesia could cause renal injury and that compound A in particular might contribute to this injury. It was reported that compound A produced renal injury dose-dependently in rats. Therefore, a reduction in compound A concentration in the circle system during low-flow anaesthesia is considered important for ensuring safety.

There are three possible explanations for the successful reduction of compound A in our circle system. The first is that the differences in compound A concentration resulted from differences in the temperature of soda lime. It was found in *in vitro*
studies that increasing the temperature of the soda lime increased the degradation of sevoflurane and the production of compound A,9,14 suggesting that reducing the temperature of soda lime should inhibit the production of compound A in the anaesthesia system.15 In our study, the mean maximum temperature of the soda lime was 43.4 °C in the control group, and temperatures were 6.4 °C lower in the carbon dioxide group and 2.6 °C lower in the water group, with no significant difference between the water and control groups. Strum, Johnson and Eger14 showed that the rate of degradation of sevoflurane was related linearly to temperature. However, in our study, the decrease in compound A concentration in the circle system was greater than the decrease in temperature of the soda lime.

The second possible reason for our results is that the differences in compound A concentration resulted from differences in the components of the soda lime. In exhausted soda lime, the components of soda lime (i.e. calcium hydroxide, potassium hydroxide and sodium hydroxide) are reduced by reactivity with carbon dioxide. It has been suggested that the hydroxyl groups present on the components of soda lime might be related to the production of the degradation products of sevoflurane.16 Therefore, the reactivity of exhausted soda lime with sevoflurane might be reduced because of a decrease in the number of hydroxyl groups, resulting in a decrease in compound A concentration in the circle system.

The third possible reason for our results is that the differences in compound A concentration resulted from differences in water content. The in vitro study showed that dry soda lime produces higher levels of sevoflurane degradation products than fresh soda lime,10 whereas the half-life of sevoflurane in Baralyme increases with increases in added water.17 Strum and Eger10 reported that the water content of soda lime decreased from 15% with fresh to 4–8.5% during routine clinical use. The water content measured in our sample of fresh or partly exhausted soda lime was similar to these values. Thus it can be said that compared with fresh soda lime, partly exhausted soda lime is drier and soda lime with water added is wetter. Considering water content by itself, our results suggested that water tended to increase the production of degradation products in the carbon dioxide group, while it tended to reduce such production in the water group. In our study, the production of compound A at 60 min after the start of measurement was greater in the carbon dioxide group than in the water group, despite the lower maximum temperature of soda lime and differences in the components of soda lime. Although this difference was not statistically significant, the same trend was noted at later times. This may have been a result of differences in the water content of the soda lime in each group.

Considering other factors that are thought to affect the generation of degradation products of sevoflurane, fresh gas flow rate and type of carbon dioxide absorbent (soda lime) were the same in the three groups, and carbon dioxide production by the patient and concentration of sevoflurane in the circle system did not differ significantly between the groups. Thus we concluded that these three contributing factors were interdependent, leading to a decrease in compound A concentration in the circle system in the carbon dioxide group and in the water group. The relative importance of these factors should be assessed in future studies.

Partly exhausted soda lime has a lower carbon dioxide absorbing capacity than fresh soda lime, and therefore the long-term use of exhausted soda lime in anaesthesia may be questioned. In our study, rebreathing was observed in three patients in the carbon dioxide group. This raises the question of the carbon dioxide absorption capacity of soda lime with water added. Our findings indicate that soda lime with water added loses its ability to absorb carbon dioxide only 1–2 h sooner than fresh soda lime, suggesting that it can be used for a period of time.

The results of our study indicated that the use of partly exhausted soda lime or soda lime with water added reduced compound A concentrations in the circle system during low-flow sevoflurane anaesthesia. In particular, soda lime with water added, although its ability to absorb carbon dioxide is decreased, reduced compound A concentrations in the circle system by a factor of 4 compared with fresh soda lime, suggesting that it may prove useful in clinical practice.

References


