Degradation products of sevoflurane during low-flow anaesthesia

H. BITO AND K. IKEDA

Summary
Low-flow (1 litre min⁻¹) sevoflurane anaesthesia was used in 16 patients undergoing laparoscopic cholecystectomy (group LSC, n = 8) or tympanoplasty (group TP, n = 8), and concentrations of sevoflurane degradation products were measured. Degradation products in the circuit were measured hourly, and end-tidal carbon dioxide concentration, inspired and end-tidal sevoflurane concentrations, and carbon dioxide elimination were monitored. The only degradation product detected was CF₂=C(CF₃)-O-CH₂F (compound A). The mean maximum concentrations of compound A were 21.6 (SEM 1.6) ppm and 19.6 (0.8) ppm in the LSC and TP groups, respectively (ns). The maximum temperatures of soda lime were 46.4 (0.5) °C and 44.8 (0.5) °C, respectively (P < 0.05). Hourly end-tidal sevoflurane concentrations and concentrations of sevoflurane degradation products were the same for both groups. Carbon dioxide elimination was the same for both groups 1 h after the start of anaesthesia, but was higher in group LSC after 2 h (P < 0.05). Intraperitoneal carbon dioxide insufflation associated with laparoscopic cholecystectomy had no effect on the concentration of sevoflurane degradation products. (Br. J. Anaesth. 1995; 74: 56-59)

Key words
Anaesthetics volatile, sevoflurane. Equipment, breathing systems.

Sevoflurane is known to react with soda lime to produce degradation products [1, 2]. The concentrations of degradation products in the breathing system during low-flow anaesthesia have been investigated [3], but there have been no quantitative studies of degradation products during low-flow anaesthesia in laparoscopic cholecystectomy. As carbon dioxide elimination by the patient is higher in laparoscopic cholecystectomy because carbon dioxide is infused into the peritoneal cavity [4], the temperature of the carbon dioxide absorbent increases. When the temperature of the carbon dioxide absorbent is high, the production of degradation products is known to be increased [5, 6]. Therefore, it is assumed that more degradation products are formed during laparoscopic cholecystectomy than other surgical procedures. Low-flow sevoflurane anaesthesia was performed in patients undergoing either laparoscopic cholecystectomy or tympanoplasty, and the concentrations of degradation products in the two groups were compared. The temperature of the carbon dioxide absorbent and carbon dioxide elimination by the patient, which is affected by the temperature of the carbon dioxide absorbent, were also measured and compared.

Patients and methods
This study was approved by the local Ethics Committee and informed consent was obtained from all patients. We studied 16 patients undergoing laparoscopic cholecystectomy (group LSC, n = 8) or tympanoplasty (group TP, n = 8), and who were judged to be ASA I or II.

Premedication comprised hydroxyzine 50 mg and atropine sulphate 0.5 mg administered i.m. 45 min before induction of anaesthesia. Anaesthesia was induced with thiopentone 4-5 mg kg⁻¹ and vecuronium 0.12-0.15 mg kg⁻¹. After tracheal intubation, the total flow rate for maintenance of anaesthesia was set at 1 litre min⁻¹. The ratio of the oxygen and nitrous oxide flow rates was controlled so that the oxygen concentration in the inspiratory limb exceeded 30%. Hourly end-tidal sevoflurane concentrations were monitored and concentrations of sevoflurane degradation products were the same for both groups. Carbon dioxide elimination was the same for both groups 1 h after the start of anaesthesia, but was higher in group LSC after 2 h (P < 0.05). Intraperitoneal carbon dioxide insufflation associated with laparoscopic cholecystectomy had no effect on the concentration of sevoflurane degradation products. (Br. J. Anaesth. 1995; 74: 56-59)

Table 1  Patient characteristics (mean (SEM or range)): LSC = Laparoscopic cholecystectomy, TP = tympanoplasty

<table>
<thead>
<tr>
<th></th>
<th>Age (yr)</th>
<th>Height (cm)</th>
<th>Body weight (kg)</th>
</tr>
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<tbody>
<tr>
<td>Group LSC</td>
<td>51.1 (22-73)</td>
<td>158.9 (3.0)</td>
<td>57.5 (3.1)</td>
</tr>
<tr>
<td>Group TP</td>
<td>53.5 (24-69)</td>
<td>159.6 (4.4)</td>
<td>61.3 (5.1)</td>
</tr>
</tbody>
</table>

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Table 2  Maximum concentration of compound A, maximum temperature of soda lime, MAC-h and anaesthesia time (mean (SEM)). LSC = Laparoscopic cholecystectomy, TP = tympanoplasty. *P < 0.05 vs group TP

<table>
<thead>
<tr>
<th></th>
<th>Max. concn compound A (ppm)</th>
<th>Max. temp. soda lime (°C)</th>
<th>MAC-h (h)</th>
<th>Anaesthesia time (h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group LSC</td>
<td>21.6 (1.6)</td>
<td>46.4 (0.5)*</td>
<td>3.17 (0.22)</td>
<td>3.08 (0.19)*</td>
</tr>
<tr>
<td>Group TP</td>
<td>19.6 (0.8)</td>
<td>44.8 (0.5)</td>
<td>3.87 (0.16)</td>
<td>3.84 (0.19)</td>
</tr>
</tbody>
</table>

Equipment used was the Modulas II anaesthesia system (Ohmeda, Madison, WI, USA).

Two temperature probes (temperature probe model 9182, Hioki Electric Co., Nagano, Japan) were inserted at points above and below the centre of the upper compartment of the canister to measure the temperature of the soda lime, and the measured values were recorded at 15-min intervals.

End-tidal carbon dioxide concentration and inspired and end-tidal sevoflurane concentrations during anaesthesia were monitored using mass spectrometry (Medical Gas Analyzer 1100, Perkin Elmer, Pomona, CA, USA). Minute carbon dioxide elimination by the patient was calculated as minute expired volume multiplied by 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 mini-mixing chamber and then measured by mass spectrometry [7]. Hourly mean values were calculated from the values measured every 1 min. Sevoflurane MAC-h exposure was calculated from the percent anaesthetic concentration and the duration of exposure. A MAC value of 2.05% was used for sevoflurane [8].

Sample gas for measurement of degradation products was collected from the inspiratory limb of the anaesthesia circuit. The concentrations of the degradation products were measured every 1 h by a gas chromatograph (model GC-9A, Shimadzu, Kyoto, Japan) equipped with a gas sampler (model MGS-5, Shimadzu, Kyoto, Japan).

A column temperature of 100 °C and an injection inlet temperature of 140 °C were used, with nitrogen as the carrier gas at a flow rate of 50 ml min⁻¹. The detector was a hydrogen flame ionization 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 by preparing standard calibration gas from stock solutions of compounds A and B supplied by Maruishi Pharmaceutical Co., Ltd. (Osaka, Japan).

All results are expressed as mean (SEM). Maximum and hourly degradation product concentrations, the temperature of the soda lime, end-tidal sevoflurane concentration and carbon dioxide elimination were measured in each patient, and groups LSC and TP were compared using repeated measures ANOVA where appropriate and Student's t tests. P values less than 0.05 were considered statistically significant.

Results

There were no differences in age, height or body weight between the two groups (table 1). Of the degradation products of sevoflurane, only \( \text{CF}_2=\text{C}(-\text{CF}_3)-\text{O}-\text{CH}_2\text{F} \) (compound A) was detected. The maximum concentration of compound A in the circuit was 21.6 (1.6) (12.2-27.0) ppm in group LSC and 19.6 (0.8) (16.1-22.6) ppm in group TP; there was no significant difference between the two groups (table 2). The maximum soda lime temperature was 46.4 (0.5) °C in group LSC and 44.8 (0.5) °C in group TP (P < 0.05) (table 2). There were no significant differences in MAC-h between the two groups (table 2).

When the concentrations of compound A in the circuit at each measurement time were compared
between the two groups, no significant differences were observed at any of the measurement times (fig. 1). End-tidal sevoflurane concentration during the measurement of degradation products also showed no difference between groups (fig. 2). Mean carbon dioxide elimination per hour did not differ significantly between the two groups 1 h after the start of anaesthesia, but values in group LSC were significantly higher than those in group TP after 2 h ($P < 0.05$) (fig. 3).

**Discussion**

During laparoscopic cholecystectomy, some of the insufflated carbon dioxide is absorbed and the amount of carbon dioxide eliminated by the patient increases [4]. Thus with low-flow anaesthetic techniques the temperature of the soda lime increases to higher levels during laparoscopic cholecystectomy than during surgical procedures not requiring a pneumoperitoneum. In the present study, carbon dioxide elimination by the patient was higher in laparoscopic cholecystectomy than in tympanoplasty, and the temperature of the soda lime was higher in the former group. It is known that the production of degradation products increases when the temperature of soda lime is high [5, 6] and it is reasonable to assume therefore, that the concentration of degradation products may be higher during laparoscopic cholecystectomy than during tympanoplasty. However, we found no significant differences in the concentrations of degradation products between the two groups in the present study. The reason for this may be that the difference in the mean soda lime temperature between the two groups was only 1.6 °C and thus was not sufficient to cause a significant difference in the concentrations of degradation products.

Factors other than the temperature of the soda lime which affect the concentrations of degradation products include sevoflurane concentration in the system [2], type of carbon dioxide absorbent used [3, 9], freshness of the carbon dioxide absorbent [3, 10] and total flow rate [11]. In the present study there were no differences in sevoflurane concentration in the circuit or the total flow rate between the two groups, and fresh soda lime was used for each patient. Therefore, factors affecting degradation product concentrations, other than the type of surgical procedure, were the same for both groups. The fact that, contrary to expectations, the concentrations of degradation products were the same in the two groups indicates that no factor other than the temperature of the soda lime was involved.

In this study, pneumoperitoneum associated with laparoscopic cholecystectomy had no effect on the concentrations of degradation products, but when carbon dioxide uptake is abnormally high for some reason, such as extraperitoneal carbon dioxide insufflation during pelviscopy [4], carbon dioxide elimination by patients appears to be higher than that observed in the present study. For this reason, it is possible that the temperature of the soda lime is increased further, resulting in increased concentrations of degradation products.

The LC$_{50}$ value of compound A in rats has been reported to be 1050–1090 ppm for 1-h inhalation and 340–490 ppm for 3-h inhalation [12]. The concentrations of compound A observed in the present study were comparable with those reported in previous studies [11, 13], and were low compared with the LC$_{50}$ in rats. In low-flow [3] or closed system [14] sevoflurane anaesthesia, it has been reported that no abnormalities in renal and liver function tests occurred. However, it is necessary to further clarify the safety of low-flow sevoflurane anaesthesia under various conditions, including low-flow anaesthesia in patients undergoing laparoscopic cholecystectomy.

**References**

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