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SHORT COMMUNICATION

The Determination of a New Inhalational Anaesthetic, Sevoflurane, Using an Internal Standard, Xenon, by Gas Chromatography/Mass Spectrometry/Selected Ion Monitoring

Kazuko Miyano,* and Yasumasa Tanifuji

Department of Anesthesiology, The Jikei University School of Medicine, 3-25-8, Nishi-shimbashi, Minatoku, Tokyo 105, Japan

Toru Obata

Division of Biochemistry, Institute of Medical Science, The Jikei University School of Medicine, 3-25-8, Nishi-shimbashi, Minatoku, Tokyo 105, Japan

A novel determination method for a new inhalation anaesthetic, sevoflurane, in a closed circuit in the presence of carbon dioxide absorbents is investigated using gas chromatography/selected ion monitoring with xenon as an internal standard. The decrease rate of sevoflurane with soda lime was 0.22%±0.158/h (mean±SD), while that with baralyme was 0.57%±0.115/h (mean±SD).

INTRODUCTION

Volatile anaesthetics are readily available as inhalational anaesthetics for general anaesthesia. Since they are circulated in an anaesthesia circuit, carbon dioxide absorbents are necessary in order to eliminate the carbon dioxide in a patient's breath. Carbon dioxide absorbents are mainly composed of alkaline substances and eliminate carbon dioxide by an exothermic neutralization reaction.

Sevoflurane is a new inhalation anaesthetic and has the property of rapid induction of and recovery from anaesthesia for a small blood/gas partition coefficient (Wallin *et al.*, 1975; Yasuda *et al.*, 1991); it is therefore expected to be a good anaesthetic for clinical use. However, the high reactivity of sevoflurane with soda lime has limited its development (Fujii *et al.*, 1987; Strum *et al.*, 1987; Tanifuji *et al.*, 1989; Miyano *et al.*, 1991). We need to know the extent of the reduction of sevoflurane by carbon dioxide absorbents after prolonged circulation and which kind of absorbent is appropriate for clinical use.

The determination of sevoflurane in a closed circuit was investigated. Since it was very difficult to prevent gas leakage from a circuit, an internal standard was added to the closed circuit at the beginning of a procedure. This study required an internal standard having chemical stability and inactivity; an inert gas was thought to be suitable. Isotopically labelled variants of the compound to be analysed approach this ideal when mass spectrometric detection is available (Gaffney *et al.*, 1971); however, in the present work it is impossible to use an isotopically labelled compound as an internal standard. We chose to use xenon because its molecular weight was closer to that of sevoflurane than those of the other inert gases.

In this study we determined sevoflurane in a closed circuit using an internal standard, xenon, and then compared the reactivity of two different kinds of carbon dioxide absorbents, soda lime and baralyme.

EXPERIMENTAL

Reagents. Soda lime was purchased from Wako Chemicals (Osaka, Japan) and baralyme was purchased from AIKA (Tokyo, Japan). The composition of soda lime is calcium hydroxide 79%, potassium hydroxide 3%, sodium hydroxide 2%, water 16% and silica 0.2%, while that of baralyme is calcium hydroxide 74%, barium hydroxide 1%, potassium hydroxide 5% and water 10%.

Circulation procedure. The closed circuit was designed using only glass and Teflon and not rubber, in order to prevent the non-specific absorption of anaesthetic into the rubber, and was composed of a ventilator, a two litre bag, connected tubes and a 600 mL glass vessel containing soda lime or baralyme.

Five per cent sevoflurane (Maruishi Pharmaceuticals Co., Osaka, Japan) was introduced into the circuit with an oxygen carrier. The circuit was saturated with sevoflurane and the circulation was started. At this point, 5 mL of xenon (Seitetsu Chemicals, Chiba, Japan) was injected into the circuit. After 15 min circulation, the gas was withdrawn and analysed, and these results were regarded as the starting values.

Analysis conditions. Gas chromatography/mass spectrometry (GC/MS) was carried out using a gas chromatograph (JEOL MS-GCG06) mass spectrometer (JEOL JMS DX-303) equipped with a data processing system (DA-5000 Version 3.01A). The column used was a chemically bonded DOP phase (2.5 mm i.d. × 3 m, 60/80 mesh). Helium was used as the carrier gas in the GC/MS. The GC/MS conditions were:

* Author to whom correspondence should be addressed.

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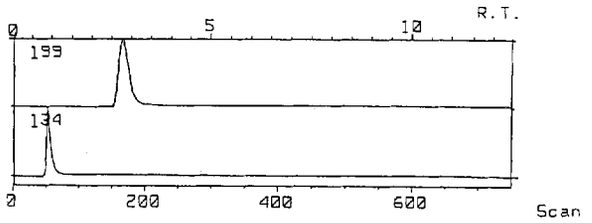

Figure 1. Mass fragmentogram of sevoflurane and xenon by SIM. The SIM output from a GC/MS instrument adjusted to monitor ion current at *m/z* 199 and 134.

injection port temperature, 100 °C; column temperature, 80 °C; ionization chamber temperature, 100 °C. The mass spectrometer was operated in the positive ion mode with electron impact ionization: electron impact (EI) ionization energy, 70 eV; trap current, 300 μA; accelerating voltage, 3.0 kV. The spectrum was recorded at a low resolution of 1:1500 by scanning the magnetic field from *m/z* 20 to 200.

RESULTS AND DISCUSSION

The mass spectrum of sevoflurane has a molecular ion at *m/e* 200 and the adjacent mass number of molecular ion at *m/e* 199. Since the intensity of the molecular ion at *m/e* 200 was weak, the appearance of a peak with the gas chromatograph/mass spectrometer focused on the more abundant fragment with mass number 199.

In the mass spectrum of xenon, there were some ions in the neighbourhood of the molecular ion at *m/e* 132. Taking into consideration the intensity of ions, *m/e* 134 was used for the registration of xenon by mass fragmentography, to avoid contamination by overlap sevoflurane fragments. The selected ion recording chromatogram is shown in Fig. 1.

Quantification depended upon the linear relationship between the percentage concentration of sevoflurane and the peak-area ratio of sevoflurane/xenon. Sevoflurane is usually used in the vicinity of 2% to 4%. The correlation coefficient of the calibration line for concentrations of sevoflurane ranging from 0.5% to 4% was 0.991. Each coefficient of variance for each concentration of sevoflurane was 4.8, 6.3, 3.3 and 4.8 ($n=6$), respectively.

The gas samples containing sevoflurane and xenon which were withdrawn in the closed circuit after circulation without any carbon dioxide absorbents were analysed. The sevoflurane/xenon ratio was constant throughout the entire experiment (mean±SD; 100%±3.88). However, we found that xenon could not be detected after a few hours circulation without using a spin bar in a bag. After circulation for 1 or 4 h without stirring, only about 9.5% and 0.5% was detected respectively; these values were expressed in terms of the percentage of the peak area before standing. After sufficient stirring by the spin bar, it was possible to detect xenon, 100%. These results suggested that the amounts of sevoflurane in an anaesthesia circuit could be determined using xenon as the internal standard, if a spin bar was used.

The circulated gas was analysed from the beginning of a circulation every two or three hours for 20 h with soda lime or baralyme. An approximately linear relationship was observed between sevoflurane decrease and time. The sevoflurane quantity in the circuit after 20 h with soda lime was 95.8%±3.11 (mean±SD), while that with baralyme was 88.8%±2.40 (mean±SD), expressed as a percentage of the original amount of sevoflurane. The decrease rate with soda lime or baralyme was 0.22%±0.158/h (mean±SD) and 0.57%±0.115/h (mean±SD), which was obtained simply by dividing the decrease quantity after 20 h of circulation by 20 h. Baralyme degraded sevoflurane to a greater degree than did soda lime.

REFERENCES

Fujii, K., Morio, M., Hanaki, C. and Tasima, T. (1987). *Hiroshima Journal of Anesthesia* **23**, s87.

Gaffney, T. E., Hammar, C.-G., Holmstedt, B. and McMahon, R. E. (1971). *Anal. Chem.* **43**, 367.

Miyano, K., Nakazawa, M., Tanifuji, Y., Kobayashi, K. and Obata, T. (1991). *Jpn. J. Anesthesiology* **40**, 384.

Strum, D. P., Johnson, B. H. and Eger II, E. I. (1987). *Anesthesiology* **67**, 779.

Tanifuji, Y., Takagi-Miyano, K., Kobayashi, K., Yasuda, N. and Eger II, E. I. (1989). *Anesth. Analg.* **68**, s285.

Yasuda, N., Eger II, E. I., Weiskopf, B. R., Tanifuji, Y. and Kobayashi, K. (1991). *Jpn. J. Anesthesiology* **40**, 1059.

Wallin, R. F., Reagan, B. M., Napoli, M. D. and Stern, I. V. (1975). *Anesth. Analg.* **54**, 758.