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ARTICLES

Mass Spectrometry Monitoring of Sevoflurane in the Breathing Circuit of an Inhalation Anesthesia Machine

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Abstract—The results of controlling the amount of inhalation anesthetics sevoflurane in the patient breathing circuit of an inhalation anesthesia machine (IAM) by mass spectrometry are presented. A vacuum system with a differential chamber providing pressure difference in the range 1×10^{5}–1.5×10^{-4} was used to inject the studied gas sample from the delivery circuit into the mass spectrometer. The concentrations of the anesthetic obtained using mass and IR spectrometry are compared. The potency of mass spectrometry for monitoring the anesthetic gas in the real time mode is demonstrated. The time dependences of the concentration of the anesthetic gas corresponding to different periods of anesthesia are given.

Keywords: anesthesia, sevoflurane, mass spectrometry, concentration, mass spectrum.

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INTRODUCTION

Nowadays lengthy operations are performed widely using multicomponent anesthesia. In this case, an inhalation anesthetic is used in addition to intravenous analgesics and anesthetics, such as fentanyl and propofol. Since the beginning of the 1990*th*, inhalation anesthetic sevoflurane has become most preferable among others ones, because, its poor solubility in blood in comparison to halothane and isoflurane opens up a possibility for the dynamic control over the anesthesia. In inhalation anesthesia machines (**IAM**), the concentration of the anesthetic is controlled using IR-spectrometers, whose operation is based on the absorption of the emission of photodiodes at $\lambda = 620$ and 940 nm [1]. The well known drawbacks of the spectrometers based on IR absorption are well known. Among these is the possibility of the overlapping of absorption spectra of molecules present in the IAM circuit. The spectrometers based on the Raman scattering of the anesthetic molecules are characterized by low sensitivity in the real time mode [2]. In the first case, the reliability of measurements and the stability of sensor calibration for the period of anesthesia seem questionable, while in the second case, low sensitivity necessitates for longer periods of exposition and a substantial increase in the time of measurement over 10 min; the measurement of the anesthetic concentration within the the breath cycle is impossible. The potencies of mass spectrometry in the control of inhalation anesthetics in a breathing circuit of IAM were demonstrated in the works [3–5]. Comparative laboratory studies of the mass spectrometry monitoring of inhalation anesthetics with IR-control were described in the papers [6, 7]; they showed a satisfactory convergence of the results obtained by the both techniques under laboratory conditions. The data on time characteristics of the spectrometers in use were not presented in the works mentioned.

In the actual paper we report a comparative study of the data of the sensor control of sevoflurane in IAM Dragger (Fabius, Julian) with mass spectrometry results recorded for the breathing circuit of IAM in the mode of a breath cycle under clinical conditions. The samples were taken from the connection unit of an endotracheal tube with an IAM connector in the course of neurosurgery operations. In the paper we show the usefulness of mass spectrometry for monitoring the concentration of anesthetic in the breathing circuit of an IAM aimed to ensure the necessary depth of anesthesia in the real-time mode.

EXPERIMENTAL

To ensure the quantification of the anesthetic in the real-time mode, we sampled gaseous mixture from the breathing circuit of IAM into the closed ion source of a Prisma quadrupole mass spectrometer (Preiffer Vacuum) with electron impact ionization. The energy of electrons was of 70 eV. The starting flow of the gaseous mixture in the IAM rotameter made 6.0 L/min. Anesthesia was maintained in the mode of low-flow lung ventilation. The flow rate of the gaseous mixture made

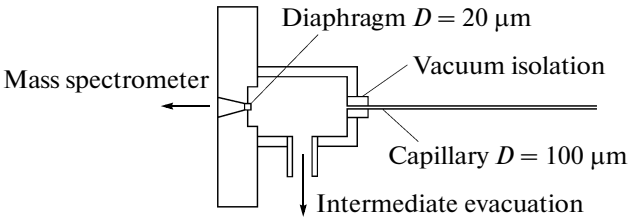

Fig. 1. Unit for the delivery of a sample into the mass spectrometer.

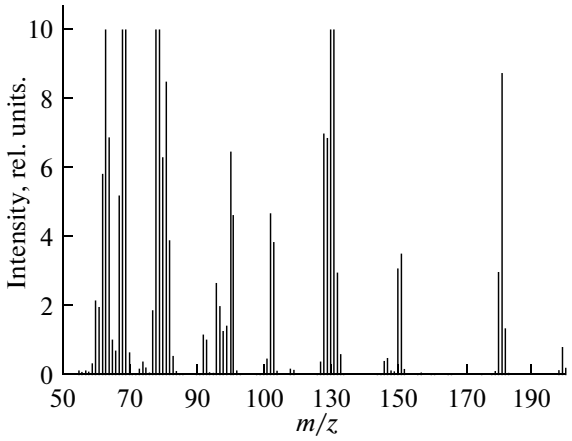

Fig. 2. Mass spectrum of a gaseous mixture in an IAM circuit in the range of m/z 55–200. Peaks with m/z 69, 131, 181, and 199 correspond to ions produced by the electron ionization of sevoflurane.

0.5 L/min. The breath volume per minute was set according to the norm of 0.06 L per a kilo of body weight at the breath frequency of 10–13 in a minute. An injector of sevoflurane was positioned outside the circuit of the circulation breathing mixture of the IAM. After tracheal intubation, the injector of sevoflurane was set at the injection value 1.5–2.0 vol % sevoflurane until its necessary concentration in the exhale mixture was attained under the control of an IR-spectrometer. The values of the anesthetic concentration preset at the injector were determined by the age, body weight of the patient, and how great the traumatic influence of the surgery was, and was governed by the minimal alveolar concentration (**MAC**) [2]. Fentanyl was delivered in 30 min in a dosage of 1.5 μg per kilo of body weight; propofol, by bolus injection. The IAM maintained the circulation of nitrous oxide and inhalation anesthetic sevoflurane in breathing circuit; the medication Sevorane from Abbot Laboratories Ltd., United Kingdom, was used. The concentration of sevoflurane was determined by the intensity of the molecular ion peak at m/z 199. The calibration was built for the readings of the anesthetic injector implemented into the IAM with no absorption of sevoflurane in the outer cycle. An additional validation of calibration was done using an external standard with a known concentration of sevoflurane. The vacuum system of sampling from the IAM circuit consisted of a capillary with an inner diameter of 100 μm and length of 2 m attached to the IAM, and a diaphragm of a diameter of 20 μm connected to the ion source of the mass spectrometer (Fig. 1). The intermediate volume of the differential evacuation system was maintained by the first step of a turbomolecular pump with an operation power of 60 L per second, which ensured the working pressure in the chamber of the mass spectrometer at 1.5×10^{-4} Pa. The pressure difference at the steps of differential evacuation made 1×10^{5}–3–1.5×10^{-4} Pa, respectively.

During anesthesia, we recorded the time dependence of peak intensity with m/z 199, corresponded to the molecular ion of sevoflurane. The quantification of sevoflurane in the breathing circuit of IAM was performed with a time resolution of 100 μsec and the detection limit not less than 0.05 vol. % in oxygen. The rate of sampling from the inhalation circuit of IAM made 10^{-6} L/min under atmospheric pressure. The delay of the mass spectrometer signal with respect to the concentration of the gaseous mixture in the front end of the capillary did not exceed 30 sec.

RESULTS AND DISCUSSION

A mass spectrum of a gas mixture present in an IAM circuit is shown in Fig. 2. The assignment of the peaks in the spectra was done in accordance to [8, 9]. The ratios m/z for sevoflurane were 69, 79, 131, 151, 181, and 199 [8]; fentanyl opioid analgesics, 146 [9]; and substances A and B, 78, 81, 113, 128, and 180 [8]. Substances A and B in our case were potentially toxic products of the interaction of sevoflurane with CO_2 absorber in breathing circuit of IAM, i.e., pentafluoroisopropenyl fluoromethyl ether $C_4H_2F_6O$ and pentafluoromethoxyisopropyl fluoromethyl ether $C_5H_6F_6O$, respectively [8].

In this work, the main attention was paid to the comparative study of the time delay of the IR-spectrometer and mass spectrometer on the changes in the anesthetic concentration in the breathing circuit of IAM, which was determined by the position of the injector lever. Anesthesia was maintained using a Draeger Vapor 2000 injector was used. In Figs. 3–5, the time dependences of sevoflurane concentration for the total period of anesthesia are presented starting from the intubation of a patient, the surgery operation itself at the low-flow mode of IAM operation (0.5 L/min), and finishing with the recovery of the patient from the anesthesia at a high flow rate of gaseous mixture in IAM of 6.0–8.0 L/min. In Fig. 3 we present two stages of sevoflurane increase in an IAM circuit up to the value of 2 vol. %, corresponding to the value preset in injector in the beginning and at the 110*th* minute of anesthesia. The delay of the readings of the IR-sensor made not less than 15 min using manual chronometry. In the entire course of anesthesia, the

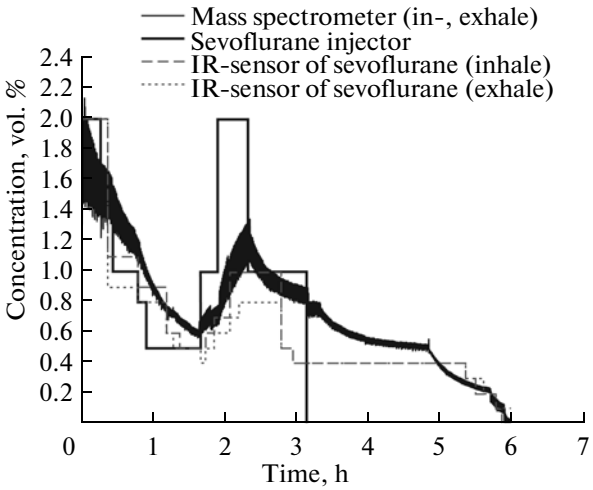

Fig. 3. Time dependence of sevoflurane concentration according to the readings of the injector, mass spectrometer, and IR-sensor (for Dragger Julian IAM).

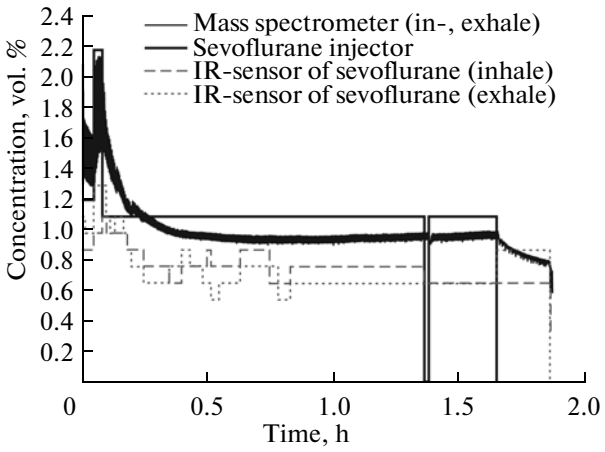

Fig. 4. Time dependence of sevoflurane concentration according to the readings of the injector, mass spectrometer, and IR-sensor (for Dragger Julian IAM).

concentration of the inhalation anesthetic did not go below 0.5 vol. %, which matched the target value for patients according to MAC. Noteworthy, the maximal delays of sensor readings occurred when the concentration of the anesthetic underwent abrupt jumps, as indicated in Figs. 3 and 5. In such cases, the Dragger Julian IAM was used to maintain anesthesia. Figure 4 presents a chronometry pattern corresponding to anesthesia at a stable flow of sevoflurane. In this case, the delay of readings of the IR-sensor made not less than 10 min. As the calibration of the mass spectrometer was not available for the entire period of anesthesia with an interval of 10–15 min, we could not perform a trustworthy comparison of IR- and mass spectrometer readings for the anesthetic concentration. This should be done shortly.

In Fig. 5, the time dependence of the concentration of sevoflurane by the data of the injector, mass spectrometer, and IR-sensor for the Dragger Julian IAM is presented. Figures 6–8 correspond to different stages of anesthesia, for which a full picture is presented in Fig. 5. The dependences are presented with different time resolutions and reflect changes in concentration over a breathing cycle. The beginning of anesthesia at the maximal concentration of sevoflurane and under the effect of intravenous anesthetics is presented in Fig. 6. The dynamics of the concentration evolution has a smooth shape, which corresponds

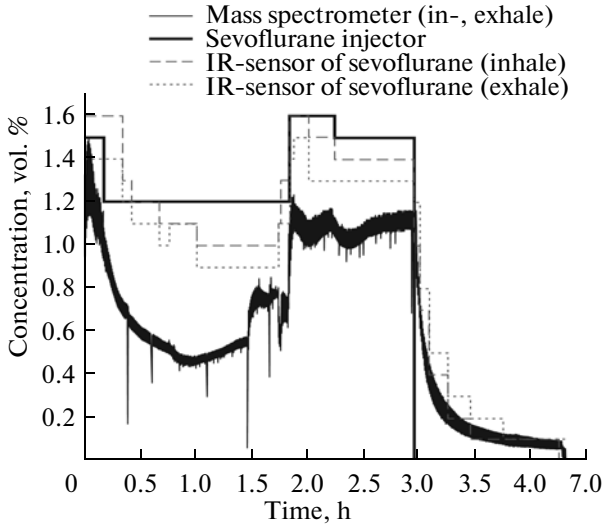

Fig. 5. Time dependence of sevoflurane concentration according to the readings of the injector, mass spectrometer, and IR-sensor (for Dragger Julian IAM).

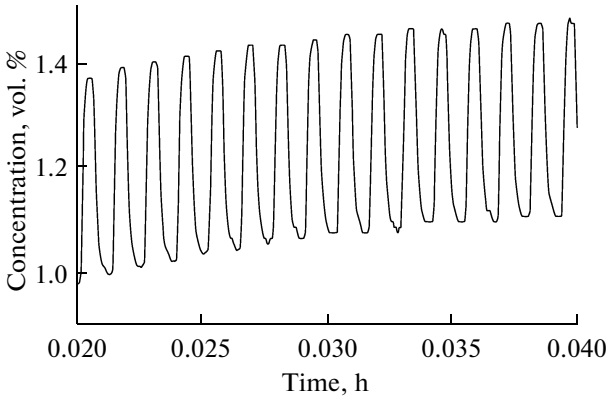

Fig. 6. Dynamics of the concentration evolution for sevoflurane at the initial stage of anesthesia over a breathing cycle.

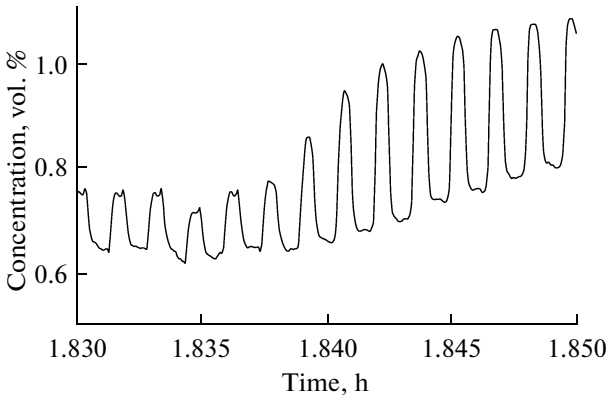

Fig. 7. Dynamics of concentration evolution for sevoflurane in an increase in the anesthetic concentration in the IAM circuit over a breathing cycle.

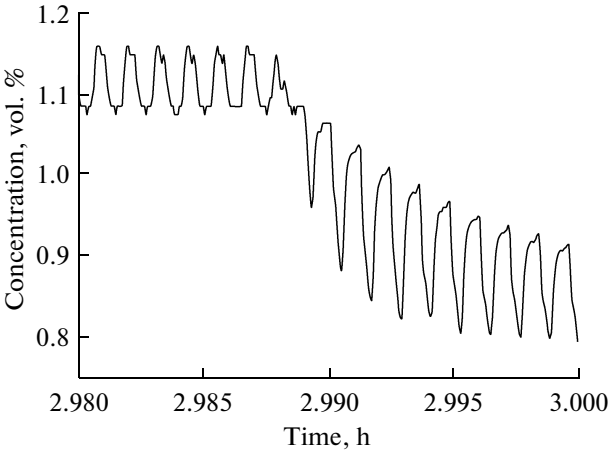

Fig. 8. Dynamics of concentration evolution for sevoflurane over a breathing cycle near the end point of anesthesia.

to the mode of blood saturation with the anesthetic. In Fig. 7, the elevation of sevoflurane concentration in the IAM circuit is presented for the change of the injector regulator from 1.2 to 1.6 vol. %. The ripped behavior of the curve in the beginning of the picture may refer either to the termination of the muscular relaxant activity or to attempted independent breath of the patient. The view of sevoflurane concentration vs. the period of breathing cycle, which is characteristic for the end point of anesthesia at the higher concentration of oxygen in the IAM circuit and the injector switched off, is presented in Fig. 8. Here we present a picture of recovery of a patient from anesthesia. In the latter case, sevoflurane released from blood, so its concentration in the exhale mixture was higher than in the inhale one.

CONCLUSIONS

In conclusion, let us mention that the use of mass spectrometry control ensures the continuous monitoring of sevoflurane in a breathing mixture and may serve a point of concern in an inhalation anesthesia machine.

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