Biological Monitoring of Occupational Exposure to Isoflurane by Measurement of Isoflurane Exhaled Breath

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The relationship between isoflurane environmental concentrations in operating rooms and the corresponding isoflurane concentration in the exhaled air of the operating personnel at the end of the exposure has been investigated. Isoflurane was retained in an adsorbent cartridge and after thermal desorption the concentration was estimated by gas chromatography. Significant correlation between environmental and exhaled air isoflurane concentrations allowed the establishment of a biological exposure index and biological exposure limits corresponding to proposed atmospheric threshold values.

For the evaluation of isoflurane in air and in exhaled breath, thermal desorption–gas chromatography techniques were developed and validated.10–12 The exhaled isoflurane is trapped in a solid adsorbent for chromatographic analysis. The method is not affected by water vapour condensation.11

The aim of this study was to propose a biological index of exposure based on the relationship between personal exposure to isoflurane in the operating theatre and its concentration in exhaled air.

EXPERIMENTAL

The study involved a total of 167 personal samples collected from anaesthetists, surgeons and nurses during their routine work in 13 surgical theatres in a Spanish hospital. The concentration of isoflurane in air was monitored continuously throughout exposure and exhaled air was sampled after exposure.

Isoflurane ambient concentrations

Isoflurane exposure was determined by using diffusive monitors attached to clothing within the breathing zone. The diffusive samplers were standard stainless-steel tubes for an ATD50 thermal desorption system (Perkin Elmer). The tubes were packed with 150 mg of conditioned Chromosorb 106.10 Before use, and during storage, the tubes were protected with storage caps; when used, a diffusion cap was fitted to allow controlled exposure to the environment. The monitors were continuously exposed in the breathing zone for the whole operation periods.

All diffusive samplers were desorbed by means of the ATD system, directly connected to a Perkin-Elmer
Table 1. Experimental conditions for thermal desorption and gas chromatography

**Thermal desorption parameters**

- Carrier gas: N₂ (68.95 kPa, 10 psi)
- Desorption: Two stages
- Oven temperature: 240°C
- Cold trap: lower temperature -30°C
- upper temperature: 240°C
- Heated transfer line: 100°C

**Gas chromatographic parameters**

- Stationary phase: Free Fatty Acid Phase
- Film thickness: 0.3 µm
- Column length: 25 m
- Column inner diameter: 0.2 mm
- Detector temperature: 70°C
- Detection: Flame ionization

8700 gas chromatograph by a heated transfer line. Operating conditions are summarized in Table 1.

The performance of this kind of sampler has been evaluated and validated. The sampler was found to collect isoflurane efficiently for up to 8 h at an uptake rate of 0.45 ml min⁻¹.¹⁰,¹³

**Ioflurane in exhaled breath**

The portable system used to take exhaled air samples has already been described.¹⁴ It consists of a Haldane-Priestley aluminium tube modified to concentrate aliquots of end-expired (alveolar) air, from one or more exhalations, in a solid adsorbent for chromatographic analysis.

Samples of exhaled air were obtained by having the subject take two or three deep breaths, inhaling and holding their breath for 10–15 s, then exhaling into the aluminium tube of the sampler until all air was expelled. Isoflurane from end-exphaled air was retained in an adsorbent cartridge. A servomotor-driven gas syringe of 50 ml capacity alternately drew in from the aluminium tube and through the adsorbent metallic tube, standard for the ATD50 thermal desorption system. The tube was packed with 200 mg of 20/40 mesh Chromosorb 106 and was sealed at the end of the procedure for transport and storage.

The total volume of end-expired air that passed through the adsorbent tube was 1 l, representing five 200-ml aliquots for each of the five consecutive exhalations. In all subjects, exhaled breath samples were collected 10 min after the end of exposure in an area separated from the site of exposure.

Table 2. Statistical parameters of the distribution of the time-weighted average of the environmental concentration and the exhaled air concentration of isoflurane

<table>
<thead>
<tr>
<th>Environment isoflurane concentration (mg m⁻³)</th>
<th>Exhaled air isoflurane concentration (mg m⁻³)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median value</td>
<td>16.62</td>
</tr>
<tr>
<td>Geometric mean</td>
<td>16.23</td>
</tr>
<tr>
<td>Geometric standard deviation</td>
<td>2.23</td>
</tr>
<tr>
<td>Range</td>
<td>1.14–157.23</td>
</tr>
<tr>
<td>Geometric mean</td>
<td>2.85</td>
</tr>
<tr>
<td>Geometric standard deviation</td>
<td>2.51</td>
</tr>
<tr>
<td>Range</td>
<td>0.15–26.09</td>
</tr>
</tbody>
</table>

All samples of exhaled breath air were desorbed following the same procedure as in the preceding section. Operating conditions are given in Table 1.

**RESULTS AND DISCUSSION**

Isoflurane in the operating rooms was always detectable. The distribution of the personal levels of isoflurane exposure for all theatre staff is shown in Fig. 1. Data were best fitted to a log-normal distribution. This type of distribution has been shown for other pollutants.¹⁵,¹⁶

Isoflurane concentrations ranged from 1.14 to 157.23 mg m⁻³ (Table 2). The results are similar to those obtained in other studies¹⁷ but higher than those found in several Canadian hospitals,¹⁸,¹⁹ where the arithmetic means ranged from 1.8 to 22.3 mg m⁻³.

The percentage of biotransformation for isoflurane is only 0.2%,²,⁴ so the best possibility for its biological monitoring is to measure the unchanged substance.

In order to obtain information about the sampling strategy, preliminary study was carried out under several exposure conditions (varying both isoflurane ambient concentration and exposure times). Alveolar air samples were taken at different times after exposure,
the first sample being collected 10 min after the end of the exposure. Personal samples in the breathing zone were also taken for each sampled subject. Isoflurane concentrations and exposure times ranged from 8.4 to 157.2 mg m$^{-3}$ and from 75 to 360 min, respectively, in order to study elimination through exhalation after different levels of exposure.

Elimination profiles of the exposition situations studied are shown in Fig. 2. After high exposure, initial exhalation concentrations were higher than after low exposure. In both cases, elimination profiles were similar to those found in anaesthetized patients\(^1,3\) as well as to those obtained for other organic solvents that were mainly eliminated by the respiratory route (perchloroethylene, for instance).\(^{20-22}\)

Figure 3 shows the distribution of measured levels of isoflurane in exhaled breath air. Exhaled air isoflurane concentrations ranged, with a log-normal distribution, from 0.15 to 26.09 mg m$^{-3}$ with a geometric mean of 2.85 mg m$^{-3}$.

A close relationship was found between the log of exposure dose, expressed as time-weighted average exposure multiplied by exposure time ($D$, mg m$^{-3}$ min), and the concentration in the exhaled air ($CAE$, mg m$^{-3}$) ($r=0.79$, $p=0.0001$), as can be seen in Fig. 4. The linear regression line fits the following equation

$$\log CAE = 0.025 + 0.77 \log D$$

The regression line does not start from the origin of the Cartesian coordinate, as has been shown for isoflurane and halothane in urine.\(^{17,23}\) This indicates that some isoflurane retained previously was not completely cleared during the resting period. This view was confirmed by the presence of isoflurane in samples of exhaled air taken 16 h after exposure.

The limit value of 2 ppm was recommended by NIOSH for all halogenated agents.\(^{24}\) This standard was given in 1977, when isoflurane was not yet in use.
More recently, the Swiss exposure standard for isoflurane and enfurane was set at a value of 10 ppm.

The proposed method can be performed easily and quickly and could also be applied for another volatile liquid anaesthetic, desflurane, the use of which is currently increasing. Obviously, the exhaled air collection must always be performed with the same methodology and sampling strategy.

REFERENCES