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Association of anesthetic toxic isoflurane gases of the indoor air of operating room, Ahvaz, Iran during 2016

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Abstract
Operating rooms (ORs) in hospital wards are very important because of special conditions of patients. The hazards of contact with low concentrations of anesthetic gases (AG) are undeniable. Nowadays AG isoflurane is one of the important pollutants which is in the air of ORs and used in anesthesia. The purpose of this study was to evaluate the level of anesthetic toxic isoflurane gases of the indoor air of Razi, Golestan and Emam educational hospitals ORs, using active sampling system during 2016. In this study, in order to sampling and detection of isoflurane concentration (ppm), a portable pump (SKC pump) and tubes (Sorbent Tube Tenax TA 250 mg) were utilized. The sampling was done in three different points of the ORs. According to this study, the “Razi” and “Emam” hospitals had the highest and the lowest isoflurane concentrations. According to the results of this study, isoflurane concentrations in three main educational hospital ORs affiliated to the Ahvaz Jundishapur University of medical sciences were 2.342, 2.15 and 2.04 ppm, respectively. According to this study, the average concentration of isoflurane in three main educational hospitals was more than recommended scales by international organizations (2 ppm) and it sounds that exposure to this amount of gas would be the cause of health disorders for staff. The results showed that the mean of isoflurane concentration in different parts of ORs with standard ventilation system was significantly lower than those ORs in which they did not have standard ventilation. While environmental health management and AG contamination in ORs have been ignored, they can cause disorders in ORs’ staffs and causing more spiritual and material costs.

Keywords
Isoflurane, anesthetics, operating room, hospital, Iran

Introduction
Current scientific evidence obtained from human and animal studies suggests that chronic exposure to anesthetic gases (AG) increase the risk of both spontaneous abortion and congenital abnormalities in offspring among female workers and wives of male workers (Byhahn et al., 2001b; Chaoul et al., 2015; Gupta et al., 2016). Risks of hepatic and renal diseases are also increased among exposed workers (Byhahn et al., 2001b; Ghimenti et al., 2015; Mierdl et al., 2003; Muir, 1978). International Agency for Research on Cancer (IARC) states there is inadequate evidence for the carcinogenicity of enflurane, halothane and isoflurane both in animals and humans (Kanmura et al., 2000; Kumar & Tripathi, 2015; Lachenmeier et al., 2009). Exposure to AG and health endpoint of the anesthesia gases such as isoflurane on human since the past have been considered by government and epidemiological researchers (Byhahn et al., 2001b; Choosong et al., 2015; Gupta et al., 2016; Mierdl et al., 2003). Enflurane and isoflurane have similar health effects for acute exposure. The most important health effects of isoflurane are irritation and redness in eyes, dryness and irritation of skin, liver and kidney damage and irritation of the mouth and throat (Byhahn et al., 2001a; Choosong et al., 2015; Dascalaki et al., 2008; Kanmura et al., 2000; Raj et al., 2003). If inhaled, headaches, dizziness, drowsiness, unconsciousness and death can occur (Bargellini et al., 2001; Izsdes et al., 2010). Isoflurane is the most commonly used organic AG. According to current guideline hundreds of staffs in operating rooms (ORs) have suffered from AG (Barash, 2009; Byhahn et al., 2001b;
Schulte-Uentrop & Goepfert, 2010). Occupational exposure may occur whenever anesthetics are used in ORs, dental offices and veterinary hospitals (Joksovic et al., 2015; Mierdl et al., 2003). The number of people who were potentially exposed was estimated to be 215,000 in 1977 (Muir, 1978). This number is probably much higher today if the increase in the health care industry since 1977 is considered. Physical properties and other descriptive information of isoflurane are colorless, molecular formula (C₃H₂OClF₅), mild ethereal and solubility (miscible with organic liquids) (Devischer et al., 2010). The detection limits of the analytical procedure are 92.8, 87.3 and 44.7 pg for isoflurane, respectively (Kumar & Tripathi, 2015). These are the amounts of each analyte that will give a response that is significantly different from the background response of a reagent blank (Muir, 1978). Ahvaz is one of seven Iranian metropolitan cities (Khaefi et al., 2016; Yari et al., 2016). Concentrations of the anesthesia gases in these educational hospitals became increased and intensified. OR staffs in Ahvaz educational hospitals, because of the major reasons, including admitted high number of cases in educational hospitals’ OR after healthcare reform and the shortage of sufficient number of operation room staffs are exposed to high anesthesia gas concentrations. The studied teratogenic showed that increased anesthesia gases concentrations especially isoflurane can increase the rate of morbidity on staffs ORs (Guirguis et al., 1990; McGregor, 2000). In recent years, several studies have shown a relation between the health effects and short- and long-term exposure with isoflurane in the location of respiratory air among the staff’s ORs (Guirguis et al., 1990; Joksovic et al., 2015; Kumar & Tripathi, 2015; Raj et al., 2003). Joksovic et al. in 2015, evaluated the early exposure to general anesthesia with isoflurane (Joksovic et al., 2015). In a similar work, Chaoul et al. studied the level of an occupational exposure to AG in ORs (Chaoul et al., 2015). Guirguis et al. associated the health effects of exposure to AG in Ontario hospital personnel (Guirguis et al., 1990). Mierdl et al. had been estimated the association between levels of inhalational anesthetics and enhancement the risk of patients’ health during cardiac surgery (Mierdl et al., 2003). In 2016, Gupta et al. have shown a determined does exposure to inhalation anesthesia in ORs (Gupta et al., 2016). Byhahn et al. in a study has shown an occupational exposure to volatile anesthetics (Byhahn et al., 2001b). According to the results of the study of Izdes et al. in 2010, high anesthesia gases concentration for short term exposure can increase the risk of glutathione, total antioxidant capacity and DNA damage in anesthesia nurses (Izdes et al., 2010).

The aim of this study was to estimate the level of anesthetic toxic isoflurane gases indoor air at Razi, Golestan and Emam educational hospitals’ ORs in Ahvaz (located in south-west of Iran), during year 2016.

**Materials and methods**

**Methods**

This cross-sectional study was conducted in 14 ORs in three main educational hospitals’ ORs. In this retrospective study, we used an active sampling system for measuring the amount of AG (isoflurane) in three main teaching hospitals at southwest of Iran during 2016.

**Sampling**

Samples were collected using a portable personal sampling pump (SKC pump: standard model) and Sorbent Tube (Tenax TA 250 mg) (SKC Inc., Eighty Four, PA) at three educational hospitals during 2016. Samples are gathered with glass sampling tubes packed with sections of (140/70 mg) Anasorb 747 (Figure 1). The sections are held in a place with a glass wool plug and two urethane foam plugs. For this estimation, they usually prepared sorbent tube which was purchased from SKC pump. The end of the sampling tube was broken immediately before the sampling. Only properly trained personnel can sample in an OR or dental office; this is necessary to be in compliance with Occupational Safety and Health Administration (OSHA) exposure control plan for blood borne pathogens (All & Business, 1994). Samples are desorbed with CS₂ and analyzed by Gas Chromatograph (GC), using a Flame Ionization Detector (FID). Air volume and sampling rate were 12 L at 0.05 L/min. Isoflurane was evaluated at two target concentrations because US National Institute for Occupational Safety and Health (NIOSH) recommended exposure limits (Control, 1988; Ghimenti et al., 2015; Muir, 1978) are considerably lower than the current ACGIH threshold limit values (TLVs) (Hygienists, 1986). After sampling for selected time, the sampling tube was sealed immediately with plastic end caps. ACGIH has recommended a higher target concentration of 75 ppm was set for isoflurane because it is a geometric isomer of enfurane. NIOSH has recommended that exposure to these halogenated AG should be controlled with a 60 min ceiling value of 2 ppm (Muir, 1978). The AG are usually administered in conjunction with nitrous oxide.

**Standard preparation and analysis**

We prepared concentrated stock standard of isoflurane in toluene. Then we were worked with analytical standards by injecting microliter amounts of concentrated stock standards into 2 mL vials containing 1.0 mL of desorption solvent delivered from the same dispenser used to desorb samples. For example, to prepare a target level standard of isoflurane, inject 10 μL of a stock solution containing 672 mg/mL of isoflurane in toluene into 1 mL of desorption solvent. At the end of the sampling, we were deleted the plastic end caps and
carefully transfer each section of the adsorbent to separate 2 mL vials. After that, we threw off the glass tube, urethane foam plugs and glass wool plug. Then, we were added 1.0 mL of desorption solvent to each vial, using the same dispenser which was used for preparation of standards. Then, we were covered the vials with polytetrafluoroethylene-lined caps and shake them for several times during the next 30 min. Testing for breakthrough was performed, using a FID to monitor the effluent from sampling tubes containing only either the 150 mg section of Anasorb CMS or 140 mg section of Anasorb 747. The amount of analyte per sampler is obtained from an appropriate calibration curve in terms of \( \text{mg/m}^3 \), uncorrected for desorption efficiency. The air concentration is calculated, using the following formulae,

\[
\text{ppmv} = \frac{24.45 \times \frac{mg}{m^3}}{mw} \tag{1}
\]

where 24.45 is the molar volume at 25°C and 101.3 kPa (760 mmHg) and molecular weight of isoflurane = 184.49.

Description of study area

The field of experiment was conducted in Ahvaz, the capital of Khuzestan province of Iran (31° 45' N, 48° 29' E) at the operation room at hospital affiliated to Ahvaz Jundishapur University of Medical Sciences, during 2015 (Geravandi et al., 2015; Goudarzi et al., 2015; Goudarzi et al., 2016; Neisi et al., 2016; Saeidimehr et al., 2015; Salmanzadeh et al., 2015). Razi, Golestan and Emam educational hospitals are a tertiary-care hospitals with 220, 450 and 900 beds, located in the southwest of Ahvaz, Iran (Figure 2).

Statistical analysis

Data analyses were performed, using SPSS version 16 (SPSS Inc., Chicago, IL). Levels of isoflurane anesthesia gas in different conditions were compared, using independent samples t-test or one-way ANOVA. Also, in this study we were assessed the effects of exhaust, ventilation and cooler system.

Ethical considerations

Sampling and data collection were done by researcher and we analyzed the isoflurane data by Excel and SPSS software’s. We were estimated the level of AG isoflurane and compared with national standard of air at Razi, Golestan and Emam educational hospitals’ ORs.

Results

This study was conducted on more than 14 ORs in three main educational hospitals’ ORs affiliated to Ahvaz Jundishapur University of medical sciences, Iran during 2016. Based on the results, 57.15% of the rooms had exhaust systems and the exhaust systems were not active in only 14.29% of these rooms. There were ventilation systems in 71.42% of these rooms and the cooler was working at 78.57% of them (Table 1).

The standard of isoflurane according to US NIOSH and California OSHA (OSHA 5155 Table AC-1) permissible exposure limits for chemical contaminants is 2 ppm (2000 \( \mu \text{g/m}^3 \)) (Checkai, 2014; Dascalaki et al., 2008). Based on the result of this study, Emam and Razi hospitals had the lowest and the highest isoflurane concentrations during 2016, respectively. Table 2 shows that the annual average of isoflurane concentration in three main educational hospitals’ ORs is higher than that of NIOSH.

Frequency distribution related to isoflurane illustrates in Figures 3–6 with three ranges in three main educational hospitals’ ORs. It should be noted that 74% of above cases are corresponded to the ORs with the concentrations of higher than 2 ppm.

Table 1. Absolute and relative distribution of the operating rooms according to the state of their ventilation systems, cooler and exhaust systems.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ventilation system</td>
<td></td>
<td></td>
</tr>
<tr>
<td>On</td>
<td>4</td>
<td>28.57</td>
</tr>
<tr>
<td>Off</td>
<td>6</td>
<td>42.85</td>
</tr>
<tr>
<td>Not exist</td>
<td>4</td>
<td>28.58</td>
</tr>
<tr>
<td>Cooler</td>
<td></td>
<td></td>
</tr>
<tr>
<td>On</td>
<td>11</td>
<td>78.57</td>
</tr>
<tr>
<td>Off</td>
<td>2</td>
<td>14.29</td>
</tr>
<tr>
<td>Not exist</td>
<td>1</td>
<td>7.14</td>
</tr>
<tr>
<td>Exhaust system</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Connect</td>
<td>8</td>
<td>57.15</td>
</tr>
<tr>
<td>Not connect</td>
<td>2</td>
<td>14.29</td>
</tr>
<tr>
<td>Not exist</td>
<td>4</td>
<td>28.56</td>
</tr>
</tbody>
</table>
Discussion

Nowadays, because of the increase of admitted patients’ cases and increased AG which are consuming in ORs, paying attention to patients and staff is very important. In this study, we evaluated the level of AG isoflurane of air at Razi, Golestan and Emam educational hospitals’ ORs of Ahvaz, Iran. According to the results of this study, recovery and reconstruction ventilation systems in ORs can be very important roles in survival and reduce the concentration of isoflurane. Results showed that Razi educational hospital is the most polluted hospital among others, during 2016. Also, based on the result of our study, the average concentrations of isoflurane in Razi and Emam hospitals had the highest and the lowest during 2016, respectively.

Al-Ghanem et al. in their study had been used Gas chromatography–mass spectrometry (GC-MS) for monitoring of anesthetics gases of OR in Jordan (Al-Ghanem et al., 2010). They demonstrated that medical staff personnel are exposed to high concentrations of AG (Al-Ghanem et al., 2010). Ventilation systems, mechanical and building factors can be the reasons of these differences in isoflurane concentration which were found during sampling, significantly among the various ORs. Based on the result which was accrued in Germany, assessment of different health endpoint related to long term exposure to concentrations of AG among ORs staff (Byhahn et al., 2001b). According to the results of Flack et al.’ study, the exposure to isoflurane anesthetics were below the standard of NIOSH recommendation (Flack, 2006). The high concentrations of isoflurane which were observed in this study were associated with the defection of ventilation and exhaust systems of Ahvaz ORs, Iran.

Mierdl et al. in their study evaluated the relationship between an occupational exposure to AG and the health effects on staff and patients of ORs (Mierdl et al., 2003). They reported that the concentration of anesthetic agents was low at most times during the study (Mierdl et al., 2003). Based on the results of our study, the concentration of isoflurane was relatively higher because of the greater concentration in Razi, Golestan and Emam educational hospitals’ ORs, old equipments and weakness in ventilation systems.

To recap the discussion it sounds that the concentrations of isoflurane in this study were higher than the standard of NIOSH and this is because of higher concentrations of isoflurane gas in ambient air of operation rooms.

**Table 2. Isoflurane concentrations in Razi, Golestan and Emam educational hospitals during 2016.**

<table>
<thead>
<tr>
<th>Operation room at hospital</th>
<th>NIOSH standard (ppm)</th>
<th>Average (ppm)</th>
<th>Min (ppm)</th>
<th>Max (µg/m³)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Razi</td>
<td>2</td>
<td>2.342</td>
<td>0.35</td>
<td>3.24</td>
</tr>
<tr>
<td>Golestan</td>
<td>2</td>
<td>2.15</td>
<td>0.21</td>
<td>3.012</td>
</tr>
<tr>
<td>Emam</td>
<td>2</td>
<td>2.04</td>
<td>– a</td>
<td>2.78</td>
</tr>
</tbody>
</table>

*Non-detectable values.

Figure 3. Measured Average concentrations of isoflurane in three main educational hospitals’ operating rooms.

Figure 4. Concentrations of isoflurane data from Razi operating rooms.

Figure 5. Concentrations of isoflurane data from Golestan operating rooms.
**Conclusion**

The isoflurane is one of the isomer in the ambient air of ORs after a performed reaction enflurane. In this study, a detailed analyzed data were carried out to find the level of AG isoflurane of air at Razi, Golestan and Emam educational hospitals’ ORs of Ahvaz (located in the south-west of Iran), during 2016. High concentration of this gas in ORs was associated with OR equipments, building characterizes, ventilation, cooler and exhaust systems. Controlling the AG especially isoflurane, careful monitoring, application of modern equipments and decreasing the emission of isoflurane which are entering to the air of operation rooms will have important roles in decreasing the amount of isoflurane.

**Limitations and strengths**

Finally, it should be mentioned that this study had some limitations such as small sample in only three hospitals. It should be noted that, similar studies should be carried out on other public and private hospitals, using large samples. Therefore, we evaluated outcomes attributed to isoflurane which may be under or overestimated due to other existing AG into the air of ORs. Also, we can prevent or reduce the exposed to AG isoflurane in OR by medication protocol and education.

**Declaration of interest**

Authors have no conflict of interests. The authors gratefully acknowledge AJUMS and the Environmental Technologies Research Center (ETRC) for financial support and providing necessary facilities to accomplish thus research with project number of ETRC-9303.

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