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STUDY OF SOME HEALTH HAZARDS AMONG OPERATING THEATER PERSONNEL DUE TO EXPOSURE TO ANESTHETIC GASES (PART I)

By

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Abstract

Introduction: The use of anesthetic gases might lead to Chromosomal Aberrations (CAs) among the operating room personnel. **Aim of work:** To monitor isoflurane air level in the environment of operating rooms denoting the use of anesthetic gases, and to assess the CAs among operating room (OR) personnel. **Materials and Methods:** Operating room personnel 184 (68 males and 116 females) were included in the study and compared with 192 other hospital areas personnel (63 males and 129 females). All subjects filled a questionnaire including personnel, family, past and present histories. All subjects were tested for chromosomal aberrations. Operating theaters were evaluated regarding the type of breathing circuits used whether open or closed, the type of anesthetic gases used, presence of air conditioning, and scavenging system. Isoflurane air level was measured using the organic method 103 by OSHA. **Results:** OR personnel had significantly higher percentage of CAs than control group (p value <0.001). Also it is higher with higher concentrations of waste anesthetic gases. There was a positive correlation between prolonged exposure to high concentrations of anesthetic gases and the occurrence of CAs among exposed OR personnel. Smoking had positive significant effect on frequency of CAs (p value = 0.017). Isoflurane air level was higher than NIOSH Recommended Exposure Limit (RELs) in most of measured points, and that the level is higher in dual open and closed circuits using theaters, also the level was higher in points near the anesthesia machine and in recovery rooms than critical care rooms. **Conclusion:** Isoflurane air level was higher than RELs in most of measured points. Personnel working in operating theaters are more at risk to

develop chromosomal aberrations than controls. **Recommendations:** Implementation of adequate and working scavenging system and air conditioning, use of closed circuits whenever possible, periodic checking of anesthetic air levels, chromosomal studies for working personnel, and replacement of any malfunctioning parts of anesthesia machine.
Key words: Chromosomal aberrations, Isoflurane, Operating room, Smoking and Duration of exposure.

Introduction

Inhalations of anesthetics are essential materials used in hospitals to induce unconsciousness in patients prior to surgical procedures. The most commonly used agents are Halothane, Enflurane, Isoflurane and sevoflurane. Nitrous Oxide is also a good analgesic for pain relief during childbirth and some dental procedures (OSHA, 2000). OSHA has not set a permissible exposure limit for WAG (Waste Anesthetic Gazes). However, under the General Duty Clause of OSHA, an employer must provide employees a work area free of recognized hazards (Krenzischek et al. 2002). In 1977, NIOSH issued a Recommended Exposure Limit (REL) for nitrous oxide (N2O) of 50 parts per million (ppm) (when used as the sole agent) expressed as a time-weighted average (TWA) during the period of anesthetic administration, and a maximum of 2 ppm (16.2 mg/m3) over a 1-hour period (as a 60 minute ceiling level) for any halogenated agent that shouldn't be exceeded during any part of the workday (OSHA, 2000).

Various complaints and disease states, as well as reproductive and developmental effects, have repeatedly been related to chronic exposure to inhalational anesthetics (Burm, 2003). Many health care professionals are potentially exposed to waste anesthetic gases and are at risk of occupational illness. These professionals include anesthesiologists, nurse anesthetists, surgical and obstetric nurses, operating room (OR) technicians, nurse aids, surgeons, anesthesia technicians, post anesthesia care nurses, dentists, dental assistants, dental hygienists, veterinarians and their assistants, emergency room staff, and radiology department personnel as Magnetic Resonance Image (MRI) and cardiovascular radiology personnel, ambulance and emergency vehicles personnel which may be provided with

anesthetic gas equipments mainly for pain relief (OSHA, 2000).

Some contamination of the operating rooms by waste anesthetic gases is unavoidable when anesthetic gases are used. The amount of contamination increases when unsealed airway devices and/or high concentrations of inhaled anesthetics are used; inhaled induction of anesthesia, for example, is especially problematic (Hall et al., 1997 and Hoerauf et al., 1997). Waste gases can escape into the room air from various components of the anesthesia delivery system. Contamination with anesthetic gases of the OR's air is determined by both the quantity of gas liberated to air from various sources during anesthesia and by the efficiency of the various means of gas removal from the ambient air of the work environment (Gustorff et al., 2002 and Shou-Huang et al., 2002). In addition to exposure occurring during surgery, anesthetic exposures can also occur in recovery rooms when patients exhale anesthetics after being brought out of surgery.

The mechanism by which the anesthetics induce DNA damage is still unclear. However when halothane or isoflurane react directly with DNA, the most feasible alkali-labile modifications may be alkylation at the N-7 position of purines. Another explanation could be that, anesthetic gases including halothane, isoflurane and sevoflurane undergo a residual metabolic oxidation or reduction giving rise to reactive intermediates that covalently bind to cellular macromolecules. Their mediated reactions may also be involved in DNA damage induction (Alleva et al., 2003). There is evidence that halothane is mutagenic in certain in vitro test systems (Garro and Phillips, 1978). The major metabolite of halothane, trifluoroacetic acid, is relatively non-reactive and it is believed to be non-toxic. However, a postulated reductive defluorination pathway may lead to toxic or even genotoxic compounds such as 1-bromo-1-chloro-2, 2-difluoroethylene, that is an alkylating agent. Cytogenetic changes (mitotic anomalies and chromosomal abnormalities) were described as an effect of halothane exposure in mammalian cells (Ferstanding, 1995).

The considerable difference in isoflurane and halothane ability to induce

DNA damage found in Jaloszynski et al., (1999) in vitro study on PBLs (Peripheral Blood Lymphocytes) may be explained, at least partially, on the basis of physical properties, because halothane is more soluble in lipids than isoflurane. Occupational exposure to nitrous oxide has been linked to abnormal DNA synthesis. The mechanism may be explained by that nitrous oxide rapidly and irreversibly oxidizing the cobalt atom in vitamin B12, so inhibits enzymes that are vitamin B12 dependent. These enzymes include thymidylate synthetase, which is necessary for DNA synthesis (Morgan, 2006).

Bilban et al., 2005 and Chandrasekhar et al., 2006 found higher CAs and MN (Micro Nucleus) frequency in the group exposed to anaesthetic gases than in controls. Also Musak et al., (2009) and Shaker et al., (2011) found higher frequency of CA and SCE (Sister Chromatid Exchange) in female staff occupationally exposed to anesthetic gases. More over Musak et al., (2013) reported significantly increased chromosomal damage among nurses and physicians occupationally exposed to sevoflurane and isoflurane. However, Hoerauf et al., (1999) found slight, but not significant, increase in the MN formation in operating room personnel. Also, Wiesnr et al., (2008) found no difference in the rate of MN among anesthetists exposed to sevoflurane than in controls. A study by Szyfter et al., (2004) had reported no genotoxic effect for halothane, isoflurane or sevoflurane using comet method in operating room personnel compared with those of controls.

Aim of work

The aim of this study was to monitor isoflurane air level in the environment of operating rooms denoting the use of anesthetic gases, and to assess the CAs among operating room personnel.

Materials and Methods

Study design: Cross sectional study.

Place and duration of the study: The study was conducted at operating theaters, recovery rooms and surgical intensive care rooms at Kasr Al Ainy hospitals during a duration of about 6 months.

Study Sample: The study was conducted among 198 operating room personnel in Kasr Al Ainy hospitals (The whole working population who accepted to be included in the study).

The only inclusion criterion was regular working in operating rooms for the past 2 years.

The exclusion criteria were taking any cytotoxic drugs or exposure to any kind of ionizing radiation for the last 6 months before conducting the study.

Accordingly 14 were excluded for being working less than 2 years, so the remaining were 184 operating room personnel (68 males and 116 females) exposed to anesthetic gases. Among them were the anesthetists (No= 31), surgeons (No = 26), nurses (No = 82), and workers (No = 45). During their work, operating room personnel were exposed to a complex mixture of anesthetic agents (halothane, isoflurane, sevoflurane, and previously nitrous oxide). The use of nitrous oxide has been stopped since 2008.

A control group of matched 192 subjects (63 male and 129 female) was selected from other departments staff of the same hospital mainly from internal medicine hospital and outpatient clinics (doctors, nurses, workers and secretaries) with no history of occupational exposure to anesthetic agents, and not taking any cytotoxic drugs or exposed to ionizing radiation during the entire previous 6 months, and not having positive hepatitis markers.

Study methods:

Operating room personnel are divided into 31 anesthetists (17%), 82 nurses (45%), 26 surgeons (14%), and 45 (24%) workers.

Some theaters use open and closed circuits for anesthesia which are: major surgery, surgery minor, improving surgical performance, orthopedics, 4th and 5th floors pediatrics, ENT and ophthalmology theaters (number of working personnel=96 with a percentage of 52%), while other theaters use closed circuits only which are: neurosurgery, gynecology, cardiothoracic and urology theaters (No=88 with a percentage of 48%).

Some theaters (neurosurgery and cardiothoracic) use isoflurane gas only (number of operating personnel =58)

with a percentage of 31%, some other theaters (ophthalmology and 4th floor pediatrics) use isoflurane, sevoflurane and occasionally halothane (No =27) (15%), while the rest of theaters use isoflurane and sevoflurane (No =99) (54%).

A) The studied group were subjected to the following:

1. **A self designed face-to-face questionnaire**, which included standard demographic data (age, gender) as well as medical history of diseases, exposure to X-rays, medication, lifestyle (smoking, alcohol), and occupational questions (years of exposure, weekly exposure hours, use of protective measures).

2. **Laboratory investigations:**

- **Collection of blood samples:** Venous blood was collected once from all the study and control group subjects in a heparinized tube for chromosomal aberration study. Blood samples were coded to avoid possible bias. The samples were transported on ice to the laboratory and were processed within 24 h.

- **Chromosomal aberrations (CAs) assay (peripheral blood lymphocytes):** The CA analysis was conducted following a standard protocol. Aliquot of 1 ml venous blood was taken from each subject in heparinized vacutainers. Whole blood was cultured in 8 ml of F-10 medium (Gibco, United Kingdom) supplemented with 20% fetal calf serum (FCS), 0.5 ml phytohaemaglutinin, 5000 IU/ml penicillin and 1000 IU/ml streptomycin (100 ugm/ml). Each culture was incubated in 5% CO2 and 95% air incubator at 37˚C for 72 h. Metaphases were obtained by adding 0.2 mg/ml colchicine to the cultures 3 h before harvesting. The cells were collected by centrifugation, resuspended in a prewarmed hypotonic solution (0.075 KCI) for 15 min at 37˚C and fixed in acetic acid: methanol (1:3 v/v). Chromosome preparations were stained with 3.3% Giemsa. The slides were analysed at 100 magnifications using a light microscope and 25 complete metaphases were screened per each individual and scored for CA frequency. The slides were analysed

by two scorers from the same laboratory.

B) In all studied theaters the following was done:

1. **Description of the workplace:** Air was conditioned by a laminar flow system with recirculation of 60% of exhausted air. The air flow entered through the upper parts of the walls and was evacuated at openings in the walls near the floor level, creating a laminar air flow. However in all operating rooms (ORs), the exhaust outlets of the anesthesia machines were not connected to a waste gas scavenging system.
2. **Each operating theatre was checked for:** -The type of breathing circuits used whether open or closed.-The type of anesthetic gases used.-Scavenging system: present or not.
3. **Environmental measurement:** Isoflurane, sevoflurane and halothane are the only anesthetic gases currently used in CUHs, with isoflurane being the only gas used in all ORs, so it was selected for environmental monitoring. OSHA ORGANIC METHOD 103: Samples are collected by drawing a known volume of air through standard size (6-mm o.d., 140/70 mg) Anasorb 747 tubes. Samples are desorbed with CS2 and analyzed by GC using a flame-ionization detector (FID). The sample can be taken at a flow rate of 0.05 L/min. Total sample volumes not exceeding 12 liters are recommended. Immediately before sampling, break off the ends of the sampling tube. All tubes should be from the same lot. Attach the sampling tube to the sampling pump with flexible, non-crimping tubing. It is desirable to utilize sampling tube holders which have a protective cover to shield the employee from the sharp, jagged end of the sampling tube. Install the tube so that the sampled air first passes through the larger section. Air being sampled should not pass through any hose or tubing before entering the sampling tube. To avoid channeling, attach the sampler vertically with the larger section pointing downward, in the worker's breathing zone. Position the sampler so it does not impede

work performance or safety. After sampling for the appropriate time, immediately remove the sampling tube and seal it with plastic end caps.

Submit the samples to the laboratory for analysis as soon as possible after sampling. If delay is unavoidable, store the samples at reduced temperature.

Standard preparation: Prepare concentrated stock standard of isoflurane in toluene. Prepare working 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.

Sample preparation: Remove the plastic end caps from the sample tube and carefully transfer each section of the adsorbent to separate 2-ml vials. Discard the glass tube, urethane foam plugs and glass wool plug. Add 1.0 ml of desorption solvent to each vial using the same dispenser as used for preparation of standards. Immediately seal the vials with polytetrafluoroethylene-lined caps.

Shake the vials vigorously several times during the next 30 min. Measure the sample with gas chromatography (GC) equipped with flame ionization detector (FID). A GC column capable of separating the analyte of interest from the desorption solvent, internal standard and any interferences. A 60-m × 0.32-mm i.d. fused silica Stabilwax-D8419 column was used in the evaluation.

GC conditions:

Zone	60°	(column)
Temperatures:	250°	(injector)
	300° (detector)	
Run time:	15 min	
Column gas flow:	1.2 mL/min (hydrogen)	
Septum purge:	1.5 mL/min (hydrogen)	
Injector size:	1.0 μL (11.3:1 split)	
Column:	60-m × 0.32-mm i.d. capillary Stabilwax-DB (1.0-μm df)	
Retention times of isoflurane:	5.50	min

FID conditions:

Hydrogen flow:	34 mL/min
Air flow:	450 mL/min
Makeup flow:	33 mL/min (nitrogen)

* We choose an operating room to represent each operating theater.

Points of sampling: We performed area sampling because of unavailability of personnel sampling pumps, but we tried to choose points representing operating personnel, and the sampling tubes were put at 160 cm of the floor at the breathing zone of the working personnel. Each sample was repeated 3 times and the arithmetic mean was calculated. *point A: at the breathing zone of working personnel on the left corner of the head of the operating table which is the usual area of the anesthetists. *In some theaters it was feasible to take other air samples and were coded as follows: *point B: at the breathing zone of working personnel in the middle of the right side of the operating table, which represents the exposure of the surgeons and scrub nurses. *point C: is measured at the breathing zone of working personnel at the periphery of the room, which represents the exposure of workers. *point D1: is measured at the breathing zone of working personnel in the recovery room close to the head of the patient. *point D2: is measured at the breathing zone of working personnel in the critical care rooms close to the head of the patient.

Consent

All personnel were told about the study and gave us an oral consent to take the blood samples.

Ethical approval

The study protocol was approved by Occupational and Environmental Medicine Department Ethical Committee, Faculty of Medicine, Cairo University.

Data management

Data were coded and entered using the statistical package SPSS version 21.Data was summarized using mean and standard deviation for the quantitative variable. Comparison of quantitative variables was done using analysis of variance (ANOVA) with multiple comparisons post hoc test when comparing more than 2 groups and using unpaired T test when comparing 2 groups. Exact test was used instead when the expected frequency is less than 5. Correlation was done to test for linear relations between quantitative variables by Pearson correlation. p-values less than 0.05 were considered as statistically significant.

Results

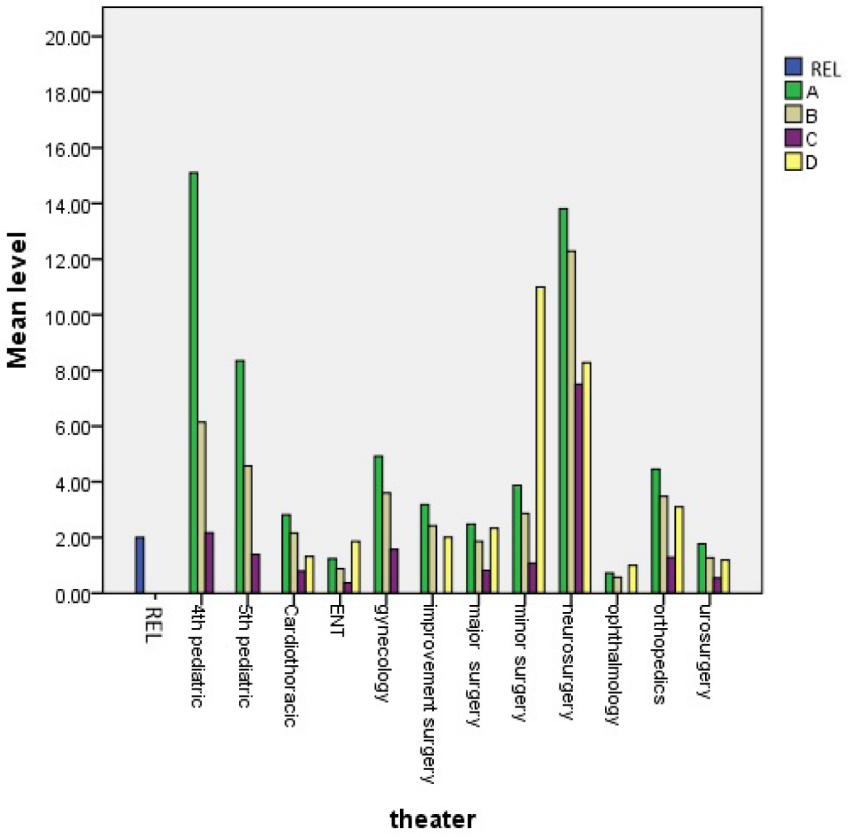

Fig.1: Mean Isoflurane air level in different theaters in (ppm).

A: at the left corner of the head of the table (representing the anesthetist)

B: at the middle of the right side of operating table (representing surgeon and nurse)

C: at the periphery of operating room (representing worker)

D1: in the recovery room.

D2: in the ICU.

The mean isoflurane air level is higher in theaters using closed circuits (4.26±4.28 ppm) than in theaters using alternate open and closed circuits (3.24±3.34), but this increase doesn't reach the level of statistical significance (p value =0.665). As neurosurgery section showed odd results, these results are excluded from the statistical analysis, accordingly the mean isoflurane air level is more in theaters using open and closed circuits (3.24±3.34 ppm) than in theaters using closed circuits only (2±1.31 ppm), but this increase doesn't reach the level of statistical significance (p value =0.333).

The mean of isoflurane air level was arranged in a descending order as follows: A (5.23±4.76 ppm)>D (3.57±3.57)>B (3.51±3.19)>C (1.75±2.09). After analysis by pairs by post hoc test, we found that the level of isoflurane in area C is significantly lower than areas A, B and D (p value = 0.01, 0.041, 0.05 respectively). The difference between other areas didn't reach statistically significant level.

This study showed that there is no statistically significant difference in comparing the exposed and control groups as regard age, sex and smoking habit ($p<0.05$)

The mean duration of working among the exposed group was 11.7 ± 7.5 years ranging from 2-35 years.

Table 1: Mean ± SD of chromosomal aberrations (CAs) among exposed and control group.

	Exposed (No =184)	Control (No=192)	p value
Total CA	5.72±8.94	3.67±12.7	**< 0.001****
Breaks	2.79±4.26	1.71±5.91	**< 0.001****
Gaps	1.86±2.91	1.40±4.84	**< 0.001****
Deletions	0.38±.85	0.02±0.12	**< 0.001****
Centromere separation	0.68±1.2	0.54±1.91	**< 0.001****

**: Highly statistically significant.

Table 1 showed that there was a statistically significant increase in total and all measured types of CAs among exposed when compared to control group.

Table 2: Mean ± SD of chromosomal aberrations (CAs) and different variables.

Variables	Total CAs (Mean ± SD)	p value
-Sex		
Male (N0:68)	7.91±10.79	**0.025***
Female (N0:116)	4.44±7.41	
- Type of Circuit		
Closed (No:88)	4.27± 7.25	0.067
Open and closed (No: 96)	7.05±10.11	
- Gases used		
Isoflurane(No:58)	4.98±7.75	0.278
Isoflurane& Sevoflurane (No:99)	5.27±8.43	
Isoflurane, Sevoflurane & Halothane (No:27)	8.96±12.28	
-Smoking		
Smokers (No:52)	8.62±11.36	**0.017***
Non smokers (No:132)	4.58±7.54	
-Job categories		
Surgeon (No:26)	5.35±10.1	0.241
Anesthetist (No:31)	4.1±8.08	
Nurse (No:82)	5.24±7.91	
Worker (No:45)	7.93±10.37	

*: Statistically significant.

Table 2 showed that the total CAs were significantly higher among males compared to females, smokers compared to non-smokers. Also it showed that total CAs were higher among personnel using both open and closed circuits (7.05±10.11) than in those using closed circuits only (4.27± 7.25), but this increase is not statistically significant (p value=0.067).

The mean value of total CAs was higher among personnel using isoflurane, sevoflurane and halothane (8.96±12.28) more than those using isoflurane and sevoflurane (5.27±8.43) or those using isoflurane only (4.98±7.75). This increase is not statistically significant (p value=0.278).

Table 3: Correlation between chromosomal aberrations and age, duration of work and smoking index.

Variables	CAs (r)	p value
Age	0.471	**<0.001****
Duration of work	0.583	**<0.001****
Smoking index	0.208	**<0.005***

*: Statistically significant.

Table 3 showed that all types of CAs are positively correlated with age, duration of exposure and smoking index.

Table 4: Frequency distribution of positive reproductive history among operating room personnel.

	Exposed (No =149)		Control (No =183)		p value
	No.	%	No.	%	
Infertility	9	6.00%	11	6.00%	0.991
Spontaneous abortion	30	20.00%	18	9.80%	**0.009***

**: Highly statistically significant. *: Statistically significant

We found that 35 of operating room personnel and 9 of controls were single so they were excluded from this comparison. Males and female were included in the study, taking into consideration that "spontaneous abortion "included histories of abortion among workers' wives.

Table 4 showed that the percentage of spontaneous abortion was significantly higher among operating room personnel (20%) than among control group (9.8%) (P value = 0.009).

Discussion

Environmental assessment of waste anesthetic gases revealed that there was no scavenging system installed in any of the operating rooms and that in very few times the air conditioning system was not working. When it came to the detection of air level of anesthetic gases, in our study one operating room was chosen to represent each operating theater, rooms vary in dimensions. Also isoflurane was chosen from the used gases to be measured as it is the one which is used in all theaters with or without other gases. Mean isoflurane air level was higher than the NIOSH RELs in point A, B, and D, and it was below it in point C as seen in.

Isoflurane had the highest level in neurosurgery and pediatric theatres (Fig. 1). The high level of isoflurane in Neurosurgery Theater despite of being closed system type is explained by the long duration of the operations, and the use of higher inspired concentration of isoflurane in hypotensive anesthesia which is used commonly in neurosurgery operations. Also there may be a source of leak that needs to be investigated. However most other individual measures are higher in theaters using open and closed circuits more than in theatres using closed circuits only (Fig. 1).

The high isoflurane level in pediatric theaters is common and can be explained by that in pediatric anesthesia open circuits are more common to use, the use of inhalational induction anesthesia, and that children are more anxious than adults and move a lot which make the mask not properly fitted during induction.

The higher air level in the 4th floor than the 5th can be explained by that in many operations done in the 5th floor a closed system is used like cardiosurgery operations. The low level in ophthalmology theaters can be explained by the use of closed circuits, the short duration of the procedures and that some operations are done using local anesthesia

Musak et al., (2013) also in their study in several hospitals in Slovakia not using scavenging system, reported increased air level of volatile anesthetics (average concentration sevoflurane and isoflurane was 200 mg/m3). This was not matched with the

study done by Mierdl et al., (2003), on waste anesthetic gas level during cardiopulmonary bypass surgery where they found that sevoflurane level didn't exceed the limit. This is explained by that in our study no scavenging system is used while in theirs it is installed.

The mean air level of isoflurane was higher in operating theaters using closed circuits only more than those using both open and closed circuits, but this increase was not statistically significant. But in individual measures the mean isoflurane level is mostly higher in theatres using open and closed circuits than in those using closed circuits only except for the neurosurgery theatre which was extraordinary high. Accordingly exclusion of the odd high levels of the neurosurgery theater from the calculation. Hence our findings revealed that isoflurane air level is higher in theaters using both open and closed circuits than in theaters using closed circuits only, but this increase doesn't reach the statistical significance level.

This was matched somehow with the study done by Raj et al., (2003) on sevoflurane air level, where they found that the lowest levels of sevoflurane were found in the dental operating theatre where a circle system with scavenging was used; the highest environmental levels with high blood, urine and breath levels were found in the MRI (Magnetic Resonance Imaging) suite where the T-piece was used with no scavenging. The highest mean sevoflurane concentrations were found in the environment samples in the oncology unit (29 ppm) and may be due to the very high turnover of patients.

Also we found that the air level of isoflurane was higher in points A, B and D, more than in point C, but this increase is not statistically significant. The highest level was in area A, the increased isoflurane level in this point and in point B can be explained by that these points are the closest to the anesthesia machine where there may be the highest exposure. The increased air level in area D1 can be explained by the fact that patient in the recovery rooms exhale the remaining of anesthetic gases directly in the air, also the number of patients in the recovery rooms is more than those in ORs.

Isoflurane air level was higher in point A which represents the anesthesiologists exposure more than point B which represents exposure of the surgeons and nurses, but this increase was not statistically significant, and both exceeded the REL (5.23, 3.51 ppm respectively). This was similar to the study done by Prokes et al., (2009) on operating room personnel (surgeons, anesthesiologists, and nurses), where they found that although members of the surgical team were exposed to approximately similar average concentrations of halothane (below TLVs), it was found that anesthesiologists in 32% of operational procedures were exposed to halothane concentrations above TLV, surgeons in 23%, instrumenting nurses in 22%.

Our work didn't coincide with the study done by Hoerauf et al., (2001), who measured sevoflurane in the breathing zone of one representative of each of three personnel groups (anesthetist, surgeon, auxiliary nurse) in operating room by means of a direct reading instrument using photoacoustic infrared spectrometry, where they found that the 2 ppm level was not exceeded in the case of the anesthetist and the surgeon, but was exceeded in 16% in the measurements for the auxiliary nurse.

Getting to comparison between the isoflurane air level in recovery rooms and ICU rooms, the study revealed that it was higher in point D1 which represents the recovery rooms more than in point D2 which represents the ICU. That is because the recovery room is commonly designed as one large room without any walls between patients, which may result in cross contamination of WAGs (Waste Anaesthetic Gases); there is narrow distance between patients; high occupancy and rapid turnover of patients; the air exchange rates of the air-conditioning system are usually lower, and the patient respires in the ambient air excreting a lot of remaining anesthetic gases, while in critical care rooms most of the patients are mechanically ventilated so the expired gases to the ambient air are minimal.

Our study showed significant increase in chromosomal aberrations (CAs) among exposed compared to the controls (P value <0.001) as shown in Table 1. Similar results were

obtained by Musak et al., (2009) where they found statistically significant increase in chromosomal aberrations in 76 personnel exposed to volatile anesthetics compared to controls in hospitals in Slovakia. The percent of smoking habit among exposed was comparable to that in our study, also females constituted the larger portion of the sample in both studies, but they didn't mention the types of volatile gases used and the presence or not of scavenging system. The sample was 54% anesthesiology physicians and 46% nurses. Recently the same author Musak et al., (2013), reported significantly increased chromosomal damage (chromosome and chromatid type) among 139 anesthesiology nurses and 108 anesthesiology physicians occupationally exposed to sevoflurane and isoflurane in several hospitals in Slovakia. In their study they found increased air level of volatile anesthetics (average concentration of sevoflurane and isoflurane was 200 mg/m3).

Another relevant study done by Shaker et al., (2011) who detected significant increase in CAs with non significant increase in SCE (Sister Chromatid Exchange) in 27 non smoking female nurses in some of the operating rooms in CUHs (Cairo University Hospitals), who were exposed to a mixture of isoflurane and sevoflurane without the use scavenging system. Moreover, our results were in accordance with the results obtained by Aldrieny et al., (2013) who examined 26 operating room personnel who were exposed to halothane and isoflurane gases with no scavenging system in Tanta university hospitals and 13 controls, and they found statistically significant increase in total CAs, breaks, gaps and deletions among exposed when compared to controls. So the condition in their hospital is nearly the same to our hospital and this explains the same results.

The current study was consistent with the study done by Paes et al., (2014), on non-smoker 15 operating room personnel (anesthesiologists, neurosurgeons, orthopedic surgeons, and general surgeons) exposed mainly to isoflurane and to a little extent to sevoflurane and N2O, and 15 unexposed controls, where they found significantly increased DNA damage among exposed

than controls as assessed by comet assay.

However, our results didn't match with the results obtained by Szyfter et al., (2004) who has reported no significant differences between 29 operating room personnel exposed to halothane, isoflurane or sevoflurane and a 20 control non-exposed group when using comet method on their PBL (Peripheral Blood Lymphocyte). This may be explained by the different parameters studied. Also they didn't mention the air levels of anesthetic gases in their study. Also, our results were not in accordance Wiesnr et al., (2008) in their study on 15 anesthetists exposed to sevoflurane and 15 control internists. They found no difference in the rate of MN (Micro Nucleus) between the exposed and the control groups. The air level of sevoflurane was 0.1-0.2 ppm, and the operating rooms in their study were air conditioned and have scavenging system. This can be explained by many facts which are: their use of scavenging system, the different parameters studied their use of sevoflurane gas only, and the low level of sevoflurane in air. But they found increase rate of sister chromatid exchange (SCE) among exposed than among controls.

On studying the effect of sex on CAs, we found that there was significant increase in CAs among males than females exposed personnel (Table 2). The high percentage of CAs among males in our study can be attributed to: a) a percent of males were smokers however non of females were smoker, b) males had significantly longer weekly working hours more than females, c) females have body structure, metabolism and hormonal processes different than males, and the health effects of exposure to chemicals can be influenced by this difference. This was against the results obtained by Musak et al., (2013), where there was no statistically significant difference in CAs among sexes. They explained the higher frequency of CAs among females more than males in their study by the more exposure of females to the anesthetic gases.

Coming to the effect of different job categories on CAs, our study showed that total CAs was higher among workers than nurses and surgeons

than anesthetists (Table 2). This can be explained by that workers have the longest exposure hours per week, followed by nurses, and that surgeons are near to the breathing circuit for the whole length of the operation more than anesthetists. This coincide with the results obtained by Musak et al., (2013) where they found in their study that CAs were more frequent among nurses than physicians, and they explained that by the longer duration of exposure for nurses. While Chandrasekhar et al. 2006 found that CAs in operating room personnel were in this descending order: technicians, anesthetists, nurses then surgeons. In their study the anesthetists and surgeons spent 6h/d and the nurses and technicians spent 8h/d in the operating theater.

Did anesthetic circuit types affect the working personnel? Our study showed that all mentioned chromosomal aberrations were higher among personnel using open and closed circuits than in those using closed circuits only (Table 2). This was approved more with the environmental results which revealed that isoflurane air level is more in theaters using open and closed circuits than in those using closed circuits only (Fig. 1).

Did anesthetic gas type added to the risk CAs? Our study showed that total CAs were higher among personnel using halothane, sevoflurane and isoflurane than in those using sevoflurane and isoflurane than in those using isoflurane alone (Table 2), but this increase is not statistically significant. This slight increase may be explained by that halothane is more lipid soluble (Jaloszynski et al., 1999).

Our results addressed the effect of age of the CAs in OR personnel, and there was positive correlation between age and chromosomal aberrations among exposed personnel (Table 3). This concurred with the study done by Shaker et al., (2011), who also found significant positive correlation between CA and age in female nurses in ORs exposed to mixture of anesthetic gases (nitrous oxide, isoflurane and sevoflurane). This is explained by that both studies were done in the same hospital. However, our results were different than the results obtained by Rozgaj and Kasuba, (2000), on 28 anesthesiologists, 16 technicians

working in non ventilated ORs in a hospital in Croatia, where the main gases used were nitrous oxide and halothane, and the results obtained by Aldrieny et al., (2013). Both studies revealed that age didn't affect CAs frequencies.

In our study we found significant positive correlation between duration of exposure and CAs (Table 3). Our results were supported by the study done by Shaker et al., (2011), who also found significant positive correlation between CAs and duration of exposure in female nurses and this can be explained by that both studies were done in the same hospital. Also our study matched with the results obtained by Aldrieny et al., (2013), which revealed that duration of exposure is positively correlated with CAs among exposed personnel. Moreover our results were similar to the results obtained by Paes et al., (2014), where they found that duration of exposure was significantly positively correlated to DNA damage.

A contradicting study was that of Chandrasekhar et al., (2006), where they found that age and duration of exposure did not have any significant effect on CAs frequency in their study on 45 operating room personnel in hospital in India, working in air conditioned rooms with laminar flow and with a scavenging system, but they found that duration of exposure affects the MN (Micro Nucleus) frequency and they explained this by that MN frequency is more sensitive technique than CAs frequency. Also the difference between their results and ours can be explained by the use of scavenging system which may decrease the cumulative effect of the gases. Also our study was opposite to the study done by Rozgaj and Kasuba (2000), where they found that duration of exposure didn't affect CAs frequencies.

Does smoking contribute to the cytogenetic damage? Our study revealed that there was significant increase in CAs among smokers compared to non smokers (Table 2) and positive correlation between smoking index and CAs among exposed personnel (Table 3). Musak et al., (2013) found that there was slight increase in total CAs among smokers, but this increase didn't reach statistical significance. However our results didn't match with the results obtained by Rozgaj and Kasuba, (2000),

where they found that smoking didn't affect CAs frequencies.

As we studied the reproductive history of the operating room personnel, we found that there was a significant increase in rate of spontaneous abortion among exposed compared to controls (Table 4). These results go in accordance with the results of the study done by Saurel-Cubizolles et al., (1994), who found the same results among female nurses in hospitals in France. They didn't mention in their study the type of the gases used, and they didn't do any environmental studies. Similar results also found by Rowland et al., (1995), where they detected that female dental assistants working in unscavenged environments with nitrous oxide for 3 hours a week or more had a 260% higher risk of spontaneous abortion than unexposed nurses. This study has a common factor with ours which is the absence of scavenging system.

Moreover, Shirangi et al., (2008) also reported that there was significant increase in the risk of spontaneous abortion in women exposed to unscavenged anesthetic gases for > or =1 h per week, in their study done on females exposed to inhalational anesthetics in veterinary hospitals.

Conclusion and Recommendations

In this study it was evident that isoflurane air level was higher than NIOSH RELs in most of measured points, and that the level was higher in dual open and closed circuits using theaters, also the level was higher in points near the anesthesia machine and in recovery rooms than critical care rooms. This rise in the air levels of WAGs can be attributed to absence of effective scavenging system of anesthetic wastes.

In our study, we found that personnel working in operating theaters and exposed to waste anesthetic gases are more at risk to develop CAs. Also there was a significant increase in rate of spontaneous abortion among exposed compared to controls. This was related to the prolonged exposure over years and working in operating rooms utilizing open anesthetic circuits rather than closed circuits, a factor which results in higher operating room concentrations of anesthetic gases. Smoking had positive significant effect on frequency of CAs.

Implementation of adequate scavenging system of waste anesthetic gases with securing adequate functionality of air conditioning systems is a must. Regular and proper maintenance of anesthesia machines and anesthetic circuits should be done. Daily checking of the anesthesia machines and their connections; making sure that none is torn or kinked or improperly fitted. Encourage the use of closed systems whenever possible. Periodic measurement of anesthetic gases air levels to ensure keeping them within the safe levels. Periodic and regular full checkup of the health status of operating room personnel (doctors, nurses and workers) and prompt recognition and management of any health problems should be done. Support the implementation of programs for smoking cessation. Enforce the use of personal protective equipments whenever possible as part of occupational health and safety rules.

Further studies are required with personal sampling of anesthetic gases to support our results regarding the relation between exposure to anesthetic gases and health hazards specifically high prevalence of chromosomal aberration and its association with different types of cancer.

Conflict of interests

There were no conflict of interests.

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