Monitoring of Volatile Anesthetics in Operating Room Personnel Using GC-MS

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Abstract

Objective: To estimate individual occupational exposure of operating room personnel to nitrous oxide, sevoflurane, isoflurane and halothane during regular working hours.

Methods: Volatile anesthetics in urine and breathing area air samples were measured in forty subjects. Passive samplers were collected after continuous five-to-seven hours of exposure. Further, thirty air samples, using passive samplers, were collected from 14 operating rooms of the Jordan University Hospital. All air and urine samples were analyzed using static headspace sampler coupled to capillary column GC-MS system.

Results: The monitored anesthetic volatile agents values of breathing area air samples were as the following (mean ± SEM, ppm): 43.2 ± 6.29, 4.16 ± 2.38, 0.19 ± 0.05 And 0.15 ± 0.10 for nitrous oxide, sevoflurane, isoflurane and halothane, respectively. Whereas, values of the post- shift urine samples (mean ± SEM, µg/l) were: 1234 ± 209, 4.3 ± 0.82, 3.75 ± 0.7 and 9.9 ± 1.2 for nitrous oxide, sevoflurane, isoflurane and halothane, respectively. Concerning operating rooms contaminations, the median and the (range) values for N_2O were 90.4 ppm (12.2 – 327), for sevoflurane they were 16.4 ppm (2.14-53.7), for isoflurane 10.7 ppm (0.41-24.9) and for halothane 0.71 ppm (0.00 8-6.05).

Conclusions: Based on the results of this study, it is obvious that operating rooms personnel were exposed to high level of anesthetic agents and therefore, it is recommended to install efficient scavenging systems inside the operating rooms beside the regular maintenance of anesthetic machines. Moreover, the awareness of operating room personnel should be increased in order to minimize possible health risk.

Abbreviations: MS= Mass Spectrometry; GC= Gas liquid Chromatography; NIOSH= United States Institute for Occupational Safety and Health; JUH: Jordan University Hospital; MeOH= Methanol; ug= microgram; v/v= Volume to volume; SIM; Single Ion Monitoring; ppm= one part per million parts; TWA= Time Weighted Average: r^2 =Correlation coefficient: SEM= Standard Error of the Mean

Keywords: Nitrous oxide, Sevoflurane, Isoflurane, Halothane, Automated GC-MS Headspace.

(J Med J 2008; Vol. 42 (1): 13- 19)

Received	***Accepted***
August 2, 2007	*February 1, 2008*

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Introduction

Inhalational anesthetics are widely used in all over the World in surgical procedures and experimental research. Anesthetic agents, beside its importance in medicine, is posing great source of chemical pollution in hospital operating rooms. The health consequences of chronic environmental exposure to anesthetic vapors by operating room personnel remain controversial. There are considerable epidemiological evidences indicating that nitrous oxide, for example, is associated with congenital malformation, spontaneous abortion and infertility. [1-5] Occupational exposure to significant concentrations of volatile anesthetic may results in headaches and neurobehavioral alterations. [6,7] Further concern that long-term chronic exposure to anesthetic agents may cause immunosuppression and genetic damage [8,9] for operating room personnel. However, except for halothane, which causes liver injury, and its teratogenic effects, at high levels, no clear cause-effect relationship has been reported for chronic exposure to any other anesthetic agent. [10-12]

Due to the increasing health risk because of operating personnel exposure to volatile anesthetic agents, the public health authorities in Western Countries provide occupational exposure recommendations in order to minimize possible health risk. For example, the United States National Institute for Occupational Safety and Health (NIOSH) recommended that an 8-h Time-Weighted Average (TWA) concentrations of N_2O should not exceed 25 ppm, less than 2ppm of any halogenated anesthetic agent if it is used alone, or below 0.5 ppm if the halogenated agent is used in combination with N_2O. [13] Such health regulations are not yet established in many developing countries. For example, in Jordan as for the author's knowledge, no regular monitoring for volatile anesthetic agents is conducted in operating rooms. Thus, the objectives of this study were to assess the extent of occupational exposure of operating rooms personnel at Jordan University Hospital to nitrous oxide, sevoflurane, isoflurane and halothane during routine work.

Methods and Techniques

Site of the study: This study was conducted in operating rooms of Jordan University Hospital (JUH). Three types of environmental and biological samples were collected to assess the level of volatile anesthetic agents.

Operating room air samples: Thirty air samples with an average of two samples per room were collected from the atmosphere of fourteen operating rooms. Air samples were collected during routine operating activities between 9:00 a.m. to 3:00 p.m. and were collected using double-bed passive sampler (Radiello Aquaria, Milan, Italy). After collection, samplers were mounted on stainless steel stands at 150 cm height, and cartridges were immediately transferred into 10ml of H2O: MeOH (60:40) mixture inside a 20-ml headspace glass vial and then sealed with PTFE rubber septum.

Personnel air samples: Operating room personnel signed informed consents in order to donate air and urine samples at the end of their working day. In the morning, and after bladder voiding, each subject was equipped with a double-bed passive sampler that was attached to the coat near the breathing area zone. [14] Air samplers were disassembled and the cartridges were collected. The cartridges were immediately transferred into 10 ml of H2O: MeOH (60:40 v/v) mixture inside a.20-ml headspace glass vial and then sealed with PTFE rubber septum.

Post- shift urine samples: Urine samples were collected from subjects at the end of the day work and 10 ml urine samples were immediately, within 5 min, [14,15] transferred via disposable syringes into a 20-ml headspace vials pre-sealed with a PTFE rubber septum containing 200 µl 9 N H_2SO_4 as antibacterial agent. [14-16] All air and urine samples were stored at -80C° and analyzed within a week of collection.

Chromatographic analysis: Samples were analyzed for anesthetic agents by headspace GC-MS method, using a static head space sampler

coupled to a shimadzu 2010 GC-MS (Tokyo, Japan). A capillary column, HP-Plot Q, 30 m x 0.32 mm ID, 20μm thickness (J and W Scientific, Agilent, Palo Alto, Calif. USA), was used to separate the components of anesthetic agents. Vials of urine and personnel air samples were mixed while heating to 41°C for 120 min.

One ml portions of vial headspace were injected into GC-MS system, while air samples of operating rooms were heated to 62°C for 2 min, and then were analyzed by injecting 1ml of vial head space into GC-MS system. The GC-MS condition for environmental and urine samples are summarized in Table (1).

Table (1): GC-MS-SIM conditions which were used for the analysis of air and urine samples.

GC and MS Parameters:
Carrier gas: helium
Flow rate: 1.2 ml/min
Injection split: 10:1
Oven temperature:
Initial 40°C (2 min), then ramp to 150°C, at rate of 11°C per min, then, column temperature was increased to 194°C within 6 min.
Run time: 22 min
Ion source temperature: 200°C
Interface temperature: 180°C

Anesthetic agent	**Retention time (min)**	**Quantifier ion**
N2O	2.667	44.0
Sevoflurane	17.705	131.0
Isoflurane	18.242	51.0
Halothane	19.317	117.0

Calibration standards: Calibration standards were prepared using compressed N_2O (Int. Ind. Med. Liquid Gas Co. Ltd, Sahab, Amman, Jordan), sevoflurane (Abbott Lab., Queenborought, Kent (UK), isoflurane and halothane (Hikma licensed Crhodia Ltd., UK). Different concentrations of anesthetic agent standards were used exactly as described in the instruction Manual of Radiollo Aquaria, Milan, Italy, edition O2/2003. Two calibration sets of standards were prepared, one for air samples and the other for urine samples. Urine sample standards, in particular, were prepared by spiking known amounts of anesthetic agents with N_2O, sevoflurane, isoflurane, and halothane into pre-sealed vials previously prepared with 10 ml of blank urine containing 200 μl of 9N H_2SO_4. Meanwhile, for personnel and room air samples, calibration standards were prepared by adding an increasing amount of analyts to 20-ml preseald vials which contained a 10 ml of H_2O: MeOH (60:40 v/v) Table (2).

Data analysis: Averages, standard deviations, standard errors and ranges were calculated for values of air and urine samples. Further, the correlation coefficient (r^2) values were derived from the linear regression curve equations.

Results and Discussion

Chromatography of anesthetic agents: A good separation of the anesthetic agents were obtained using the capillary column and temperature program. Table (2) presents the retention times of nitrous oxide, sevoflurane, isoflurane and halothane as follows: 2.67, 17.71, 18.24 and 19.32 min, respectively. Further, good correlation coeffient values were obtained for a wide range of standard curve values that were used in this study. The calibration plots were linear for N_2O, sevoflurane, isoflurane and halothane (Table 2).

Monitoring data of anesthetic volatile agents: Table (3) reports the concentration of anesthetic agents in the atmospheric air of operating rooms. The average ± SEM values of nitrous oxide, sevoflurane, isoflurane and halothane in the fourteen operating rooms were: 90.44 ± 24.43 ppm, 16.38 ± 4.78 ppm, 10.7 ± 2.25 ppm and 0.71 + 0.48 ppm, respectively. The results indicated that Cardiothoracic operating room has the highest N_2O level followed by the Day case operating room, while the least was the Gynecology operating room (Table 3). Generally, the average concentration of nitrous oxide, sevoflurane, isoflurane, and halothane in this study exceeded by many folds the NIOSH recommended exposure limit, 25 ppm for nitrous oxide and 0.5 ppm for anesthetic halogens (Table 3).

Table (4) reports the personnel breathing area values of N_2O, sevoflurane, isoflurane and halothane. The average (ppm) of volatile agents in 40 subjects were: 43.16 ± 6.29, 4.16 ± 2.38, 0.19 ± 0.05 and 0.15 ± 0.1, for N_2O, sevoflurane, isoflurane and halothane, respectively. Again, the average values for both N_2O and sevoflurane exceeded the NIOSH recommended exposure limits.

Table (5) reports the anesthetic agents' values in the post shift urine samples of eighteen subjects. The average (µg/1) for nitrous oxide, sevoflurane, isoflurane and halothane were: 1234 ± 209, 4.3 ± 0.82, 3.75 ± 0.7 and 9.9 ± 1.2, respectively.

The results of this work reveal high levels of N_2O and sevoflurane in most personnel air and post-shift urine samples. These finding are suggesting several sources for contamination that may be attributed to the high levels of anesthetic agents such as: leaks from the circuits of the anesthetic machines that provide nitrous oxide and other halides from the central gas system. This leak if it happened might result in considerable contamination of the operating room. [17] Another important source of contamination is the leak during induction and during maintenance of anesthesia from the patient's airways such as the mouth and the nose. Further source of contamination is the lack of efficient scavenging system as in our case which may contribute considerably to air pollution in operating rooms. Finally, the flow rate of fresh gas which is used during surgery has to be reduced whenever possible especially when anesthesia is maintained with other inhalational agents. [18- 22]

In conclusion, the levels of anesthetic agents found in this study are generally exceeding the international recommended exposure limits which are 25 ppm for nitrous oxide and 0.5 ppm for anesthetic halogens.

Recommendations: Based on the findings of this study, it is pertinent to carry out certain measures in the operating rooms in order to reduce the pollution level of anesthetic agents and to protect room personnel. These measures are:

1- Conducting a routine monitoring of the volatile anesthetic agents from time to time.
2- Installing efficient scavenging systems in all operating rooms.
3- Repairing or replacing all connections of anesthetic machines from time to time.

Acknowledgment: This research was supported by the Deanship of Research, University of Jordan, Grant Number 927, Amman, Jordan. The authors would like to acknowledge the technical assistant of Mr. Osama Al-Yamani for running GC-MS system, and the technical assistant of Mr. Amer Imraish and Wafa Al-Shaer for her skillful secretarial assistance.

Table (2): Typical standard curve concentrations of volatile anesthetic agents which were used in urine or air sample analysis. The proper concentrations of the anesthetic agents were introduced to 20ml head space glass vial presealed with a PTFE rubber septum according to Instruction Manual of Radidiollo Aquaria, edition 02/2003, Milan, Italy.

	Mass of anesthetic agents introduced to vials (µg)			
Vial Number	***N_2O***	***Sevoflurane***	***Isoflurane***	***Halothane***
0	*0.0*	*0.0*	*0.0*	*0.0*
1	*18.0*	*1.53*	*1.53*	*0.94*
2	*35.9*	*3.06*	*3.06*	*1.87*
3	*71.8*	*7.63*	*7.65*	*4.68*
4	*179*	*15.3*	*15.3*	*9.35*
5	*359*	*30*	*30.6*	*18.7*
	Values of Correlation Coeffient (r^2)			
Urine:	*0.9091*	*0.959*	*0.975*	*0.9819*
Air:	*0.9998*	*0.993*	*0.9942*	*0.9942*

Table (3): Average values of anesthetic agents (ppm) of duplicate air samples which were collected from 14 operating rooms at University of Jordan Hospital.

Operating room	*Level of N_2O (ppm)*	*Level of Sevoflurane (ppm)*	*Level of Isoflurane (ppm)*	*Level of Halothane (ppm)*
Urology	*12.2*	*9.11*	*0.41*	*0.008*
Orthopaedics	*41.4*	*3.73*	*9.87*	*0.059*
General Sugery(1)	*38.6*	*2.57*	*11.40*	*0.031*
General Sugery(2)	*27.8*	*11.40*	*14.50*	*0.104*
Gyneacology(1)	*75.3*	*17.90*	*1.66*	*0.408*
Gyneacology (2)	*58.1*	*40.60*	*1.33*	*0.300*
Cardiothoracic	*327*	*12.70*	*13.50*	*0.050*
Plastic Surgery	*43.8*	*2.14*	*18.40*	*0.110*
Paediatrics Sugery	*37.5*	*9.95*	*0.71*	*6.050*
Neuro- Surgery	*25.4*	*7.01*	*7.74*	*0.230*
ENT	*211*	*53.70*	*3.81*	*0.460*
Ophthamology(1)	*131*	*5.20*	*24.90*	*0.000*
Ophthamology(2)	*187*	*3.56*	*21.00*	*0.000*
Day- case Surgery	*50.6*	*49.80*	*20.30*	*0.000*
Average	***90.4***	***16.4***	***10.7***	***0.71***
Standard Deviation	***91.4***	***17.9***	***8.42***	***1.78***
SEM	***24.43***	***4.78***	***2.25***	***0.84***
Range	***12.2-327***	***2.14-53.7***	***0.41-24.9***	***0.008-6.050***

Table (4): Values of personnel breathing zone samples of forty subjects as monitor by the headspace GC-MS (total ion current) technique.

Parameter	**Nitrous oxide (ppm)**	**Sevoflurane (ppm)**	**Isoflurane (ppm)**	**Halothane (ppm)**
Mean	43.16	4.16	0.19	0.15
SD	39.27	14.86	0.28	0.56
SE	6.29	2.38	0.045	0.104
Range	0.00-135.99	0.02-73.07	0.00-1.28	0.00-3.89

Table (5): Values of post-shift urine samples of 18 subjects as monitored by the headspace GC-MS. Total ion current mode was used to quantitate for N_2O levels, while single ion monitoring (SIM) technique was used in the quantitation of sevoflurane, isoflurane and halothane.

Parameter	*Nitrous oxide (µg/l)*	*Sevoflurane (µg/l)*	*Isoflurane (µg/l)*	*Halothane (µg/l)*
Mean	*1234*	*4.3*	*3.75*	*9.9*
SD	*836*	*5.0*	*4.3*	*7.0*
SE	*209*	*0.82*	*0.7*	*1.2*
Range	*247-3182*	*0.0-30.0*	*0.0-20*	*1.0-35*

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قياس مستوى أدوية التخدير في الطاقم الطبي العامل في غرف العمليات بواسطة جهاز مقياس الكتلة والغاز الكروماتوغراف

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الملخص

الهدف: إن الهدف من هذا البحث هو قياس مدى تعرض بعض أفراد الطاقم الطبي (الجراحين، المخدرين، الممرضين، الفنيين...) لأدوية التخدير المستخدمة في غرف العمليات في مستشفى الجامعة الأردنية خلال العمل الروتيني.

فقد تم قياس مدى التعرض لأدوية اكسيد النيتروجين، سيفو فلورين، أيزو فلورين، الهالوثين في عينات الزفيركذلك تم قياس هذه الأدوية في عينات بول نفس الأشخاص، كذلك تم جمع عينات هواء من 14 غرفة عمليات مختلفة في مستشفى الجامعة الأردنية ما بين الساعة الثامنة صباحا حتى الساعة الثالثة بعد الظهر. و قد استخدم في تحليل هذه العينات جهاز مقياس الكتلة المتصل بجهاز الغاز الكروموتوغراف.

النتائج: ظهر في نتائج تحليل العينات أن مستوى أدوية التخدير المستخدمة في غرف العمليات كان عالياً جدا و يزيد في غالبيته عن الحد المسموح به وكانت نتائج التحليل أكبر من مثيلاتها في الدول المتقدمة

يعزى ارتفاع قيم هذه المواد في عينات البول و الهواء إلى أمور مختلفة وإن هذه التركيزات العالية لأدوية التخديرقد تؤثر سلبيا على صحة الطاقم الطبي إذا استمر تعرض العاملين لهذه الأدوية لفترات زمنية طويلة نسبيا.

الخلاصة: يوصي الباحثون بالآتي:

1- قياس أدوية التخدير في غرف العمليات بين الحين و الآخر و على فترات زمنية قصيرة نسبيا.

2- تركيب أجهزة إدمصاص (فلترات) عالية الكفاءة في غرف العمليات لتقلل من مدى تعرض الطاقم الطبي لهذه الأدوية.

3- صيانة أجهزة التخدير و كذلك استبدال البرابيش من حين لآخر.

الكلمات الدالة: أكسيد النيتروجين، سيفو فلورين، أيزو فلورين، الهالوثين، جهاز مقياس الكتلة المتصل بجهاز الغاز الكروموتوغراف.