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POTENTIAL HEALTH EFFECTS WITHIN OCCUPATIONAL EXPOSURE TO ANESTHETICS OF HEALTH CARE WORKERS

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Abstract. Aim. To assess respiratory system response in long time low-level occupational exposure to anesthetics (AE) and to identify appropriate prophylactic measures. **Materials and Methods**. Cross-section study on 128 health care workers occupationally exposed to AE (halothane, enflurane, isoflurane) *vs* matched controls. GC exposure evaluation, clinical examination, immunochemistry, respiratory function tests and oxidative stress markers (SOD, TBARS) were performed. To assess the possible effect of AE on the immune function, peripheral lymphocyte subpopulations, NK cells percentage and NK cytotoxic activity were determined in a subgroup (n=33). **Results**. AE concentrations in workplaces air were under but close to TLV. Irritative respiratory symptoms prevailed. Discrete distal obstructions were found in 45.3% of workers *vs* 22.8% in controls (χ^2=10.1, p<0.01, OR=2.7, CI:1.4-5.2). SOD and TBARS were significantly higher in exposed (p<0.01). Serum immunoglobulins changes suggested alteration of the humoral immune response. The anaesthesiologist subgroup had a slightly reduced percentage of specific cytotoxicity (12.34%) versus exposed (16.06%). **Conclusions**. It seems that under TLV occupational exposure to anaesthetic gases could interfere with defence mechanisms. Further research could sustain the reconsideration of exposure standards - a suitable prophylactic approach.
Key words: respiratory health effects, occupational exposure, anesthetics, exposure standards

Rezumat. Scop. Evaluarea răspunsului aparatului respirator în expunerea ocupațională la anestezice (AE) de nivele reduse, pe termen lung şi identificarea măsurilor profilactice potrivite. **Material si metodă**. Studiu transversal pe 128 subiecți – personal medical expus ocupațional la AE (halotan, enfluran, izofluran) *vs* martori adecvați. S-au realizat: evaluarea expunerii prin gaz-cromatografie, examen clinic, probe funcționale ventilatorii, teste imunochimice şi martori de stres oxidativ (superoxid dismutaza, radicali liberi). Pentru a evalua posibilul efect al AE asupra funcției imune, s-au determinat, în cadrul unui subgrup (n=33), subpopulațiile limfocitare periferice, procentajul şi activitatea citotoxică a limfocitelor NK. **Rezultate**. Concentrațiile AE în aerul locurilor de muncă au atins nivele apropiate de limitele admisibile, fără însă a le depăşi. Examenul clinic a arătat că simptomele iritative respiratorii au fost cele mai frecvente. S-au găsit obstrucții ventilatorii distale discrete la 45,3% dintre persoanele expuse din personalul medical față de 22,8% la lotul martor (χ2=10,1, p<0.01, OR=2,7, CI95%=1,4-5,2). Superoxid dismutaza şi radicalii liberi au fost semnificativ mai mari la lotul expus (p<0,05). Modificările imunoglobulinelor serice au sugerat modificarea răspunsului umoral imun. Subgrupul de anesteziști a avut procentaje uşor

mai mici ale citotoxicității specifice (12,34%) față de lotul expus (16,06%). **Concluzii**. Se pare că expunerea ocupațională la gaze anestezice, chiar la nivele sub limitele admisibile, poate interfera cu mecanismele de apărare. Studii suplimentare viitoare ar putea motiva necesitatea reconsiderării standardelor de expunere. Este o abordare profilactică ce poate fi considerată ca adecvată în această situație.
Cuvinte cheie: efecte respiratorii, expunere ocupațională, anestezice, standarde de expunere

INTRODUCTION

Some data in scientific literature pointed out possibility that occupational exposure to anesthetics (AE) could interfere with health status of the involved health care workers (1, 3, 5, 12, 16).

The aim of the study was to assess respiratory system response in long-term low-level occupational exposure to volatile AE and to identify appropriate prophylactic measures (14).

The study hypothesis states that long-term low-level occupational exposure to frequently used volatile AE for general anesthesia during surgery could impair the health status of health care workers.

An epidemiological study on 128 health care workers (anesthesiology personnel and surgeons) occupationally exposed to volatile AE (halothane, enflurane, isoflurane) *vs* 87 matched controls was performed.

The exposed personnel and the controls were comparable concerning age (38.6 *vs* 37.7 years) and length of service (12.3 *vs* 11.9 years) homogeneity and distribution. Both lots were also comparable for other potential confounding factors (smoking, drug and alcohol consumption, dietary habits, extra-occupational exposure to irritative substances). In both lots people have jobs with similar physical solicitation; they live in the same town, in similar environments.

MATERIALS AND METHODS

Considering the relevant data in literature, exposure evaluation of volatile AE (halothane, enflurane, isoflurane) has been done by GC in the air of each specific workplace (operating rooms, intensive care units) in order to quantify as well as possible the exposure for every workplace (6, 8, 13, 15). Microclimate measurements were aimed to better assess the AE potential absorption degree.

The detailed investigation of health status comprised careful occupational and medical anamnesis, clinical examination, biochemical and immuno-chemical investigations (immunoglobulins A, G, E, and M), respiratory function tests. In order to test the genotoxic potential of AE occupational exposure we performed a cytogenetic investigation: micronuclei (MN) test in oral mucosa exfoliated cells (4, 9).

Oxidative stress markers have also been done: whole blood superoxide dismutase (SOD) and Thiobarbituric Acid Reactive Substances (TBARS) (7).

To assess the possible effect of AE on the immune function, peripheral lymphocyte subpopulations, NK cells percentage and NK cytotoxic activity were determined in a subgroup (n = 33 anesthesiologists) (11).

RESULTS

Exposure evaluation of AE revealed that concentrations in workplaces air were under but close to TLV (fig. 1).

The investigation of microclimate revealed conditions (especially high temperatures and low ventilation efficiency) which could facilitate the respiratory absorption.

The health status investigation revealed irritative respiratory symptoms, allergic conditions (dermatitis, rhinitis, laryngitis, asthma, conjunctivitis), cardiovascular changes, including arterial hypertension and EKG changes (arrhythmias, conduction disturbances, ischemia), arthropathies and musculoskeletal disorders, digestive apparatus disorders (chronic hepatitis, duodenal and gastric ulcers, cholecystitis).

Prevalences are shown in figure 2.

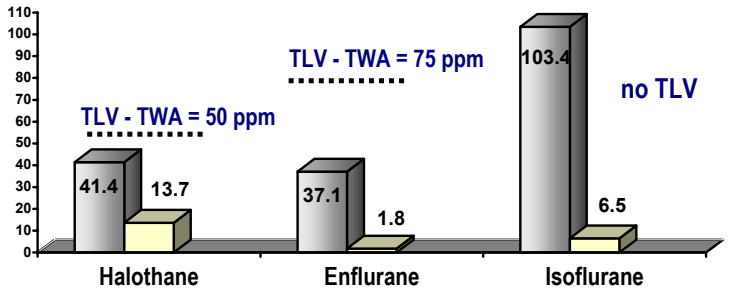


Fig.1. Measured concentrations of volatile anesthetics (ppm)

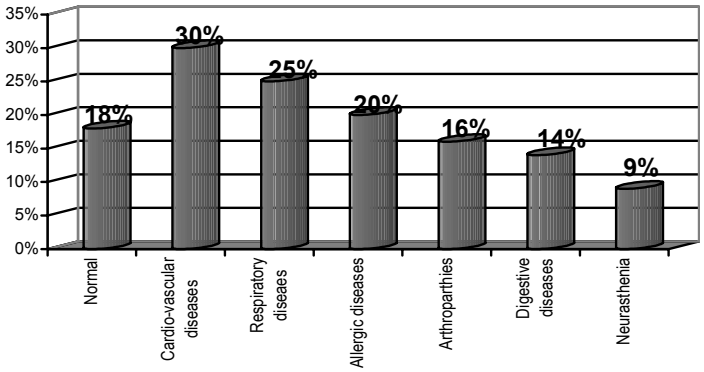


Fig. 2. The prevalence of clinical entities (%)

From clinical point of view we found that irritative respiratory symptoms prevailed in exposed health care workers (33.6%), with a significant difference versus controls (Yates' chi square = 8.41, p=0.0037, OR=2.88, 95% CI: 1.37-6.13). We also found rather frequent headaches, dizziness and nausea.

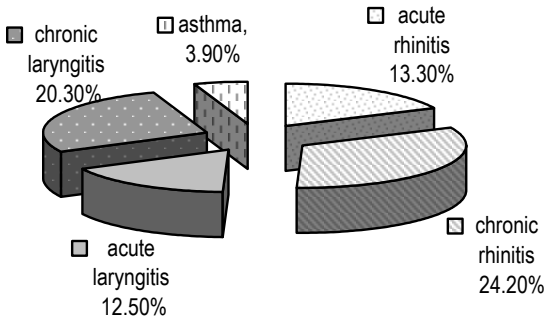


Fig. 3. The distribution of respiratory clinical entities

Considering the respiratory clinical entities (25.8% in exposed, *vs* 13.8% in controls - Yates' chi square = 3.8, p=0.05, OR=2.17, 95% CI: 1.00-4.80), we found acute rhinitis, chronic rhinitis, acute and chronic laryngitis, acute and chronic bronchitis and even asthma (fig. 3).

Spirometric investigations revealed that 52.34% of the exposed versus 28.74% of the controls had obstructive dysfunction (Yates' chi square = 10.85, p = 0.0009, OR = 2.72, 95% CI: 1.47-5.08).

Discrete distal obstructions were found in 45.3% of workers *vs* 22.8% in controls (Yates' chi square =10.1, p=0.0013, OR=2.7, 95%CI: 1.4-5.2). The distribution of obstructive dysfunction is shown in table 1.

We have found a medium correlation (R = 0.44, p = 0.001) between the obstructive syndromes and the presence of the respiratory irritative symptoms. Also a slight correlation (R = 0.38, p=0.016) was found between the obstructive syndromes and the intensity of occupational exposure (fig. 4).

Table 1. Obstructive syndromes in exposed *versus* controls

	Normal subjects	Obstructions			
		Total obstructions	Distal Obstructive Syndrome FEV1 > 80% FEV1/VC > 80% FEF25-75%,MEF50%, MEF25%, PEF, MEF75%, < 80%	Slight obstructions FEV1 < 80% FEV1/VC < 80%	Moderate and severe obstructions FEV1< 55%
Exposed workers	61	67 52.34%	58 45.31%	7 5.47%	2 1.56%
Controls	62	25 28.74%	20 22.89%	5 5.74%	0 0%
Significance of difference		p=0.0013	p=0.0006	p=0.46	p=0.12

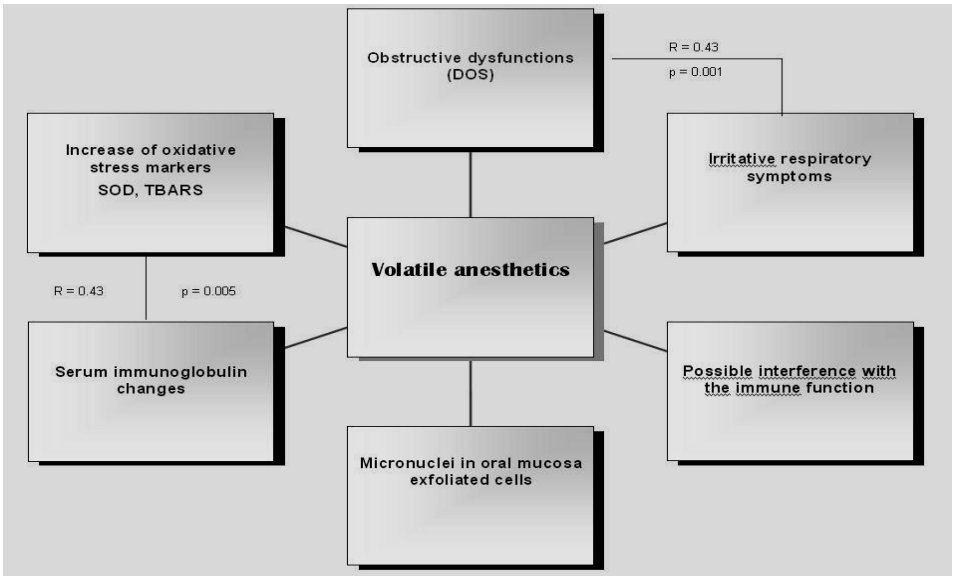


Fig. 4. Main findings in the occupational exposure to volatile anaesthetics.

Abnormal high immunoglobulins values were found in exposed as follow (fig. 5):

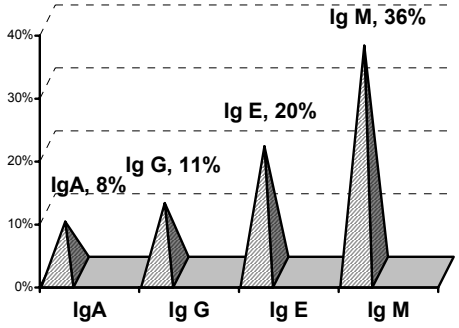


Fig. 5. Abnormal high immunoglobulins in exposed

The differences *vs* control were significant for IgE and IgM ($p<0.05$)
Ig A level correlated with Ig M and Ig G ($r=0.34$, $p=0.001$, $r=0.31$, $p=0.003$).
Serum immunoglobulins changes suggested an alteration of the humoral immune response.
The blood oxidative balance was affected as shown by raised SOD activity in 55.2 % of exposed versus 10.1 % in controls and TBARS serum level raised above the upper reference limit in 83.1 % of exposed compared to 11.5 % in controls (fig. 6).
SOD and TBARS were also significantly higher in exposed (t test = 2.9, $p=0.004$, respectively $t=3.3$, $p=0.001$) and slightly correlated with intensity of exposure ($R = 0.30$, $p= .051$).

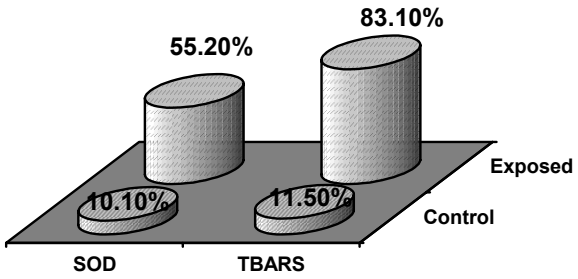
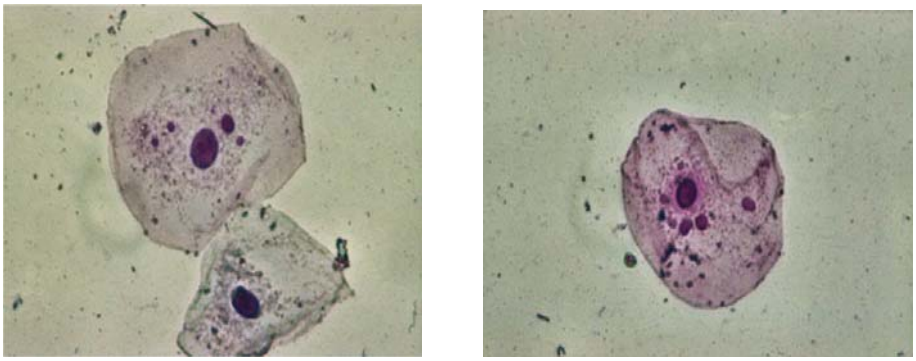


Fig. 6. Oxidative stress markers in exposed *vs* control

The cytogenetical investigation has shown that micronuclei (MN) in oral mucosa exfoliated cells were more frequent in exposed (9.4% *vs* 2.3%, chi square = 4.26, p=0.04, OR=4.4 95%CI: 0.9 - 29.2)- see figure 7 (a, b).



(a) **(b)**

Fig. 7. MN in oral mucosa

The assessment of the immune function by studying the NK peripheral lymphocites (numerical and cytotoxic aspects) revealed the following results:

- there were no significant differences concerning NK cells number in AE exposed personnel versus control;
- the percentage of specific cytotoxicity was slightly reduced in AE exposed personnel (12.34%) versus exposed (16.06%).

CONCLUSIONS

- Some of the multifactorial diseases found in health care workers could have a pathogenic connection with the specific stress, overstressing workloads and long time shifts. So these health disorders could be considered as occupational conditioned diseases and the working conditions could influence their evolution.
- It seems that under TLV occupational exposure to anaesthetic gases could interfere with defence mechanisms.
- We found frequent irritative respiratory symptoms associated with obstructive dysfunction (mainly distal obstructive syndrome), with serum immunoglobulins changes that suggested an alteration of the humoral immune response, and also associated with an increase of oxidative stress markers. These data correlate with some findings of other researchers.
- The assessment of the possible effect of AE on the immune function suggests that anesthetic gases could interfere with the immune function of the occupationally exposed subjects.
- Our findings seems to support the necessity of closely survey the immune status of exposed anesthetists,

as well as the other biological modified parameters in order to completely understand their underlying action mechanisms.

- Further research could sustain the reconsideration of exposure standards, which seems to be a suitable prophylactic approach, especially considering some other European and international recommendations (2, 17).

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