

Formaldehyde-related clinical symptoms reported by medical students during gross anatomy cadaver dissection

Subiektywne objawy kliniczne u studentów medycyny związane z ekspozycją na formaldehyd podczas zajęć prosektoryjnych z anatomii

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ABSTRACT

Introduction. Formaldehyde is a noxious gas used as a tissue preservative of cadavers in autopsy rooms. Therefore, exposure to higher concentrations applies particularly to laboratory staff, anatomists and medical students. Prolonged exposure to formaldehyde is associated with clinical complications.

Objective. To assess whether exposure to repeated inhalation of low concentrations of formaldehyde (FA) experienced during a gross anatomy course triggers subjective clinical symptoms in medical students.

Material and methods. All 198 first-year medical students of the Medical University of Lublin, Poland (28% with allergy history and 72% without allergy history; 69% male and 31% female) responded to a questionnaire concerning their subjective FA-related clinical symptoms. Differences in proportions of experienced symptoms between allergic vs. nonallergic, and female vs. males were compared by the Mann-Whitney *U* test.

Results. Even though formaldehyde concentrations in the gross anatomy laboratory were relatively low (0.47–0.57 mg/m³), medical students experienced various reactions (lacrimation in 85.9%, red eyes, dry and itchy eyes, runny nose, sneezing, and headache in > 50% of students, cough in 44%, and dry throat or throat irritation in 42% of students). Among students with a history of allergy, eye, nose, skin and respiratory system symptoms occurred more frequently in comparison to nonallergic students. Female individuals demonstrated higher sensitivity to FA exposure.

Conclusions. Exposure to formaldehyde may result in development of clinical symptoms in medical students. Particularly unpleasant symptoms may be experienced by individuals with allergy history. It is necessary to decrease formaldehyde concentrations in the anatomy dissection laboratory.

STRESZCZENIE

Wprowadzenie. Formaldehyd to szkodliwa substancja chemiczna, której wodny roztwór jest powszechnie stosowany jako środek konserwujący w prosektoriach anatomicznych. Osobami szczególnie narażonymi na ekspozycję na formaldehyd są studenci medycyny oraz per-

sonel laboratoryjny. Długotrwała ekspozycja na formaldehyd często wiąże się z pojawieniem się różnorodnych objawów klinicznych.

Cel pracy. Ocena subiektywnych objawów klinicznych u studentów medycyny, którzy byli narażeni na wdychanie formaldehydu w niskim stężeniu podczas kursu anatomii.

Materiał i metodyka. Stu dziewięćdziesięciu ośmiu studentów pierwszego roku medycyny (28% z alergią w wywiadzie i 72% bez historii alergii; 69% mężczyzn i 31% kobiet) uczestniczyło w badaniu przeprowadzonym za pomocą ankiety dotyczącej subiektywnych objawów klinicznych związanych z ekspozycją na formaldehyd. Analiza różnic w częstości występowania objawów klinicznych pomiędzy alergikami i osobami bez alergii oraz pomiędzy mężczyznami i kobietami została przeprowadzona przy użyciu testu *U* Manna-Whitneya.

Wyniki. Pomimo niskiego stężenia formaldehydu w salach prosektoryjnych (0,47–0,57 mg/m³) studenci medycyny doświadczali różnorodnych objawów klinicznych. Łzawienie obserwowano u 85,9% studentów, zaczerwienienie oczu, suchość i swędzenie oczu, katar, kichanie i ból głowy u ponad 50% studentów, natomiast kaszel oraz suchość lub podrażnienie gardła u odpowiednio 44% i 42% studentów. U studentów z alergią w wywiadzie częściej występowały objawy dotyczące oczu, nosa, skóry i układu oddechowego w porównaniu ze studentami bez alergii. U kobiet stwierdzono większą wrażliwość na ekspozycję na formaldehyd w porównaniu z mężczyznami.

Wnioski. Ekspozycja na formaldehyd może spowodować u studentów medycyny rozwój objawów klinicznych. Szczególnie nieprzyjemnych objawów mogą doświadczać osoby z alergią w wywiadzie. W celu zmniejszenia działań niepożądanych formaldehydu konieczne jest zmniejszenie jego stężenia w prosektoriami anatomicznych.

INTRODUCTION

Formaldehyde (formalin, FA) is a noxious, flammable gas which was discovered in 1856 by August Wilheld Von Hofmann [1]. Since then, formalin has been used in many branches of industry (chemical, textile, cosmetic, wood). Formaldehyde may be present in a variety of ordinary consumer goods and emitted from many products, e.g. building materials, resins, glues, fiberboard, paper, fabrics, and household cleaning products [2]. Prolonged exposure to formaldehyde is commonly associated with both allergic and non-allergic systemic complications [3]. Formaldehyde toxicity is related to mucosa irritation, particularly to the eyes and to the upper respiratory tract [4, 5]. Acute clinical symptoms include headache, dermatitis, and asthma [6]. In sensitive individuals, acute symptoms can be observed at a very low concentration of FA (0.012 mg/m³). Exposure to concentrations of about 1 ppm (1.23 mg/m³) can cause watering of the eyes and irritation of the upper respiratory passages (e.g. a cough). Higher levels (10–20 ppm; 12.5–25 mg/m³) may induce tightening in the chest, a sense of pressure in the head, and pal-

pitations [2]. Formalin is commonly used in some medical branches and research, e.g., as a tissue preservative of cadavers in autopsy rooms. Therefore, exposure to higher concentrations applies mainly to laboratory staff, anatomists and paramedical workers [7, 8]. The process of embalming in a mixture of formalin, fixatives, preservatives, germicides, buffers, wetting agents, anticoagulants, dyes, and perfuming agents aims to stop decomposition of cadavers and help to maintain proper anatomical conditions [9].

The gross anatomy course is the core course during preclinical training in medical universities worldwide [10]. The course program includes fresh cadaver dissections or prosections [11, 12]. During these dissection classes, medical and dental students are exposed to formaldehyde vapors emitted from cadavers [3, 4]. Inhalation is considered to be the primary route of exposure; however, the area of formalin absorbance includes the lungs, gastrointestinal tract, and skin [13, 14]. Several reports have evidenced that formalin inhibits learning and hinders memory abilities in mice [15, 16]. A relationship between formaldehyde inhalation and increased incidence of nasal squamous cell carcinomas in animals (rats and

B6C3F1 mice) has been revealed [17]. Although humans and animals may differ in their susceptibility to specific cancer-causing agents, the International Agency for Research on Cancer classified formaldehyde as a group 1 human carcinogen [2, 18]. The genotoxic and mutagenic abilities of formaldehyde are probably related to the formation of DNA-protein crosslinks (DPC) in target tissues [19]. Formation of DPC in the nasal respiratory mucosa due to chronic inhalation of formaldehyde has been evidenced [20]. Epidemiological studies revealed evidence for the carcinogenicity of formalin and reported that industrial workers who are exposed to formaldehyde or formaldehyde-containing products are at increased risk of nasopharyngeal and hypopharyngeal cancers [17, 21, 22]. However, there was no association with the highest formaldehyde exposure and lung cancer or leukemia [23, 24].

OBJECTIVE

The aim of the study was to assess whether exposure to repeated inhalation of a low level of FA experienced during a gross anatomy course triggers subjective clinical symptoms in medical students.

MATERIAL AND METHODS

The study was performed in the Department of Human Anatomy, Medical University of Lublin, Poland. The study population consisted of the first-year medical students, the participants of a gross anatomy course with cadaver dissection as part of the laboratory classes. Laboratory rooms measured 5.5 × 7.2 × 3.5 m and had one door and two windows. Each anatomy dissection room had general ventilation and was equipped with one stainless steel dissecting work table. All anatomy dissection rooms fulfilled the requirements of the National Labor Inspectorate. Atmospheric formaldehyde concentration levels, detected by high-performance liquid chromatography, were 0.47–0.57 mg/m³, i.e. within the range of indoor air limit values for FA emissions in Poland set by the Ministry of Labor and Social Policy (Regulation from 29 November 2002; Dz. U. Nr 217, poz. 1833).

In total, 198 first-year medical students completed the questionnaire survey. Among all participants, 69 were male and 129 female, with the age range 19–22 years. The mean duration of formalin exposure was 4 h per week during the course lasting for 30 weeks (15 weeks in fall and 15 weeks in the spring semester).

The questionnaire was distributed after the objective structured examination in anatomy (OSEA) at the end of the gross anatomy course in June 2015. Before the investigations, each participant was in-

formed about the aim of the study and agreed to answer the questionnaire completely anonymously. A three-section questionnaire was developed. The first section included questions about demographic factors and allergy history. The second part consisted of questions related to 24 subjective allergy symptoms experienced after the gross anatomy course. We evaluated the symptoms relating to: (i) eyes: redness, dryness and itching, excessive lacrimation, deterioration in eyesight; (ii) nose: runny nose, nose bleeding, sneezing, alterations in odor perception; (iii) respiratory system: dry throat and throat irritation, cough, respiratory distress; (iv) digestive system: nausea, vomiting, lack of appetite, GI disturbances, increased appetite, excessive salivation; (v) nervous system: headache, prolonged sleeping time, decreased perception; (vi) skin: rash, dryness and itching, redness; and (vii) general symptom: fatigability. The symptoms were assessed using a 5-point Likert scale (1 = poor, 2 = below moderate, 3 = moderate, 4 = above moderate, 5 = strong). The third section evaluated the influence of formalin on learning and memory processes and included four multiple choice questions with three possible options.

Statistical analysis

For statistical purposes, the study population was divided (i) by allergy history (with allergy history vs. without allergy history), and (ii) by sex (male vs. female). Differences between groups of respondents were analyzed using the Mann-Whitney *U* test. Differences of *p* less than 0.05 were considered to be significant. Statistical analysis was performed using SPSS version 16.0 (SPSS, Inc., Chicago, IL, USA).

RESULTS

The characteristics of the study group are shown in Table 1. All 198 students responded to the questionnaires. The mean age of respondents was 20.40 ± 1.46 years; the majority were female (*n* = 129). There were no significant differences in mean age between males and females. Fifty-six (28.3%) students reported an allergy history, including 28 (14.1%) with hay fever, 16 (8.1%) with alimentary allergy and 11 (5.6%) with atopic dermatitis.

All the students reported the smell of formaldehyde in the anatomy dissection room. Most of the respondents (80%) found the moderate unpleasant odor of FA not affecting the class performance and students' achievements. Irrespective of the study group, the students stated that these symptoms did not occur in other buildings of the campus.

Excessive lacrimation (170; 85.9%) after exposure to FA in the anatomy dissection room was the most frequently reported. Red, dry and itchy eyes, run-

Table 1. Characteristics of the study group and the type of allergy symptoms reported by students with an allergy history*Tabela 1.* Charakterystyka grupy badanej i typy objawów alergicznych u studentów medycyny z alergią w wywiadzie

Parameter	Total population (N = 198)	Male (N = 69)	Female (N = 129)
Age, mean ± SD [years]	20.40 ± 1.46	20.33 ± 1.75	20.43 ± 1.29
Students with allergy history, n (%)	56 (28.3)	12 (17.4)	44 (34.1)
Type of allergy symptoms, n (%):			
Hay fever	28 (14.1)	7 (10.1)	21 (16.3)
Alimentary allergy	16 (8.1)	3 (4.3)	13 (10.1)
Atopic dermatitis	11 (5.6)	1 (1.4)	10 (7.8)
Allergic conjunctivitis	10 (5.1)	0 (0.0)	10 (7.8)
Bronchial asthma	6 (3.0)	1 (1.4)	5 (3.9)
Hives	3 (1.5)	0 (0.0)	3 (2.3)

ny nose, sneezing, and headache were commonly noted subjective symptoms (in > 50% of students). Among respiratory system related symptoms, cough (44%) and dry throat or throat irritation (42%) were frequently present. Digestive system symptoms were experienced only by 6.6% (vomiting) to 23% (increased appetite) of participants. Skin problems were experienced by < 20% of students. Only a few students (13; 6.6%) complained of nose bleeding.

Students with allergy history revealed significantly higher occurrence of a runny nose and sneezing in comparison to students without allergy history; allergic vs. nonallergic – 66.1% vs. 51.4% for a runny nose; 67.9% vs. 50.0% for sneezing (Fig. 1).

The subjective reactions to FA were primarily below moderate to moderate severity; however, students with allergy history reported more intensive symptoms related to eyes, nose, respiratory system, and skin compared to students without allergy history (Table 2).

No significant differences in the frequency of reported subjective clinical symptoms were observed between females and males, but symptoms related to eyes, nose and the digestive tract reported by females were more severe (Table 3).

DISCUSSION

In Poland, new teaching methods, e.g. medical simulation and problem-based learning, have been implemented into gross anatomy courses [10, 11]. However, the traditional methodology of anatomy teaching, including cadaveric dissections or prosecutions, remains an integral part of the curriculum, and both medical and dental students cannot proceed to the next step of their education without this practice [9]. During the gross anatomy course, our students

are subjected to repeated inhalation of formaldehyde. Although the atmospheric formaldehyde concentration levels were within the range of indoor air limit values accepted in Polish law, our students experienced various clinical symptoms after the exposure to FA. The most common undesirable effects were related to the eyes (irritation, lacrimation) and nose (a runny nose). This observation is in agreement with many other studies revealing that exposure of medical students to FA provoked eye irritation and resulted in itching, burning, soreness, pain, or conjunctivitis [4, 9, 13]. For example, Lang *et al.* found that FA increased nasal problems similar to that experienced by our students (dryness, bleeding) [25]. Akbar-Khanzadeh and Mlynek found a predominance of the eye irritation (in 82% of students) and nose problems (in 76% of students) [26]. Usually eye and nasal irritation did not occur in parallel because the eyes are more sensitive; moreover, the experienced symptoms to some extent depended on individual sensitivity to chemicals/toxicants [25].

Formaldehyde is soluble in water; therefore it is rapidly absorbed in the respiratory and gastrointestinal tracts [6]. Low-level FA exposure resulted in the development of respiratory symptoms in 30–50% of our students. Throat dryness and upper respiratory tract problems were also reported by Onyije and Avwioro [9]. Wantke *et al.* [27] and Norbäck *et al.* [28] evidenced such symptoms in 45–50% of people. Digestive system problems including vomiting have also been experienced by our students. Exposure to formaldehyde and prolonged contact with FA may result in different gastrointestinal symptoms; even hemorrhage and ulceration of the digestive tract have been observed [2, 3].

In our study group, FA adverse effects on the skin were experienced to a lesser extent, which was pre-

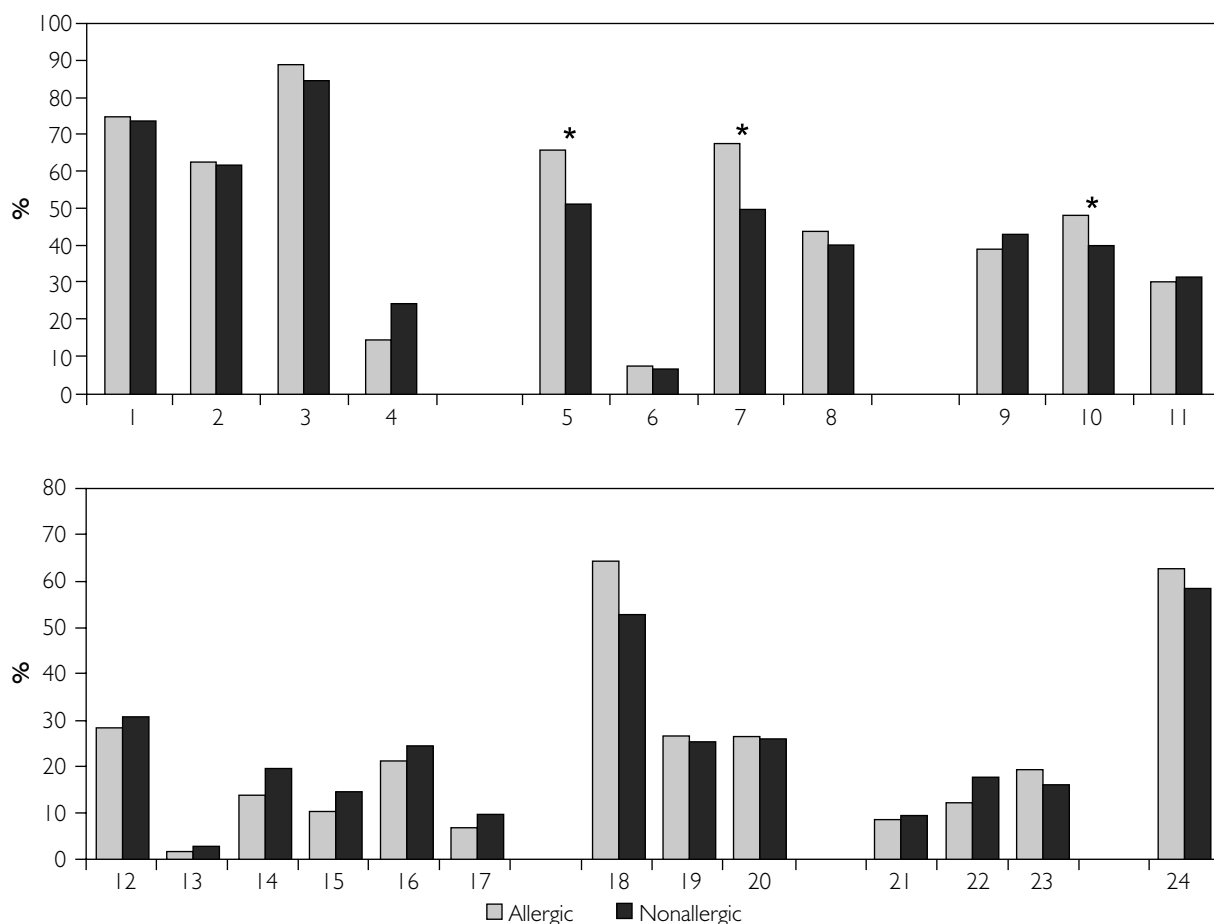


Figure 1. Percentages of allergic and nonallergic students reporting subjective clinical symptoms after exposure to formaldehyde. Clinical symptoms related to the eyes: 1 – redness, 2 – dryness and itching, 3 – excessive lacrimation, 4 – deterioration in eyesight; clinical symptoms related to the nose: 5 – runny nose, 6 – nose bleeding, 7 – sneezing, 8 – alterations in odor perception; clinical symptoms related to the respiratory system: 9 – dry throat and throat irritation, 10 – cough, 11 – respiratory distress; clinical symptoms related to the digestive system: 12 – nausea, 13 – vomiting, 14 – lack of appetite, 15 – GI disturbances, 16 – increased appetite, 17 – excessive salivation; clinical symptoms related to the nervous system: 18 – headache, 19 – prolonged sleeping time, 20 – decreased perception; clinical symptoms related to the skin: 21 – rash, 22 – dryness and itching, 23 – redness; general symptom: 24 – fatigability. *Statistically significant difference between allergic and nonallergic students by Mann-Whitney U test, $p < 0.05$

Rycina 1. Odsetek studentów medycyny z alergią oraz bez alergii w wywiadzie zgłaszających subiektywne objawy kliniczne po ekspozycji na formalinę. Objawy kliniczne dotyczące oczu: 1 – zaczerwienienie, 2 – suchość i świąd, 3 – wzmożone łzawienie, 4 – zaburzenia widzenia; objawy kliniczne dotyczące nosa: 5 – katar, 6 – krwawienie, 7 – kichanie, 8 – zaburzenia węchu; objawy kliniczne dotyczące układu oddechowego: 9 – suchość i podrażnienie gardła, 10 – kaszel, 11 – zaburzenia oddychania; objawy kliniczne dotyczące układu pokarmowego: 12 – nudności, 13 – wymioty, 14 – brak apetytu, 15 – zaburzenia trawienia, 16 – wzmożony apetyt, 17 – zwiększone wydzielanie śliny; objawy kliniczne dotyczące układu nerwowego: 18 – ból głowy, 19 – wzmożona senność, 20 – obniżona percepcja; objawy kliniczne dotyczące skóry: 21 – wysypka, 22 – suchość i świąd, 23 – zaczerwienienie; objawy ogólne: 24 – zmęczenie. *Statystycznie istotne różnice pomiędzy studentami medycyny z alergią i bez alergii w wywiadzie w teście U Manna-Whitneya, $p < 0,05$

sumably related to use of protective gloves, a common practice during contact with cadavers. In the literature, severe irritant effects of FA to the skin were reported, but after direct contact with formaldehyde containing liquids [3, 4]. Skin irritation reported by some of our students may be related to a systemic allergic reaction, as most severe skin problems were reported by allergic students.

The students with allergy history reported more severe symptoms (compared to nonallergic students) related to eyes, nose, respiratory system, and skin. Allergic people are more sensitive to toxic substanc-

es than nonallergic people; therefore they may be less able to tolerate even low formaldehyde concentrations and as a result of a lower sensitivity threshold develop symptoms more quickly. In allergic people, there is a risk of development of allergic sensitization to inhalant allergens, and symptoms commonly occur [29]. This may explain the more severe reaction of allergenic students in the form of nose and respiratory system related symptoms after FA inhalation, the main route of its exposure [30]. However, it is still unclear whether sensitization and FA-related symptoms are induced by formaldehyde-specific IgE [31,

Table 2. Subjective symptoms of allergic and nonallergic students exposed to formaldehyde (FA) during cadaver dissection (mean values for Likert scale \pm SD)

Tabela 2. Subiektywne objawy u studentów medycyny z alergią i bez alergii w wywiadzie po ekspozycji na formalinę podczas zajęć w prosektorium (wartości skali Likerta podane jako średnia \pm odchylenie standardowe)

Students	Symptoms related to						
	Eyes*	Nose*	Respiratory system*	Digestive system	Nervous system	Skin*	Fatigability
Allergic	3.4 \pm 1.7	2.9 \pm 1.3	3.1 \pm 1.2	2.6 \pm 1.3	2.2 \pm 1.1	2.8 \pm 1.3	2.7 \pm 1.5
Nonallergic	2.6 \pm 1.4	2.1 \pm 1.2	2.0 \pm 1.3	2.5 \pm 1.4	2.0 \pm 1.2	1.9 \pm 1.1	2.5 \pm 1.2

*Statistically significant difference between allergic and nonallergic students by Mann-Whitney U test, $p < 0.05$.

Table 3. Subjective symptoms of male and female students exposed to formaldehyde (FA) during cadaver dissection (mean values for Likert scale \pm SD)

Tabela 3. Subiektywne objawy u studentów medycyny po ekspozycji na formalinę podczas zajęć w prosektorium w zależności od płci (wartości skali Likerta podane jako średnia \pm odchylenie standardowe)

Students	Symptoms related to						
	Eyes*	Nose*	Respiratory system	Digestive system*	Nervous system	Skin	Fatigability
Male	2.1 \pm 1.1	1.9 \pm 1.0	2.2 \pm 1.1	1.9 \pm 1.0	2.3 \pm 1.1	2.6 \pm 1.2	2.8 \pm 1.4
Female	2.7 \pm 1.3	2.6 \pm 1.2	2.0 \pm 1.0	2.5 \pm 1.1	2.2 \pm 1.0	2.4 \pm 1.2	2.6 \pm 1.3

*Statistically significant difference between male and female students by Mann-Whitney U test, $p < 0.05$.

32]. Moreover, the role of other factors in the development of unpleasant symptoms during cadaveric dissection and formaldehyde exposure would not be excluded, for example, airborne allergenic pollen, smoking or stress-induced sensitization, as hypothesized by some authors [28, 33]. In fact, it has been documented that formaldehyde mixed with particles is more aggressive for organs' mucosa [34]. In a few particularly sensitive people, mucosa irritation in particular organs might induce mucosal hypersensitivity to histamine [13]. This mechanism may explain the presence of symptoms in students without allergy history or increased sensitivity of allergic students.

Our study further demonstrates more severe clinical manifestation to FA exposure in females. In general, the prevalence of many autoimmune and inflammatory diseases is higher in females than in males. Higher sensitization in females is associated with more pronounced B cell- and T cell-mediated immunity and stronger antibody responses to various foreign antigens [35, 36].

Unpleasant effects related to formaldehyde smell and FA-related symptoms did not discourage our students from coming to the dissecting room. They did not report problems with the class performance, or the perception of knowledge regarding anatomy. The formaldehyde smell and clinical symptoms did not have an impact on our students' attitudes. Hisamitsu *et al.* reported that the effects of medical students' exposure to FA during cadaver dissection are temporary, and usually clinical symptoms observed

during the dissection course are transient and disappeared after a few days of exposure [13].

Given the fact that formaldehyde is toxic and is classified as a dangerous substance according to the EU Dangerous Preparations Directive (1999/45/EC), it is of particular importance to stress that the adverse effects of FA on medical students can be improved by lowering the FA concentrations in anatomy dissection rooms. Primarily, student instructions before dissection, easy access to adequate personal protective equipment as well as different technological solutions are recommended as effective ways to minimize harmful FA effects [37]. Hence the Medical University of Lublin and the Department of Anatomy have established guidelines which recommend how to avoid exposure to formaldehyde in anatomy dissection rooms. The students have been informed about the potential health hazards of formaldehyde. In our department students are required to wear aprons or anatomy lab coat, lab shoes, hat, gloves and a face mask. Optionally students may use protective eyewear. It is accepted that medical face masks limit FA absorption considerably, reduce irritation and burning of the mucosa of the mouth and upper respiratory tract and decrease symptoms from the respiratory tract following inhalation [2, 38]. Also, gloves are recommended to protect against dermal contact with FA while dissecting cadavers [39].

The toxic effects could be reduced by lowering the concentrations of FA while controlling the airflow by opening windows or doors, and the use of ventilators

[37]. In our laboratory rooms, the central ventilation system operates to circulate the air; the system brings fresh air into the laboratory room and allows one to control FA emission. The dissecting work table has a drainage system which allows reduced exposure to embalming solution and FA. These technological solutions are effective and meet the required standard criteria of the FA concentration in acceptable levels of formaldehyde in our laboratory rooms.

It is widely agreed that anatomy is a core knowledge for various medical specialists and other health care professionals [10, 40]. Anatomy learned by cadaveric dissection has many proven benefits, i.e. students can explore the organization of the human body and investigate the functional anatomy. Due to technology development, the methods of teaching will undergo changes. The modern simulation technology allows one to perform virtual dissection and is being adopted by many of the world's medical schools [11, 40]. However, 'traditional' cadaveric dissection remains one of the most efficient methods of teaching anatomy for both undergraduate and postgraduate students. Cadaveric-based teaching is of particular importance during surgical training for residents and specialists in general surgery, urology, cardiothoracic surgery and neurosurgery, as well as radiologists and pathologists [11, 40, 41].

Despite known toxic effects of FA in humans, it is still popular because of low costs and effectiveness. However, there has been a recent increase of interest in alternative conservatives for formaldehyde-based embalming. A possible choice is ethanol glycerin fixation with thymol or formaldehyde neutralization with ammonium carbonate to reduce the FA level. These methods are recommended for use in gross anatomy laboratories [6, 42].

CONCLUSIONS

In some medical students exposure to FA gas at concentrations of 0.47–0.57 mg/m³ may result in subjective sensory irritation, in different groups of medical students (male and female, allergic and nonallergic). Particularly unpleasant symptoms may be experienced by individuals with allergic history. Therefore, it is necessary to reduce formaldehyde levels further in the anatomy dissection laboratories.

Conflict of interest

The authors declare no conflict of interest.

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