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Original Article

STUDY OF THE TOXIC EFFECTS OF FORMALDEHYDE VAPOURS WITHIN THE DISSECTION HALL ON THE FIRST YEAR INDIAN MEDICAL STUDENTS

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ABSTRACT

Introduction: Formaldehyde has been used since decades as a time tested embalming fluid material either alone or in mixture with methyl alcohol, thymol crystals, glycerin and water. We in Medical College, Raigarh use 37% formaldehyde, 7% methyl alcohol and the remaining water to prepare embalming solution for cadavers. The concentration of formaldehyde is usually expressed in terms of parts per million (1 ppm= 1.248 mg/cu.m.). Vapours emanating out of the cadavers within the dissection hall is a potential source of health hazard for all medical professionals, student, faculty or technicians. The discomfort includes irritation to the mucous membrane of the nose, respiratory tract, eyes and also causes allergic reaction of the skin.

Materials and Methods: Keeping track of the unconsciously caused complaints, we made a sincere attempt to chalk out the effects of formaldehyde fumes on 100 first MBBS students of Medical College, Raigarh (C.G) as they are virgin in terms of formalin exposure.

Results: The obtained results were quite dramatic. Maximum number of students was positive as among the various symptoms described.

Discussion: Medical students during their dissection course are exposed to formaldehyde, whose exposure is recently considered to be one of the causes of multiple chemical sensitivity. The present study broadly reflects the toxic effects over the first MBBS Indian medical students

Conclusion: The presentation also recommends possible methods for reduction of formalin exposure so that the medical students can enter the dissection hall without any mental tension of toxicity of formalin vapours.

KEY WORDS: Formaldehyde, Toxicity, MBBS students, Dissection, Questionnaire.

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INTRODUCTION

Formalin (Commercial name) [1] CH2 (OH) 2 & HO (CH2O) N.H is 37-50% aqueous solution of dissolved formaldehyde CH2O [2] (37% by weight or 40% by volume of formaldehyde gas in water) [1]. Formaldehyde was discovered in 1856 by the British Chemist, August Wilheld Von Hofmann [2]. It is a noxious, flammable gas, extremely soluble in water. Formalin is a colorless (at room temperature) [1] irritant which gives out pungent formaldehyde vapors and is widely used in the medical field as fungicide, germicide, disinfectant and preservative [3] solution in Anatomy mortuary (Cadaveric

preservative) , Anatomical and Pathological gross specimens in medical institutes and hospitals and in wood and plastic industries [4]. Formaldehyde is also used extensively in the chemical, adhesive, paint, plastic, construction, textile, paper, and cosmetic industries; in the manufacture of pressed wood products (urea resins in plywood wall paneling, particle board, and fiber board); in fertilizers; in permanent press products and other textiles; in paper; and in glue (Bernstein et al., 1984). It is also formed during the burning of organic materials and is found in tobacco smoke (U.S. Environmental Protection Agency [U.S.EPA], 2011).

A cadaver in a medical school is embalmed via the infusion of chemical substances into the body tissues that include formalin (which contains formaldehyde), alcohol, glycerin, carbolic acid, and dye [4]. Those substances have specific roles (e.g., fixative, preservation, denaturation, solidification of tissue protein, disinfection and maintenance of the integrity of the anatomic relation germicides, buffers, wetting agents, anticoagulants, dyes, perfuming agents, etc.) [3], and they are usually infused via the femoral arteries or the internal carotid arteries (Coleman and Kogan, 1998). This helps to preserve the cadaver by maintaining, as far as possible, a life-like state, and in the process, retaining the normal anatomical relations as are required for dissection purposes [3]. The formulation for the preparation of embalming fluid varies. It depends on the laboratory and other factors like the size, extent of edema and stage of decomposition of the cadaver [3].

Thus anatomists, technicians in biological science laboratories, and medical school students in dissection hall are regularly exposed to formaldehyde. The level of exposure to that agent depends on the time spent in the anatomy practical hall and museums, working conditions there and the type of embalming performed (Pabst 1987). Excessive formaldehyde vapor in the working area can be caused by a work environment that facilitates the spillage of formalin; poor condition of cadavers, which causes embalming fluid to leak; a high formaldehyde concentration in the air (>0.50 ppm) or in cadaveric tissues (0.22 ppm); poor ventilation in the dissection rooms; lack of strict and appropriate guidelines for handling embalmed Cadavers and prosected specimens; or ignorance of consequences of formalin exposure (Balmes, 2004).

The threshold limit value for formaldehyde is 0.3 ppm, which must never be exceeded (American Conference of Governmental Industrial Hygienists, 2001). The legal airborne permissible exposure limits are 0.75 ppm averaged over an eight-hour work shift and 2 Ppm not to be exceeded during any 15 minute work period (Formaldehyde, Occupational Safety and Health Standards, 1998). The recommended airborne exposure limits are 0.016 ppm averaged over a 10-hour work shift and0.1 ppm not to be exceeded during any 15-minute work period (Agency for Toxic Substances and Disease Registry [ATSDR], 1999).

Although formalin is extensively used in different fields, its toxicity is frequently ignored [4]. In the body, formaldehyde quickly metabolizes to formic acid [4]. The measurement of formate (formic acid minus 1 hydrogen ion) levels indicates the severity of formaldehyde intoxication. The concentration of formaldehyde in the air is often expressed in terms of parts per million (ppm) (1 ppm = 1.248 mg/m) [1].

The toxic effects of formaldehyde exposure can be classified as follows: irritation of mucous membrane, contact dermatitis, teratogenicity, and carcinogenicity (NIOSH, 2009). Upper airway irritation is the commonest respiratory effect found after exposure to formalin as 95% of inhaled formalin is absorbed through upper respiratory tract most frequently above 1ppm [5,6]. Symptoms of upper airway irritation include dry or sore throat, itching and burning sensations of the nose and nasal congestion. Tolerance to this level of exposure may develop within 1-2 hours [6]. This tolerance can permit workers remaining in an environment of gradually increasing formaldehyde concentrations to be unaware of their increasingly hazardous exposure [6]. Adverse effects of inhaling formaldehyde becomes more as the concentration level of it increases [6]. The common symptoms from acute exposure to formalin manifest as irritation of the throat, nose, eyes and skin [7]. It can also cause neurophysiologic effects, irritation of upper

respiratory tract which can potentially exacerbate asthma symptoms and other respiratory illnesses, also dyspnea, coughing, burning of nose, eyes, and pharynx [7]. Chronic exposure can cause bronchitis and pneumonia [7]. When it is swallowed, it can result in sudden death [7]. Occupational data suggests that significant changes may occur in lung function, respiratory system and cardiac function following prolonged exposure to formalin in work places [8]. It is well known that formaldehyde can cause sick house syndrome (sick building syndrome) which is characterized by mucosal irritation, headache, nausea and chest symptoms [8]. Formaldehyde is also a hapten and formaldehyde-protein complex may be immunogenic [3].

In the US, the permissible limits of occupational exposure to formaldehyde are 3 ppm in a time-weight average breathing zone during an 8-hour period, a ceiling concentration of 5 ppm and an acceptable maximum peak of 10 ppm for no longer than 30 minutes during a one day shift [11].

A sound anatomical knowledge and dissection of the human body remains the cornerstone of the first year medical students in their medical curriculum. Exposure to formaldehyde in the department of anatomy is continuous and higher than its use in other areas [3]. The Anatomy faculty, students, embalmers and histopathology technicians are continuously exposed to the toxic vapors' of formaldehyde. Hence the anatomy dissection laboratory represents a significant emotional challenge to many medical students [9]. The present study was therefore conducted to assess the following for the first year medical students within the dissection hall of the department of Anatomy.

1.The effects of acute exposure to formaldehyde.

2.To explain the probable pathophysiology of the toxicity.

3.To chalk out possible preventable measures to reduce its toxicity.

Review of literature: Exposure to moderate levels of formaldehyde (1-3 ppm) can result in eye and upper respiratory tract irritation [13, 14, 15] states that most people cannot tolerate exposures to more than 5 ppm formaldehyde in air; above 10-20 ppm symptoms become severe and shortness of breath occurs. High concentrations of formaldehyde may result in nasal obstruction, pulmonary edema, choking, dyspnea, and chest tightness [16, 17]. A medical intern with known atopy and exposure to formaldehyde over a period of 1 week developed dyspnea, chest tightness, and edema, following a final 2 hour exposure to high concentrations of formaldehyde [16]. Five workers exposed to high concentrations of formaldehyde from urea-formaldehyde foam insulation experienced intolerable eye and upper respiratory tract irritation, choking, marked dyspnea, and nasal obstruction [10]. Numerous acute controlled and occupational human exposure studies have been conducted with both asthmatic and normal subjects to investigate formaldehyde's irritative and pulmonary effects [10].

Concentrations of formaldehyde in the human exposure studies ranged as high as 3 ppm for up to 3 hours. The major findings in these studies were mild to moderate eye and upper respiratory tract irritation, typical of mild discomfort from formaldehyde exposure [10].

In a human irritation study by Weber-Tschoppe et al. (1977), 33 subjects were exposed to formaldehyde at concentrations ranging from 0.03-3.2 ppm (0.04-4.0 mg/m^3) for 35 minutes. Thresholds were 1.2 ppm (1.5 mg/m^3) for eye and nose irritation, 1.7 ppm (2.1 mg/m^3) for eye blinking, and 2.1 ppm (2.6 mg/m^3) for throat irritation [13, 10].

Kulle et al. (1987) exposed non-asthmatic humans to up to 3.0 ppm (3.7 mg/m^3) formaldehyde in a controlled environmental chamber for 3 hours. Significant dose-response relationships were seen with odor and eye irritation. At 0.5 ppm for 3 hours, none of 9 subjects had eye irritation. At 1.0 ppm, 3 of 19 subjects reported mild eye irritation and one experienced moderate irritation. At 2.0 ppm, 6 subjects reported mild and 4 reported moderate eye irritation. Nasal flow resistance was increased at 3.0 ppm but not at 2.0 ppm (2.5 mg/m^3) [10, 14].

Eleven healthy subjects and nine patients with formalin skin sensitization were exposed to 0.5 mg/m^3 formaldehyde for 2 hours (Pazdrak et al., 1993) [18]. Nasal lavage was performed prior

to and 5 to 10 minutes, 4 hours, and 18 hours after exposure. Rhinitis was reported and increases in the number and proportion of eosinophils, elevated albumin and increased protein levels were noted in nasal lavage fluid 4 and 18 hours after exposure. No differences were found between patients with skin sensitization and healthy subjects [10].

In a study by Green et al. (1987), volunteer asthmatic and normal subjects exposed to formaldehyde developed clinically significant decrements in pulmonary function. Exposure to 3 ppm formaldehyde for 1 hour resulted in clinically significant reductions of FEV (defined as > 20% or more) and FEV /FVC (ratio 70% or less) in 5 individuals in the study (2 of 16 asthmatics, 2 of 22 normal subjects, and one clinically normal subject with hyperactive airways). Other than mild nose and throat irritation, no severe respiratory signs and symptoms were apparently reported [19, 10].

Sim and Pattle (1957) exposed twelve men to 17.3 mg/m³ (13.9 ppm) formaldehyde for 30 minutes. This concentration caused "considerable nasal and eye irritation when they first entered the chamber; but despite the continued mild lacrimation for some period of time, there was no marked response (pulmonary or cardiovascular) to the exposure." The eye irritation was not severe, according to the authors, and resolved after 10 minutes in the chamber [10, 20].

Kriebel and associates (1993) studied 24 physical therapy students dissecting cadavers for 3 h per week for 10 weeks. Measured formaldehyde exposures in the breathing zone ranged from 0.49 to 0.93 ppm (geometric mean – SD = 0.73 ± 1.22). There was a pronounced increase in irritant symptoms over the duration of the each laboratory period, but this effect was stronger at the beginning of the study period. Peak expiratory flow (PEF) declined over the 10 week study by an average of 10 L/min (statistically significant trend in random-effects regression models). Fourteen weeks after ceasing exposures, the group mean baseline PEF had returned to the pre-exposure level. Rhinitis and a wide range of asthma-like conditions can result from exposure to formaldehyde [10]. Some studies have reported that workers exposed to low concentrations may develop severe prolonged asthma attacks after prior exposure; this suggests that they may have become sensitized (Feinman, 1988) [15].

Formaldehyde provocation of human subjects, occupationally exposed to formaldehyde and suffering from asthma-like symptoms such as wheezing, shortness of breath, or rhinitis, occasionally resulted in pulmonary function decrements (2 to 33% response rate) consistent with immediate, delayed, or both immediate and delayed bronco-constriction (Nordman et al., 1985; Burge et al., 1985; Henrick and Lane, 1977; Wallenstein et al., 1978) [10].

Walrath et al, (1980) presented a study of the carcinogenic effects of formaldehyde on embalmers at the CIIT conference in New York and concluded that embalmers showed a slightly elevated mortality from cancer, significant levels of arteriosclerotic heart disease and a low incidence of pneumonia deaths [11].

MATERIALS AND METHODS

The study was carried out at the department of human Anatomy of Medical College, Raigarh (C.G) (having MCI recognized 50 admission per year) over a period of 2 years (2013-2014) on 100 1st year MBBS students (both male and female). Luckily each year had a male: female ratio of 1:1. A letter of ethical clearance was granted from the ethical committee of the medical college. The students were intimated about the purpose of the study and duly signed informed consent was taken thus eliminating the chances of participant bias [9]. The students were in the age group of 18-20 years, healthy, non-overweight, non-smoker with no history of cardiac, pulmonary, dermatological system or epileptic disorder and with no previous exposure to formaldehyde fumes [13, 4, 9, 11] (inclusion criteria & exclusion criteria). The health status of the student was confirmed by a through medical examination. The students were unconsciously routinely exposed to formaldehyde fumes during the dissection hours (2 hours each day for 6 days a week). The students were informed about the source of cadavers, method of embalming of cadavers and embalming solution, legal arrangements, disposal and burial of cadavers. The students were

distributed with questionnaire pertaining to symptoms arising due to inhalation of formaldehyde fumes within the dissection hall [3, 4, 11] (Questionnaire 1). These symptoms were graded on a scale of 0-3 as follows: Grade 0: Not recognizable; Grade 1: Mildly recognizable; Grade 2: Moderately recognizable and irritating; Grade 3: Severely recognizable, Intolerable and requiring medical support. The students were also asked to clarify which among the symptoms was the first to develop and which among them was the most intolerable (Questionnaire 2) [3, 4, 9, 11]. Among 100 case sheets distributed 3 were not returned and 1 student was a known case of bronchial asthma and 2 were known smokers. These 6 case sheets were placed under exclusion criteria. Hence total 94 cases were evaluated for the study. Following the obtained results 3 graphs were plotted – Graph 1 showing the percentage severity of each significant symptom, Graph 2 showing the incidence of the significant first symptom and graph 3 showing the most irritable symptom as a measure among all symptoms.

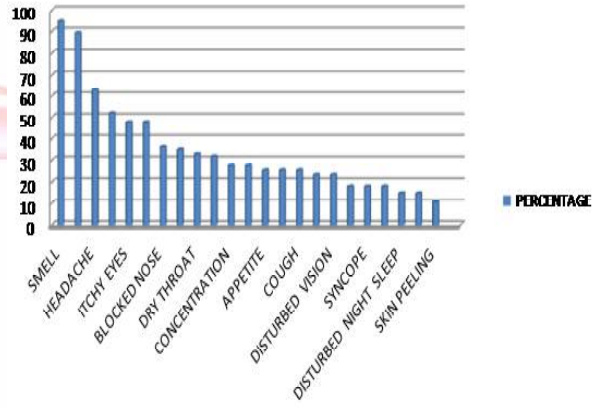
RESULTS

The obtained results were tabulated. Results are shown in table 1 and 2.

Unpleasant smell was seen in 94.68% students, running nose was complained by 52.12% students, redness of the eyes disturbed 47.87 students, unusual tiredness was felt by 31.92% participants, excessive lacrimation troubled 89.36% students, sleeping time was prolonged in 18.09% subjects, itching eyes was a symptom in 47.87% students, vision was blurred in 23.41% students, unusual thirst was felt by 18.08 students, disturbed respiration 23.45%, dry throat was seen in 32.98% students, nausea was felt by 38.3% subjects, headache was complained by 62.77% students, sleep at night was disturbed in 14.9% students, dryness of the nose was seen in 27.66% students, blocked nose was a complain in 36.17% subjects, deviated appetite was a symptom in 25.54% participants, syncopal attack troubled 18.08% students, eruptions within the skin was seen in 23.41% subjects, itchiness of the skin of the hands was a symptom in 25.53% participants, 24.47% students had complained of dry cough, 25.53% students had sore throat, tingling of the nose disturbed in 35.1% students, disturbed concentration was a problem in 27.67% students, 14.89% students felt weakness with formaldehyde inhalation, 18.08% students were restless with formalin inhalation, skin peeling was a symptom in 10.64% students, discoloration of the nails was not a significant symptom. Among the numerous symptoms, some symptoms were expressed even after the dissection hours. They include 4.26% as post dissection vomiting, 5.32% as post dissection nausea, 19.14% students with post dissection reduced hunger and 29.79% with post dissection redness of the eyes.

72.34% students experienced unpleasant smell as the first symptom, 26.60% students said the same symptom to be the most irritable, 53.19% students experienced excessive lacrimation as the most troublesome symptom. Among the other symptoms none were much significant in terms of incidence and irritability.

Graph 1: Percentage severity of each significant symptom.



Graph 2: Incidence of significant first symptoms.

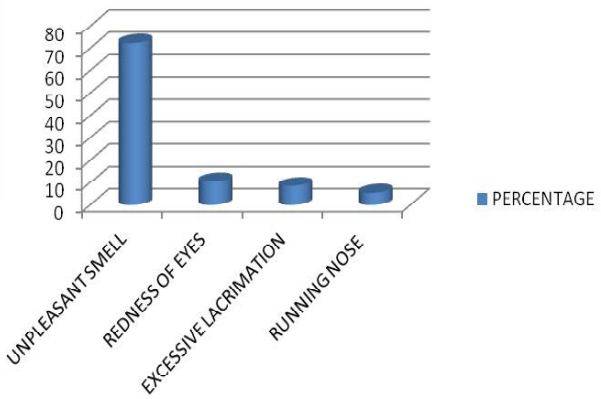


Table 1: Symptoms due to formaldehyde exposure (their grading, frequency and extent).

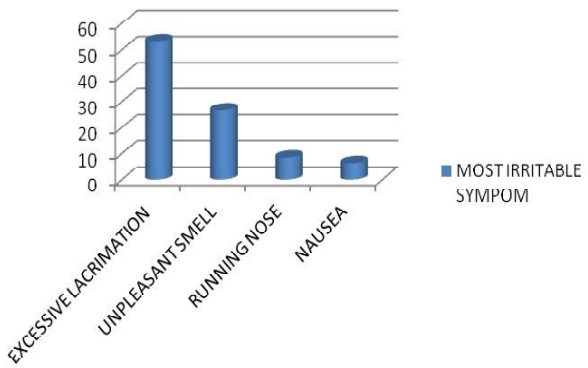
Symptoms	Gradation			
	Grade 0	Grade 1	Grade 2	Grade 3
1. Unpleasant smell	05/94 (5.3%)	32/94 (34.04%)	44/94 (46.81%)	13/94 (13.83%)
2. Excessive lacrimation (Watery eyes)	10/94 (10.64%)	55/94 (58.51%)	24/94 (25.53%)	05/94 (5.32%)
3. Headache	35/94 (37.23&)	33/94 (35.11%)	17/94 (18.09%)	09/94 (9.57%)
4. Running nose	45/94 (47.87%)	35/94 (37.23%)	08/94 (8.51%)	06/94 (6.38%)
5. Redness of the eyes	50/94 (53.19%)	35/94 (37.23%)	07/94 (7.45%)	03/94 (3.19%)
6. Itching or sore eyes	49/94 (52.13%)	34/94 (36.17%)	08/94 (8.51%)	03/94 (3.19%)
7. Nausea	58/94 (61.70%)	25/94 (26.60%)	10/94 (10.64%)	01/94 (1.06%)
8. Congested nose	60/94	26/94 (27.66%)	06/94 (6.38%)	02/94 (2.13%)
9. Tingling sensation of the nose	60/94 (63.83%)	21/94 (22.34%)	06/94 (6.38%)	06/94 (6.38%)
10. Dry or soreness in throat	63/94 (67.02%)	14/94 (14.89%)	15/94 (15.96%)	02/94 (2.13%)
11. Unusual tiredness or dizziness	67/94 (71.28)	20/94 (21.28%)	07/94 (7.45%)	00/94 (0%)
12. Post dissection redness of eyes	66/94 (70.21%)	24/94 (25.53%)	04/94 (4.26%)	00/94 (0%)
13. Low concentration	68/94 (72.34%)	20/94 (21.28%)	04/94 (4.26%)	02/94 (2.13%)
14. Dryness or soreness of nose	68/94 (72.34%)	16/94 (17.02%)	07/94 (7.45%)	03/94 (3.19%)
15. Disturbed appetite	70/94 (74.47%)	15/94 (15.96%)	07/94 (7.45%)	02/94 (2.13%)
16. Soreness of throat	70/94 (74.47%)	22/94 (23.40%)	02/94 (2.13%)	00/94 (0%)
17. Itching or sore skin on hands	70/100 (74.47%)	14/94 (14.89%)	05/94 (5.32%)	05/94 (5.32%)
18. Cough (Dry / Productive)	71/94 (75.53%)	23/94 (24.47%) (Dry)	00/94 (0%)	00/94 (0%)
19. Respiration difficulties	72/94 (76.60%)	14/94 (14.89%)	07/94 (7.45%)	01/94 (1.06%)
20. Blurring of vision	72/94 (76.60%)	12/94 (12.77%)	08/94 (8.51%)	02/94 (2.13%)
21. Skin eruptions	72/94 76.60%)	12/94 (12.77%)	06/94 (6.38%)	04/94 (4.26%)
22. Post dissection decreased hunger	76/94 (80.85%)	09/94 (9.57%)	06/94 (6.38%)	03/94 (3.19%)
23. Prolonged sleeping time	77/94 (81.91%)	12/94 (12.77%)	03/94 (3.19%)	02/94 (2.13%)
24. Restlessness	77/94 (81.91%)	16/94 (17.02%)	01/94 (1.06%)	00/94 (0%)
25. Fainting episode	77/94 (81.91%)	14/94 (14.89%)	01/94 (1.06%)	02/94 (2.13%)
26. Unusual thirst	77/94 (81.91%)	14/94 (14.89%)	02/94 (2.13%)	01/94 (1.06%)
27. Disturbed sleep at night	80/94 (85.11%)	10/94 (10.64%)	04/94 (4.26%)	00/94 (0%)
28. Weakness	80/94 (85.10%)	11/94 (11.70%)	03/94 (3.19%)	00/94 (0%)
29. Peeling of skin	84/94 (89.36%)	08/94 (8.51%)	02/94 (2.13%)	00/94 (0%)
30. Post dissection nausea	89/94 (94.68%)	04/94 (4.26%)	01/94 (1.06%)	00/94 (0%)
31. Post dissection vomiting	90/94 (95.74%)	04/94 (4.26%)	00/94 (0%)	00/94 (0%)
32. Discoloring of nails	93/94 (98.94%)	01/94 (1.06%)	00/94 (0%)	00/94 (0%)

Any previous history of allergy, cardiovascular disorder or pulmonary disorder or are you a smoker? Specify separately.

Table 2: Table showing incidence of occurrence and severity of the symptoms of formaldehyde inhalation.

Symptoms	Symptom appearing first	Most irritable symptom
1. Unpleasant smell	68/94 (72.34%)	25/94 (26.60%)
2. Running nose	05/94 (5.32%)	08/94 (8.51%)
3. Redness of the eyes	10/94 (10.64%)	02/94 (2.13%)
4. Unusual tiredness or dizziness	01/94 (1.06%)	00/94 (0%)
5. Excessive lacrimation (Watery eyes)	08/94 (8.51%)	50/94 (53.19%)
6. Prolonged sleeping time	00/100 (0%)	00/94 (0%)
7. Itching or sore eyes	00/94 (0%)	00/94 (0%)
8. Blurring of vision	00/94 (0%)	00/94 (0%)
9. Unusual thirst	00/94 (0%)	00/94 (0%)
10. Respiratory distress	00/94 (0%)	00/94 (0%)
11. Dry or sore throat	00/94 (0%)	00/94 (0%)
12. Nausea	01/94 (1.06%)	06/94 6.38%)
13. Headache	00/94 (0%)	02/94 (2.13%)
14. Disturbed nocturnal sleep	00/94 (0%)	00/94 (0%)
15. Dry or sore nose	00/94 (0%)	00/94 (0%)
16. Congested nose	00/94 (0%)	00/94 (0%)
17. Disturbed appetite	00/94 (0%)	00/94 (0%)
18. Fainting episode	00/94 (0%)	00/94 (0%)
19. Skin rash	00/94 (0%)	01/94 (1.06%)
20. Itching or sore skin on hands	00/94 (0%)	00/94 (0%)
21. Cough (Dry / Productive)	00/94 (0%)	00/94 (0%)
22. Irritation of throat	01/94 (1.06%)	00/94 (0%)
23. Tingling sensation of the nose	00/94 (0%)	00/94 (0%)
24. Low concentration	00/94 (0%)	00/94 (0%)
25. Weakness	00/94 (0%)	00/94 (0%)
26. Restlessness	00/94 (0%)	00/94 (0%)
27. Peeling of skin	00/94 (0%)	00/94 (0%)
28. Discoloring of nails	00/94 (0%)	00/94 (0%)
29. Post dissection vomiting	00/94 (0%)	00/94 (0%)
30. Post dissection nausea	00/94 (0%)	00/94 (0%)
31. Post dissection decreased appetite	00/94 (0%)	00/94 (0%)
32. Post dissection redness of eyes	00/94 (0%)	00/94 (0%)

Graph 3: Most irritable symptom.



DISCUSSION

Formaldehyde gas is produced by oxidation of methyl alcohol [8]. Medical students during their dissection course are exposed to formaldehyde, whose exposure is recently considered to be one of the causes of multiple chemical sensitivity [8]. The present study elucidates the toxic effects over the first MBBS Indian students due to their timely unconscious exposure to formaldehyde fumes arising from the formaldehyde embalmed cadaver within the dissection hall of Anatomy. These effects were quantified in a tabulated chronological order of (1) appearance of symptoms experienced (2) symptom which has the first incidence and (3) the most disturbing symptom among all. All the symptoms were presented in drawn bar graph with heir obtained percentage. The most disturbing, troubled and symptom appearing first was found to be the unpleasant smell of formalin (68/94=72.34%). (Table 1, 2).This observation is in agreement with a report from Japan, where formaldehyde has been considered a probable cause of nasopharyngeal tumors in humans, and that is why the Japan Ministry of Education, Culture, Sports, Science and Technology (MEXT) has set guidelines which recommends decreasing use of gaseous formaldehyde in gross anatomy dissection laboratories [3]. It is also in keeping with the work done in Vienna, where exposure due to inhalation of the fumes of formaldehyde caused shortness of breath, mild irritation of the upper respiratory tract, and compromised pulmonary function. Inhaled formaldehyde vapor in large doses has been associated with cancers in laboratory animals, particularly of the upper airways [3]. 53.19% (50/94) (Table 2) students complained about excessive lacrimation as the symptom which was most excruciatingly felt and troubled as they were exposed to formaldehyde vapours for the first time. Excessive exposure of the eyes to formaldehyde could lead to poor vision latter in life, which was in agreement with reports from Belgium and India that formaldehyde caused irritation of the eyes [3]. Formaldehyde may also affect assimilation during dissection because when one is tired, dizzy and having other symptoms such as headache, little or nothing can be grasped while dissecting [3]. However, only 26

out of 94 (27.67%) (Table 1) students believed that formaldehyde would strongly affect their assimilation. In this research, we found that one of the most common effects of formaldehyde—"skin-related diseases," [3] had a low incidence. The reason behind this is that being a small group of 17 students in a batch (out of 50) and being a new medical college there is a shortage of cadavers, hence 1 or 2 were made group leaders of each batch. The group in-charge took active participation in the dissection and were taught by lecturers and practical instructors, who used protective wears in the hands and other parts of the body—making skin symptoms as the least ranked effect of formaldehyde (10.64%) (Table 1).

The exact mechanism by which formaldehyde exerts its irritant, corrosive, and cytotoxic effects is not known.

Aldehydes as a group (within formaldehyde) are reactive chemicals with a highly electronegative oxygen atom making it react easily with nucleophilic sites on cell membranes and in body tissues and fluids such as the amino groups in protein and DNA forming cross links between protein and DNA *in vivo* [12, 21].

Casanova-Schmitz et al. (1984a) reported that the predominant route of formaldehyde metabolism was metabolic incorporation into macromolecules (DNA, RNA, and proteins) in the respiratory and olfactory mucosa and bone marrow. Concentrations of cross linked macromolecule in respiratory and olfactory mucosa tissues increased linearly with dose; at all doses, the concentrations within respiratory mucosa tissues were approximately two to three times that in olfactory mucosa tissues [12, 22]. Later studies by Casanova et al. (1991a, 1991b) described the formation of DNA-protein cross links in the respiratory tract measured in male Fischer 344 rats as well as in Rhesus monkeys. Concentrations of DNA-protein cross links were greatest in the middle turbinate tissues and lowest in the nasopharyngeal tissues, no evidence of cross link formation was seen in the sinus or lung tissues at any exposure concentration [12, 23].

The mechanism by which formaldehyde exerts its toxicological effects is not known; however, it is known that formaldehyde readily combines with free, un-protonated amino groups of amino acids to yield hydroxyl-methyl amino acid derivatives and a proton (H+), which is believed to be related to its germicidal properties. Higher concentrations will precipitate protein [12, 24].

Either one of these mechanistic properties or perhaps other unknown properties may be responsible for the irritation effects seen with formaldehyde exposure [12]. It is probable that formaldehyde toxicity occurs when intracellular levels saturate formaldehyde dehydrogenase activity, overwhelming the natural protection against formaldehyde, and allowing the un-metabolized intact molecule to exert its effects locally [12]. The primary metabolite of formaldehyde, formate, is not expected to be as reactive as formaldehyde itself and is subject to excretion as a salt in the urine, entrance into the one-carbon metabolic pool for incorporation into other cellular components, or further metabolism to carbon dioxide [12].

The toxicity of formaldehyde is route-dependent. Irritation at the point of contact is seen by inhalation, oral, and dermal routes. High doses are cytotoxic and result in degeneration and necrosis of mucosal and epithelial cell layers. These observations are consistent with the hypothesis that toxic effects are mediated by formaldehyde itself and not by metabolites. No specific target molecule has been identified, although DNA-protein cross links have been identified [12, 25].

An example of a local effect of formaldehyde vapor was demonstrated in the rat nasal epithelium. In rat studies where cell turnover was measured (a measure of formaldehyde cytotoxicity), the no-effect level is approximately 2 ppm (Monticello et al. 1991; Swenberg et al. 1983) for 6 hours/day exposures for 9 days. At higher concentrations (6, 10, or 15 ppm), higher rates of cell turnover were seen (Monticello et al. 1991), and a dose-response was observed. Similar results were seen by Wilmer et al. 1987, 1989 [12].

Studies have shown that formaldehyde concentration in the inspired air may be more important than exposure duration in determining the extent of nasal damage (Wilmer et al. 1987, 1989). Monticello et al. (1996) also determined that the nasal cell target population size,

increased cell proliferation of specific target cells, and the nonlinear kinetics of formaldehyde binding to DNA explain why specific regions of the rat nose are more prone to develop formaldehyde-induced nasal squamous cell carcinomas than other sites in the nasal cavity [12].

Correlation of regional and nonlinear formaldehyde-induced nasal cancer with proliferating populations of cells has been studied by Monticello et al. (1996). The majority of formaldehyde induced neoplasm's consisted of squamous cell carcinomas and polyploidy adenomas; however, cell proliferation was not affected by formaldehyde exposures of 6.01 ppm or less [12].

Although there is evidence to suggest that exposure concentration is more important than exposure duration in determining the extent of formaldehyde-induced nasal epithelial damage. First, a single high dose (40 ppm) for acute durations is not likely sufficient to induce squamous cell carcinoma cancer (Bhalla et al. 1990; Monteiro-Riviere and Popp 1986; Wilmer et al. 1987); repeated exposures for protracted durations are required to induce nasal cancer in rats. Second, the data indicate that a sequence of cellular events must occur in order to induce nasal carcinomas. This cellular and tissue damage inflicted by unmetabolized formaldehyde is then followed by a regenerative hyperplasia and metaplasia phase (Chang et al. 1983; Feron et al. 1988; Rusch et al. 1983; Wilmer et al. 1987; Woutersen et al. 1987, 1989), which results in increased cell-turnover rates within the mucosa [12].

Formaldehyde has been demonstrated to be genotoxic (Basler et al. 1985; Donovan et al. 1983; Grafstrom et al. 1985, 1993; Rithidech et al. 1987; Snyder and Van Houten 1986; Valencia et al. 1989; Woodruff et al. 1985; Yager et al. 1986). The DNA damage that occurs in the altered cells is carried into subsequent cell populations and thereby greatly enhances the progression of pre-neoplastic cells to cancer. In this manner, formaldehyde likely can act as a complete carcinogen (providing initiation, promotion, and progression) with repeated and prolonged duration of exposure at cytotoxic concentrations. Point mutations in the p53 tumor suppressor gene were found in 5 of 11 nasal tumors examined from rats exposed to 15 ppm formaldehyde for 2 years (Recio et al. 1992) [12].

Sometimes binding of formaldehyde to endogenous proteins may result in formation of neo-antigens. Such neo-antigens may elicit an immune response that might account for the occurrence of asthma and other respiratory symptoms [3]. Thus formaldehyde present in formalin definitely has a toxic effect on various body tissues which can adversely affect the health of I MBBS students [3]. So, proper precautions should be taken to prevent formalin toxicity. Considering this issue World Health Organization (WHO) has developed a guideline for formaldehyde in non-occupational settings at 100 ppb (0.1 mg/m3) for 30 minutes. This guideline was developed to protect against sensory irritation in the general population, but WHO states that it also represents an exposure level at which there is negligible risk of upper respiratory tract cancer in humans (Neeraj R, Rastogi SK in 2007).

Recommendations and outlook: Our study has the advantage of being a longitudinal study. Our subjects are our own Medical College students of the same age group who are known and the same subjects were examined by questionnaire. Hence individual variations were almost negligible. The disadvantage of the study being that the exact concentration of formaldehyde exposure cannot be determined and measured. But it was definitely at a concentration which causes nose, eye, and skin irritation. Environmental evaluation conducted in Anatomy laboratory showed formalin levels ranging from 0.02 ppm to 2.7 ppm may cause significant exposure to cause to cause symptoms of irritation for most of the exposed subjects [8]. Our study may be extended to a larger number of subjects. The study may involve the lung function effects of formalin by involving the study once a year so that chronic effects of formalin exposure may also be elicited. Environmental air concentration of gradual decrease or gradual increase levels of formalin vapours may be measured to chalk out the varied effects of formalin at varied concentration levels.

Wei et al revealed that subjective symptoms during the Anatomy dissection course were

related to the period spent in the dissection room [8]. Their study suggests that shortening the time of each Anatomy dissection practical class and reduction of the number of cadaver tables could help to reduce the symptoms [8].

Dissection has been a time tested method of teaching Anatomy so that the students can endeavor and learn the subject with a in Toto 3 dimensional tactile and spatial view that cannot be achieved with the modern computerized teaching aids. The students learn to respect dying and the dead and attain control over their mixed emotional feelings. The Anatomy dissection laboratory represents a significant emotional challenge to the newly joined medical students [9]. Hence to overcome the biological ill effects of formaldehyde over the medical professionals certain recommendations can be put forward:

1. Medical professionals should be made aware of the possible adverse health hazards of formalin inhalation.

2. The Anatomy dissection hall should have adequate ventilation systems. According to the American Conference of Governmental Industrial Hygienists (2001), the ventilation rate should exceed 15 room changes per hour [4].

3. Negative pressure ventilation and monitoring systems should be installed (within the dissection halls) to reduce the exposure of formaldehyde vapours [4].

4. Cadaveric waste should be properly discarded within labeled plastic bags and the bags should be opened outside in open environment allowing the fumes of formalin to escape.

5.Protective laboratory coats, goggles and gloves should be advised for the professionals so that direct skin contact with the agent becomes minimized.

6. Avoid usage of contact lenses within the dissection hall.

7. Installation of multiple eyes washing water jets within the dissection hall.

8. Formalin collection containers beneath the dissection table should be emptied regularly.

9. Excess formalin spillage within the dissection hall should not be advocated and if possible the excess fluid should be immediately drained. Embalming should be done by trained professionals.

10. Nitrile gloves or 2 pairs of latex gloves should be made mandatory for dissection procedure. Medical professionals allergic to latex should be advised plastic gloves for dissection and embalming procedure.

11.Pregnant professionals should keep themselves away from the formalin fumes. Students who become pregnant during the Anatomy course should immediately inform the teachers about the same and should take up the course after delivery. Pregnant students within the dissection hall should wear properly fitted double masks meant for reduction of formalin exposure. They should be advised to dissect no longer than one hour and to take 15 minutes break after each session [4].

12. Asthmatic students should wear full face or half face respirator during dissection [4].

13. Coleman R recommended use of specialized dissection beds with a fitted internal motor and replaceable active carbon filter system that causes down flow of the formaldehyde rich vapors 5.

14. Whitehead MC et al found that influ-trace and perfect solution may be substituted with regular formaldehyde solution to lower the concentration of formaldehyde within the cadaver vasculature.

15. As for the other alternative chemicals in place of formaldehyde, Frolich et al in 1984 had tried using phenoxy-ethanol as its non-toxic substitute. It proved to be impractical as the amount required was large i.e. about 600 litres for each cadaver, needing continuous immersion to prevent mould formation and the fixation process taking 5 to 10 months. Glutaraldehyde is an aldehyde related to formaldehyde, with similar fixation qualities. It would be a feasible alternative, but because of the volumes that would be required, it is prohibitively expensive [11].

16.It has also been proved that arterial injection is the lowest exposure procedure in the embalming operation and has the least impact on total overall exposure values, so these should be practiced during embalming. Some researcher also believes that ethanol glycerin

fixation with thymol conservation can be a potential alternative to formaldehyde and phenol embalming. (Hammer N Loffler S, 2012) [3, 5].

17. Nowadays there is a legal requirement for the use of formaldehyde in embalming fluids in the United States of America [11]. The same if possible may be brought forward in Indian subcontinent.

CONCLUSION

In spite of the adverse effects of formaldehyde fumes, knowingly or unconsciously most medical professionals either students or faculty or technicians or embalmers are repeatedly exposed to the vapors of the agent and most of the time considering the Indian scenario professionals are unaware of the toxic effects. Formaldehyde remains the most potent agent to be used as an embalming solution or to be mixed with other similar solution as its use is economical, excellent preservative and fixing solution and widely accepted antifungal agent. Hence its use should be properly monitored and embalming and dissection specialists should always take the added burden to follow the above mentioned recommendations so that the toxic effects of formalin can be reduced for the benefit of the subject of Anatomy in a broad sense. Large multiple longitudinal studies with a large sample size adopting the precautionary measures is the need of the hour.

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