

Original Article

## Effects of Formalin on Pulmonary Function Tests of Medical Students in Anatomy Dissection Laboratory

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### Summary of the manuscript

Formalin is used for preservation of cadavers in anatomy dissection laboratories which vaporizes at normal room temperature and causes respiratory problems. The present study has been conducted to assess the effects of formalin vapors on pulmonary function tests of first year medical students in the anatomy dissection hall. Sixty medical students of Rama Medical College Hospital & Research Centre, Mandhana, Kanpur; were selected for this study. The lung function tests (FVC, FEV<sub>1</sub>, FEV<sub>1</sub>%, FEF<sub>25-75</sub>, PEF and Vmax<sub>25%</sub>) using computerized spirometry, were done on four occasions; before exposure (basal), 1 month (acute effects), 6 months and 11 months (chronic effects) after exposure to formalin vapors. The results of the study showed statistically significant ( $p < 0.001$ ) decrease in values of FVC, FEV<sub>1</sub>, PEF and FEF<sub>25-75</sub> as acute effects of formalin exposure. However on chronic exposure the dynamic lung functions normalized back to basal levels within 6 to 11 months. The study reflects that formalin is a noxious chemical and an occupational hazard; causing decreased pulmonary functions in medical students exposed to formalin during anatomy dissection which on chronic exposure are restored back to basal levels by adaptive compensatory changes. Further studies are required to elucidate these compensatory mechanisms at the cellular level.

### Introduction

Formalin has been used as fixative chemical since ages for preserving cadavers and other biological specimens. It is extensively used by both medical

and dental colleges in anatomy dissection laboratory and pathology specimen museum. Formalin contains 37% of formaldehyde which readily vaporizes at room temperature. Many research papers and industrial reports have indicated that upper respiratory tract is the critical target of the toxicity of air borne formaldehyde and suggest that exposure to formaldehyde is associated with adverse effects on respiratory health (1-4). Symptoms of upper airway irritation, including, sore throat, itching, burning sensation of the nose and nasal congestions have been reported after formalin exposure (5). Formalin is also utilised by manufacturers of resins, plywood

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and leather goods however the exposure to formaldehyde among medical students and instructors in department of anatomy is continuous and higher than its use in other fields (6). In view of its widespread use and subsequent toxicity; exposure to formaldehyde is considered a significant human health hazard (7). However few studies have been carried out to study the effects of formalin vapours on pulmonary function tests of medical students especially in tropical hot and humid conditions such as that prevailing in our study area of Kanpur. Hence the main objective of this study is to evaluate the acute and chronic effects of formalin vapours on the pulmonary function tests of medical students.

## Material and Methods

The present study was carried out on 60 first year medical students (45 males and 15 females) of Rama Medical College Hospital & Research Centre, Mandhana, Kanpur for a period of one year. The study was approved by the institutional medical ethics committee of Rama Medical College, Hospital & Research Center. Students aged between 18–25 years of both gender, found medically fit after general medical examination; as per the hospital protocol were included in the study. Students with a history of smoking, any chronic respiratory disease or systemic illness like diabetes or hypertension were excluded from the study. Students with any congenital anomalies of spine and thoracic cage or any connective tissue and musculo skeletal disorders; compromising the pulmonary functions were also excluded from the study. A written informed consent was obtained from the students enrolled in the study after eligibility screening. The subjects were exposed to formalin vapors 2 hours each day in the anatomy dissection laboratory throughout the academic year (August, 2014 to August, 2015), to study both the acute and chronic effects of formalin exposure. The seasonal variations in the PFT were not evaluated in the present study; as all the PFT were scheduled in summer or monsoon season and none in the winter season as per the working protocol. Formalin at a concentration of 2-3 ppm was used in the anatomy dissection hall; which is prepared by mixing the commercially available formalin solution with tap water in the proportion of 3:1.3 (8). However the exact

concentration of formaldehyde exposure in the students could not be determined, which is one of the limitations of the study. The anthropometric measurements like height and weight were recorded and BMI was calculated. The study was carried out by 'Spiro Exel' a PC based, computerized software of Pulmonary Function Tests; providing a detailed analysis of both predicted and derived values. The subjects were familiarized with the equipment and all the measurements were done following the guidelines of the American Thoracic Society (9). In our study all the major parameters of pulmonary function tests such as Forced Vital Capacity (FVC), Forced Expiratory Volume in first second (FEV1), FEV1/FVC ratio, Forced Expiratory Flow between 25% and 75% of vital capacity ( $FEF_{25-75}$ ), Peak Expiratory Flow Rate (PEFR) including the  $V_{max_{25\%}}$  were recorded. Computer printouts with graphic curves were obtained (10). The lung function tests were repeated twice on each occasion for each subject and the maximum reading was selected for analysis. The pulmonary functions were tested on four occasions :-

- 1) Before exposure to formalin (basal levels)
- 2) 1 month of exposure to formalin (acute effects)
- 3) 6 months of exposure to formalin (chronic effects)
- 4) 11 months of exposure to formalin (chronic effects)

On each occasion clinical complaints of the students were recorded for correlation with the variations in the pulmonary function tests.

### Statistical analysis

The data was collected and subjected to statistical analysis using SPSS version 21.0. After recording the anthropometric profile and calculating the BMI, the basal values of the pulmonary function tests were compared with 1 month exposure to formalin vapors by Paired Student's t test to evaluate the acute changes. The pulmonary function test values at 1 month of formalin exposure, reflecting the acute reaction were further compared with the 6 months

and 11 months of formalin exposure to evaluate the chronic effects. Variability in all dynamic pulmonary function tests within the subjects and across the time were analyzed by repeated measures ANOVA and Post Hoc Bonferroni test. The level of significance was set at  $P < 0.05$ .

## Results

The mean anthropometric values and the mean basal values of pulmonary function test parameters of the first year medical students enrolled in our study; measured before the formalin exposure are recorded in Table-I. No clinical complaints pertaining to upper respiratory tract were recorded among the students.

All the pulmonary function test values after 1 month of formalin exposure showed statistically significant decrease as compared to the basal levels recorded before the exposure; except for  $V_{max}$  which did show

TABLE I : Anthropometric profile and basal pulmonary function test parameters (n=60).

Baseline parameters	Mean values
Age (years)	21.75±1.37
Height (cm)	170.32±10.91
Weight (kg)	71.29±14.54
BMI (kg/m <sup>2</sup> )	24.37±3.88
Basal FVC (L)	5.00±3.76
Basal FEV1 (L)	3.76±0.65
Basal FEV1%	93.75±3.79
Basal FEF <sub>25-75</sub> (L/s)	6.20±1.24
Basal PEFR (L/s)	9.49±1.89
$V_{max_{25\%}}$ (L)	5.81±2.32

Values in mean±SD.

a statistically significant decrease; as reflected in Table-II. However it was observed in our study that the decrease in the mean FVC and FEF<sub>25-75</sub> values was statistically significant with  $P < 0.01$ ; whereas the decrease in the mean FEV1, FEV1% and PEFR values was statistically highly significant with  $P < 0.001$ . The students simultaneously complained of upper respiratory tract symptoms of burning of eyes and nose, lacrimation, nasal congestion and itching of the skin.

It was observed in our study that the mean FEV1, FEV1% and FEF<sub>25-75</sub> values at 6 months and 11 months of formalin exposure reported an increase back to the basal levels (recorded before the exposure) when compared to the mean values recorded at 1 month of exposure; which was statistically highly significant ( $P < 0.001$ ). On the other hand the mean PEFR values at 6 months and 11 months of formalin exposure reported an increase which was statistically significant with  $P < 0.01$ . However the mean FVC values at 6 months – 4.14±0.72 and 11 months – 4.43±0.73 of formalin exposure; when compared to the mean values at 1

TABLE II : Comparison of pulmonary function tests before exposure and after 1 month of formalin exposure (n=60).

PFT parameters	Before exposure (basal levels)	After exposure (acute effects)
FVC (L)	5.00±3.76	3.34±0.76**
FEV1 (L)	3.76±0.65	3.02±0.61***
FEV1%	93.75±3.79	87.27±5.05***
FEF <sub>25-75</sub> (L/s)	6.20±1.24	4.94±1.01**
PEFR (L/s)	9.49±1.89	7.62±1.66***
$V_{max_{25\%}}$ (L)	5.81±2.32	4.98±2.05 <sup>NS</sup>

Values in mean±SD. \*\*= $P < 0.01$ , \*\*\*= $P < 0.001$ , <sup>NS</sup>=not significant.

TABLE III : Comparison of pulmonary function tests before and after exposure to formalin as a function of time (n=60).

Parameters	Before exposure (basal levels)	1 month of exposure (acute effects)	6 months of exposure (chronic effects)	11 months of exposure (chronic effects)
FVC(L)	5.00±3.76	3.34±0.76**	4.14±0.72 <sup>NS</sup>	4.43±0.73 <sup>NS</sup>
FEV1 (L)	3.76±0.65	3.02±0.61***	3.72±0.55 <sup>\$\$\$</sup>	3.74±0.53 <sup>\$\$\$</sup>
FEV1%	93.75±3.79	87.27±5.05***	92.87±3.57 <sup>\$\$\$</sup>	93.61±3.69 <sup>\$\$\$</sup>
FEF <sub>25-75</sub> (L/s)	6.20±1.24	4.94±1.01**	5.96±1.37 <sup>\$\$\$</sup>	6.11±1.50 <sup>\$\$\$</sup>
PEFR (L/s)	9.49±1.89	7.62±1.66***	8.81±1.89 <sup>\$\$</sup>	8.88±1.85 <sup>\$\$</sup>
$V_{max_{25\%}}$ (L)	5.81±2.32	4.98±2.05 <sup>NS</sup>	5.67±2.04 <sup>NS</sup>	5.49±2.09 <sup>NS</sup>

Values in mean±SD.\* = comparison of values with basal levels, <sup>\$</sup> = comparison with 1 month of formalin exposure values. \*\* =  $P < 0.01$ , \*\*\* =  $P < 0.001$ , <sup>\$\$</sup> =  $P < 0.01$ , <sup>\$\$\$</sup> =  $P < 0.001$ , <sup>NS</sup> = not significant.

month of exposure –  $3.34 \pm 0.76$  L; reported an increase back to the basal levels which was not statistically significant. There were no clinical complaints pertaining to upper respiratory tract among the students confirming our pulmonary function test findings.

## Discussion

The present study was conducted to evaluate the acute and chronic effects of exposure to formalin fumes in first year medical students in their anatomy dissection laboratories. It was observed in our study that the basal pulmonary function values of our students were on higher side of the normal reference range; with peak expiratory flow measurements PEFR being slightly more on the higher side (Table – I). It is seen in the literature that various reference values, specially pertaining to PEFR, have been published; which vary by population, environment, ethnic group, age, sex, height and weight of the subjects (10, 11, 12). As such, we also observe from Table – I that the mean height as well as weight (lean body mass) of our subjects is on the higher side of the normal range as compared to other Indian studies; which could be the reason why our model of study predicts higher values. Variations in the reference range of pulmonary functions, PEFR in particular and the various factors affecting it, is a subject which requires further research and evaluation.

From our study it is reflected that the pulmonary function test values after 1 month of formalin exposure showed statistically significant decrease as compared to the basal levels recorded before the exposure; except for Vmax which did not show statistically significant decrease (Table – II). The marked decrease in all the parameters of pulmonary functions as seen in our study are in accordance with the adverse tropical weather condition of Kanpur area, which is highly hot and humid with high heat index. The common clinical complaints recorded by the students after 1 month of formalin exposure included burning of eyes and nose, lacrimation, irritation of airways, nasal congestion and itching of skin.

All these findings confirm the acute adverse effects

of formalin which are caused due to broncho constriction attributed to the hypersensitivity reaction (5). The binding of formaldehyde to endogenous proteins creates haptens that can elicit an immune response. Studies have shown that exposure to formaldehyde has been associated with immunological hypersensitivity leading to distinct acute and chronic effects.

Chronic exposure to formaldehyde has been associated with immunological hypersensitivity as reflected by elevated circulating IgE and IgG autoantibodies to human serum albumin. In addition, a decrease in the proportion of T cells is observed indicating altered immunity (13).

A study done earlier by Farah Khaliq et al, reported decrease in FVC immediately after 2 hours of exposure to formalin, indicating broncho constriction on acute exposure to formalin. A decrease in values of FEV1 immediately after exposure was observed but it was not statistically significant (5). Akbar-Khanzadeh et al, evaluated acute pulmonary response in group of 34 workers exposed to formalin in gross anatomy dissection hall; they also reported decrease in FVC but FEV1/FVC ratio increased during exposure (14). In another study by Kilburn KH et al, histology technicians were shown to have reduced pulmonary function, as measured by FVC, FEV1 and FEF<sub>25-75</sub> compared with controls (15).

Contrary to the present study Chia et al; studied 150 first-year medical students exposed to formaldehyde during the dissection of cadavers in a gross anatomy laboratory and reported no significant differences in the pre- and post-exposure mean FEV1 and FVC (16).

However Wei et al revealed that subjective symptoms were related to the period spent in the anatomy dissection hall. 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 symptom (17). There have been an increasing number of reports of students suffering from various clinical symptoms including burning of eyes, lacrimation, irritation of airways and dermatitis; which has a higher prevalence during gross anatomy dissection period (18).

It was also observed in the present study that the mean FEV<sub>1</sub>, FEV<sub>1</sub>% and FEF<sub>25-75</sub> values at 6 months and 11 months of formalin exposure reported an increase back to the basal levels when compared to the mean values recorded at 1 month of exposure; which was statistically highly significant ( $P < 0.001$ ) as depicted in Table – III. The mean FVC values at 6 months and 11 months of formalin exposure also reported an increase back to the basal levels but were not statistically significant. No clinical complaints were recorded at 6 and 11 months of exposure, confirming the pulmonary function test findings. It is reflected from these findings that the long term exposure to formalin results in desensitization of the subjects which can be attributed to some adaptive compensatory changes in the respiratory system. It is also suggested that the broncho constriction caused in the acute phase is only mild and transient thus confirming the dynamic nature of pulmonary function parameters (19). In a similar study, Shrivastava and Saxena observed decrease in FEV<sub>1</sub> on acute exposure to formalin but it was not statistically significant however the basal values were restored after 11 months of exposure to formalin vapours; which are in affirmation to the results of our study (20). However the mechanisms involved in the reversal of the pulmonary functions back to normal levels after chronic exposure are yet to be elucidated.

Occupational data suggests that only small but significant changes may occur in lungs following prolonged exposure in the work place (21). A prospective study by Alexanderson R et al, evaluating the lung function tests and immunoglobulin levels have reported significant decrease in FVC, FEF<sub>25-75</sub> and FEV<sub>1</sub>% in wood worker who were exposed to formaldehyde since 4 years, however these decrements returned to normal after 4 weeks of non exposure showing reversibility of pulmonary function tests following cessation of exposure (19). Meanwhile in another study by Malaka T et al, the effect of formaldehyde exposure in plywood workers resulted in significantly reduced FEV<sub>1</sub>, FEV<sub>1</sub>/FVC ratio, FEF<sub>25-75</sub> but not FVC (22). Studies in rats and mice using high concentration of formaldehyde over an extremely long period have reported to result in squamous carcinoma of nose (23). Formaldehyde at

relatively high exposure doses may also precipitate bronchial asthma. Therefore the approach to formaldehyde-induced symptoms should be one of careful documentation of objective physiologic changes (24). Studies have found formaldehyde to be toxic, allergenic, and carcinogenic (25). The formaldehyde production is increasing worldwide due to its wide spread use, but due to its toxicity and carcinogenic properties many European countries have restricted its use and import and have recently banned its use as a biocide (including embalming) under the Biocidal Products Directive (26, 27).

For the numerous health challenges that formaldehyde causes on the students in anatomy dissection hall, it cannot be considered as an ideal chemical for embalming of cadaver. However the increased formaldehyde fumes in the dissection rooms and embalming rooms are due to; 1) poor working practices leading to spillages of fluid during embalming, 2) poor condition of cadavers causing embalming fluid to leak out of the cadaver, 3) using high concentrations of formaldehyde in the embalming fluid, and 4) poor ventilation of dissection rooms. Medical students, teachers and laboratory technicians are exposed to formaldehyde fumes on regular basis during the daily dissection schedules; they should be informed of potential health hazards of formalin. Attempts should be done to reduce the concentration of formaldehyde and by using other chemicals like glutaraldehyde, which can serve a good substitute for formaldehyde (28). As quoted by BS Mitchell "Reduction in formaldehyde concentration is not deleterious to specimen preservation, but leads to a safer working environment" (29). Despite its toxic effects formaldehyde remains the popular choice as a tissue fixative because of its undoubted efficiency, and consistency of results that are obtained. Thus by decreasing the concentration of formalin in standardized cadaver embalming fluid and improving the ventilation of our dissection laboratories improved we can eliminate about 90% of the ill effects of embalming formalin (8). The present study also paves the way for further studies on chronic effects of formalin especially understanding the adaptive compensatory changes taking place in the respiratory system at the cellular level.

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