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Effects of formaldehyde inhalation on cardiopulmonary functions on medical students of College of Health Sciences, Nnamdi Azikiwe University during dissection classes

Okonkwo Chukwudi Onyeka[1], Metu Stephanie Chiemerie[1], Maduka Stephen Ozoemena[2], Oguaka Victor Nwabunwanne[2]

[1]Department of Human Physiology, Faculty of Basic Medical Sciences, College of Health Sciences, Nnamdi Azikiwe University, Nnewi, Nigeria

[2]Department of Human Biochemistry, Faculty of Basic Medical Science, College of Health Sciences, Nnamdi Azikiwe University, Nnewi, Nigeria

ABSTRACT

Background/Aim: Formaldehyde (FA) is the simplest aldehyde and is also known as methanol or formalin. It is used for preservation of cadavers in anatomy dissection laboratories which vaporizes at normal room temperature. The present study has been conducted to assess the effects of FA vapor on cardiopulmonary functions of medical students in the anatomy dissection hall.

Subjects/Methodology: Sixty medical students of College of Health Sciences, Nnamdi Azikiwe University, Okofia, Nnewi were randomly selected for this study. The cardiac function tests [blood pressure (BP) and heart rate (HR)] were done using electronic sphygmomanometer and the lung function tests (Tidal Volume (VT), Vital Capacity (VC), Forced Expiratory Volume (FEV1) and Flow Volume Loop (FVL)) were done using electronic spirometry, three times after exposure to FA vapor.

Results: The results of the study showed statistically significant ($p < 0.05$) decrease in values of Forced Vital Capacity (FVC), FEV1, and Forced Vital Time (FVT), also, the result showed statistically significant increase in systolic BP and statistically insignificant ($p > 0.05$) increase in HR and decrease in diastolic BP and FEV% as acute effects of FA exposure.

Conclusion: This study reflects that FA is a noxious chemical and an occupational hazard; causing decreased pulmonary functions in medical students exposed to formalin during anatomy dissection. Further studies are required to elucidate these compensatory mechanisms.

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KEYWORDS

Formaldehyde; cardiopulmonary function; respiratory status

Introduction

Formaldehyde (FA) (H_2CO), the simplest aldehyde [1], existed in the pre-biological atmosphere of the primordial earth [2] and is also present in the outer galaxies [3]. FA is a water soluble, colorless, pungent, irritating, and highly reactive gas. Forty percent solution of FA in water is known as formalin [4,5]. This compound was first described in 1855 by Alexander Butlerov, while its chemical synthesis by methanol dehydration was first achieved in 1867 by August Wilhelm von Hofmann [6]. More than 46 billion pounds of FA is produced worldwide annually [7] and is mostly used widely in construction, textile, household furniture, productions, medicals, disinfectants, chemical, and pharmaceutical industries. FA heavily impacts on everyday consumer and is produced endogenously in all living organism, including humans, but exposure to ubiquitous exogenous sources such as indoors, outdoors, at work, in residents, in food, and medicine poses a significant threat to public health [8].

In medicine, formalin is used in the preservation of surgical specimens, for the treatment of uncontrolled intravesical hemorrhage [9,10] and

Contact Okonkwo Chukwudi O. ✉ profonyekaokonkwo@yahoomail.com Department of Human Physiology, Faculty of Basic Medical Sciences, College of Health Sciences, Nnamdi Azikiwe University, Nnewi, Nigeria.

radiation induced hemorrhagic proctitis [11–16] and cystitis, and to prevent hydatid cysts dissemination [17]. It is also a physiological intermediary metabolite in mammals. The endogenous FA is rapidly metabolized to formate or enters the one carbon pool via tetrahydrofolate [4]. Formate, as the sodium salt, is one of the simplest endogenous forms of carbon in man and is the intermediate in many anabolic and catabolic reactions. Formate or FA has been shown to be involved in single carbon transfers from many essential amino acids including glycine, histidine, tryptophan, and serine and in the synthesis of purines, pyrimidines, methionine, and cholase [18]. It is a noxious, flammable gas, extremely soluble in water.

FA is a colorless (at room temperature) [19] irritant which gives out pungent FA vapors and is widely used in the medical field as fungicide, germicide, disinfectant, and preservative solution [20]. The toxic effects of FA exposure can be classified as follows: irritation of mucous membrane, contact dermatitis, teratogenicity, and carcinogenicity. Excess exposure to exogenous FA can induce carcinogenesis and cardiovascular dysfunction, possibly due to the formation of DNA–protein crosslinks [21]. 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 1 ppm [22,23]. 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 [23].

Adverse effects of inhaling FA become more as the concentration level of it increases [23]. The common symptoms from acute exposure to formalin manifest as irritation of the throat, nose, eyes, and skin [24]. It can also cause neurophysiologic effects, irritation of upper respiratory tract which can potentially exacerbate asthma symptoms and other respiratory illnesses, and also, dyspnea, coughing, burning of nose, eyes, and pharynx [24]. Chronic exposure can cause bronchitis and pneumonia [24]. FA has been reported to cause an assortment of acute and chronic health effects [25]. Due to its high water solubility, more than 95% of inhaled FA is absorbed in the upper respiratory tract [26,27] and very little FA, if any, will reach the alveolar membranes of the lungs [28]. The toxic effects of FA on the upper respiratory tract are described as an irritant and as a sensitizer [25].

When it is swallowed, it can result in sudden death [24]. It is well known that FA can cause sick house syndrome (sick building syndrome) which is characterized by mucosal irritation, headache, nausea, and chest symptoms [29]. FA is also a hapten and formaldehyde–protein complex which may be immunogenic [20]. Several animal studies found that long-term exposure to FA could enhance bronchial responsiveness in rodents [30,31].

In this study, students are exposed to FA during dissection class to estimate its effect on their cardiopulmonary functions.

Materials/Subjects and Methods

Materials

The materials used in this experiment include:

Sixty students

Spirometer

Electronic sphygmomanometer

Cotton swab

Weighing balance

Meter rule

Sample size

The sample size calculation formula by Fischer was used to calculate sample size [32];

$$n = Z^2\, p\, (1 - p)/d^2$$

Where n = sample size

Z = Z statistic for a level of confidence

P = expected prevalence or proportion (in proportion of one; if 20%, p = 0.2), and

d = precision or margin of error (in proportion of one; if 5%, d = 0.05).

Z = 95% (1.96)

p = 4% (0.04)

d = 5% (0.05)

$$1.96^2 \times 0.04\ (1 - 0.04)/0.05^2 = 59.00.$$

Research location

This research project was carried out during dissection class in College of Health Sciences, Nnamdi Azikiwe University Okofia, Nnewi Campus, Anambra State, Nigeria.

Human subjects

Thirty students (male & female) volunteered and took part in my research work during dissection class in College of Health Sciences-Nnewi, Anambra State serving as the test group. Also, another 30 students (male & female) volunteered assisted in my research work serving as the control group.

Table 1. Shows the anthropometric parameters of the control group in this study.

	N	Minimum	Maximum	Mean ± SD
Age (Years)	30	18.00	27.00	22.40 ± 1.99
Weight (kg)	30	42.00	83.00	63.36 ± 9.11
Height (m)	30	1.56	1.93	1.72 ± 0.08
BMI (kg/m^2)	30	26.90	46.60	36.58 ± 3.27
SBP (mmHg)	30	101.00	140.00	118.96 ± 10.20
DBP (mmHg)	30	56.00	91.00	73.60 ± 7.35
Heart rate (bpm)	30	52.00	101.00	78.86 ± 11.00

SD = standard deviation.

Table 2. Shows the anthropometric parameters of the test group in this study.

	N	Minimum	Maximum	Mean ± SD
Age (Years)	30	17.00	22.00	19.56 ± 1.19
Weight (kg)	30	60.00	94.00	69.83 ± 6.95
Height (m)	30	1.56	1.83	1.71 ± 0.07
BMI (kg/m^2)	30	35.60	46.00	40.69 ± 4.20
SBP (mmHg)	30	96.00	147.00	113.30 ± 10.70
DBP (mmHg)	30	61.00	97.00	74.13 ± 7.11
HR (bpm)	30	54.00	92.00	75.40 ± 9.98

SD = standard deviation.

Groups

The 60 students were grouped into two, test group consisting of male and female students and control group consisting of male and female students.

Exposure to formaldehyde

The control group has never been exposed to FA. Meanwhile, the test group was exposed to FA for 6 hours per week for a period of 6 months. The exposure was done in the dissection room.

Estimation of cardiopulmonary functions

The cardiopulmonary functions, blood pressure (BP), heart rate (HR), Forced Expiratory Volume (FEV1), Forced Vital Capacity (FVC), Forced Vital Time (FVT), and FEV%, provide the information on the cardiopulmonary state of the subjects used in this study.

Procedure

BP and HR of the subjects were measured using electronic sphygmomanometer, afterwards the subjects blew into the mouthpiece of the spirometer for three times (FEV1, FVC, and FVT) while their data were recorded. The mean of the pulmonary parameters was later calculated. This was done for all the 60 subjects.

Calculation

FEV% = FEV1/FVC

Body Mass Index (BMI) = Weight (kg)/Height (m^2).

Statistical analysis

Data were analyzed using SPSS version 23. This was done using the one-way analysis of variance. The results were subjected to descriptive statistics. An independent *T*-test was used in comparing the control group and test group of the cardiopulmonary functions [systolic blood pressure (SBP), diastolic blood pressure (DBP), FEV1, FVC, FVT, and FEV%]. Gender differences between the test groups. Data were considered significant at $p < 0.05$.

Results

Table 1 shows the anthropometric parameters of the control group in this study. Result from the Table 1 revealed the anthropometric data of the control group in this study. The minimum and maximum age for this study was between 18 and 27 years with a mean of 22.40 ± 1.99, the weight of the participants was between 42.00 and 83 kg with a mean of 63.36 ± 9.11, the height was between 1.56 and 1.93 m with a mean of 1.72 ± 0.08, the BMI was between 26.90 and 46.00 kg/m^2 with a mean of 36.58 ± 3.27, the SBP was between 101.00 and 140 mmHg with a mean of 118.96 ± 10.20, DBP was between 56.00 and 91.00 mmHg with a mean of 73.60 ± 7.35, and the HR was between 52 and 101 bpm with a mean of 78.86 ± 11.00.

Table 2 shows the anthropometric parameters of the test group used in this study. Result from the Table 2 revealed the anthropometric data of the test group in this study. The minimum and maximum age

Table 3. Shows comparison between control and test group of cardiopulmonary functions (FEV1, FVC, FEV%, FVT, SBP, DBP, and HR).

Cardiopulmonary parameters	Control	Test group	*P*-value	*T*-value
	Mean ± SD	Mean ± SD		
HR (BPM)	75.40 ± 9.98	78.86 ± 11.00	0.206	0.698
SBP (mmHg)	113.30 ± 10.70	118.96 ± 10.20	0.040*	0.546
DBP (mmHg)	74.13 ± 7.11	73.60 ± 7.35	0.776	0.285
FVT	1.39 ± 0.44	1.03 ± 0.44	0.002*	0.714
FVC (L)	1.45 ± 0.45	0.82 ± 0.43	0.000*	5.436
FEV1 (L)	1.35 ± 0.36	0.83 ± 0.40	0.000*	5.227
FEV%	1.00 ± 0.30	0.94 ± 0.19	0.363	0.916

SD = standard deviation.

Table 4. Shows comparison of gender in test group of cardiopulmonary functions (FEV1, FVC, FEV%, FVT, SBP, DBP, and HR).

Cardiopulmonary parameters	Gender	Mean ± SD	*P*-value	*T*-value
FEV1	Male	1.01 ± 0.43	0.010*	2.747
	Female	0.65 ± 0.27		
FVC	Male	1.07 ± 0.48	0.001*	3.805
	Female	0.58 ± 0.13		
FVT	Male	1.20 ± 0.51	0.031*	2.277
	Female	0.86 ± 0.27		
FEV%	Male	0.87 ± 0.26	0.053	
	Female	1.01 ± 0.01		-2.016
SBP	Male	124.60 ± 11.09		
	Female	113.3 ± 4.98	0.001*	3.588
DBP	Male	74.40 ± 9.80		
	Female	72.80 ± 3.80	0.560	0.589
Heart rate	Male	76.86 ± 12.86		
	Female	80.86 ± 8.74	0.328	-0.996

SD = standard deviation.

for this study was between 17 and 22 years with a mean of 19.56 ± 1.19, the weight of the participants was between 460.00 and 94.00 kg with a mean of 69.83 ± 6.95, the height was between 1.56 and 1.83 m with a mean of 1.71 ± 0.07, the BMI was between 35.60 and 46.00 kg/m^2 with a mean of 40.69 ± 4.20, the SBP was between 96.00 and 147.00 mmHg with a mean of 113.30 ± 10.70, DBP was between 61.00 and 97.00 mmHg with a mean of 74.13 ± 7.11, and the HR was between 54 and 92 bpm with a mean of 75.40 ± 9.98.

Table 3 displays the comparison between the control and the test groups for cardiopulmonary functions (FEV1, FVC, FEV%, FVT, SBP, DBP, and HR). Data were analyzed using student independent *T*-test for comparing the control group with the test group and values were considered significant at $P < 0.05$. (Figures 1 and 2). *$P < 0.05$ means significant and $P > 0.05$ means not significant. Result from the study revealed that there was an insignificant increase in HR when comparing the control group (75.40 ± 9.98) to the test group (78.86 ± 11.00). For SBP, there was a significant increase when comparing the control group (113.30 ± 10.70) to the test group (118.96 ± 10.20). For DBP, there was an insignificant decrease when comparing the control group (74.13 ± 7.11) to the test group (73.60 ± 7.35). (These are shown in figure 1). For FVT, there was a significant decrease when comparing the control group (1.39 ± 0.44) to the test group (1.03 ± 0.44). For FVC, there was a significant decrease when comparing the control group (1.45 ± 0.45) to the test group (0.82 ± 0.43). For FEV1, there was a significant decrease when comparing the control group (1.35 ± 0.36) to the test group (0.83 ± 0.40). For FEV%, there was an insignificant decrease when comparing the control group (1.00 ± 0.30) to the test group (0.94 ± 0.19). (See figure 2).

Table 4 shows the comparison between the performances of the males and the females of test group for cardiopulmonary functions (FEV1, FVC, FEV%, FVT, SBP, DBP, and HR). Data were analyzed using student independent *T*-test for comparing

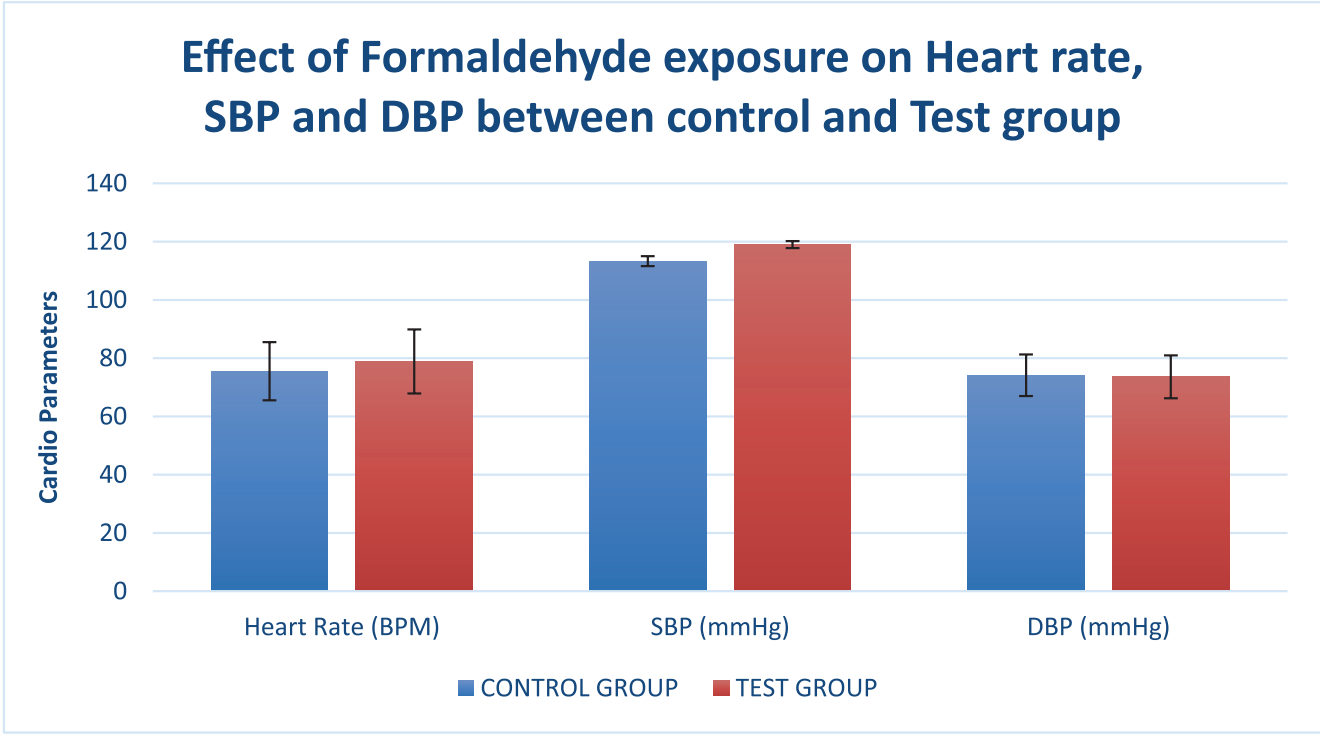

Figure 1. Bar chart showing the effects of FA exposure on the HR, SBP, and DBP between the control and test groups.

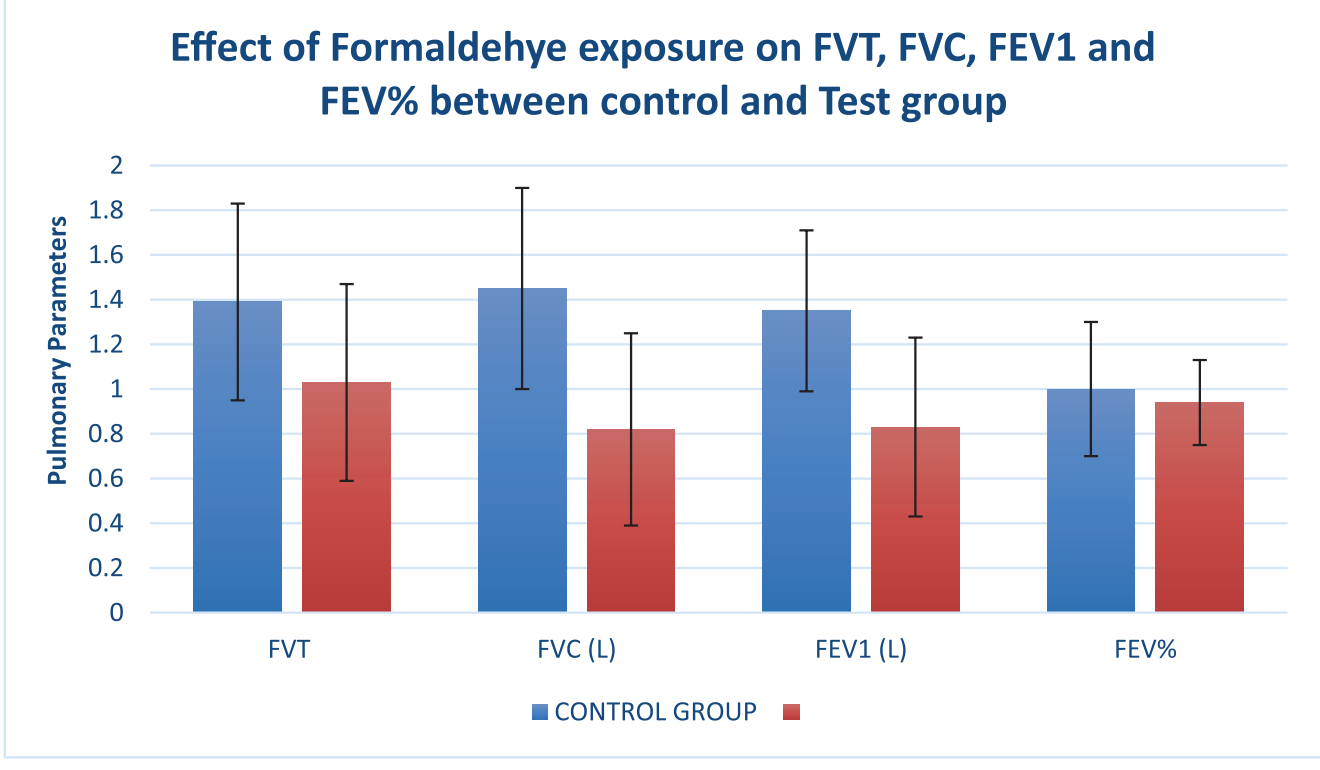

Figure 2. Bar chart showing the effects of FA exposure on FVT, FVC, FEV1, and FEV% between control and test groups.

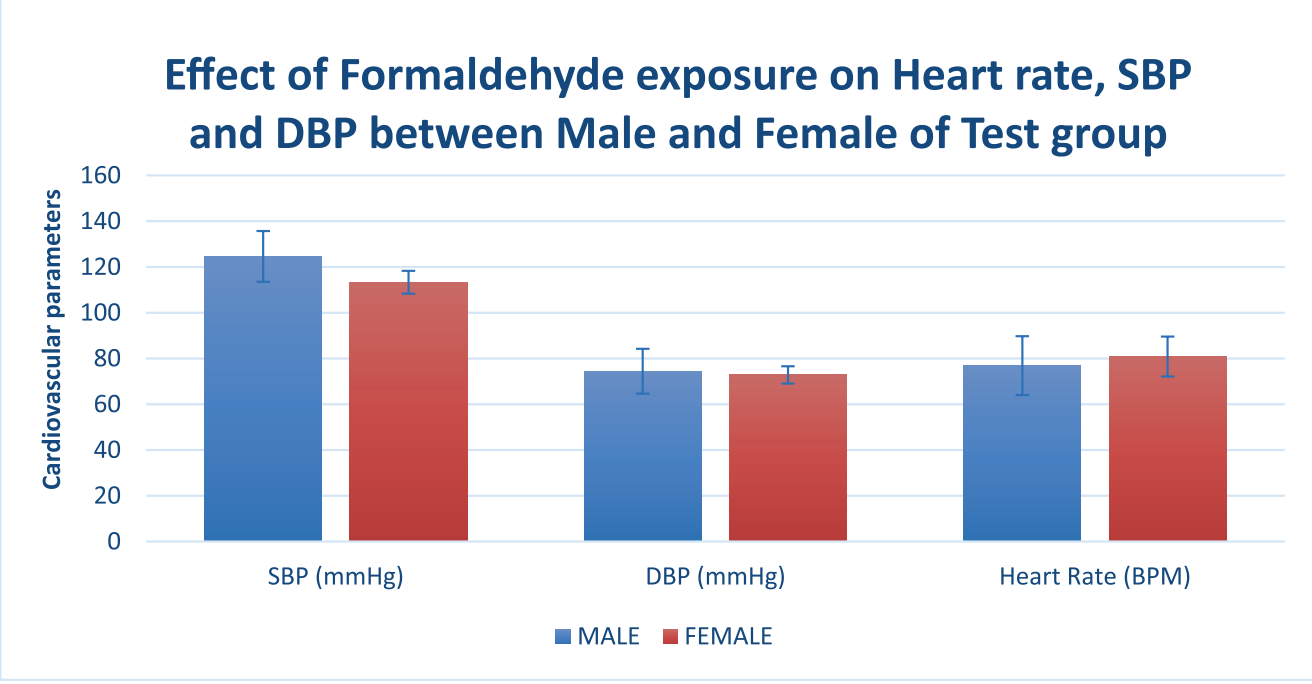

Figure 3. Bar chart shows the effect of FA exposure on HR, SBP, and DBP between the male and female of test groups.

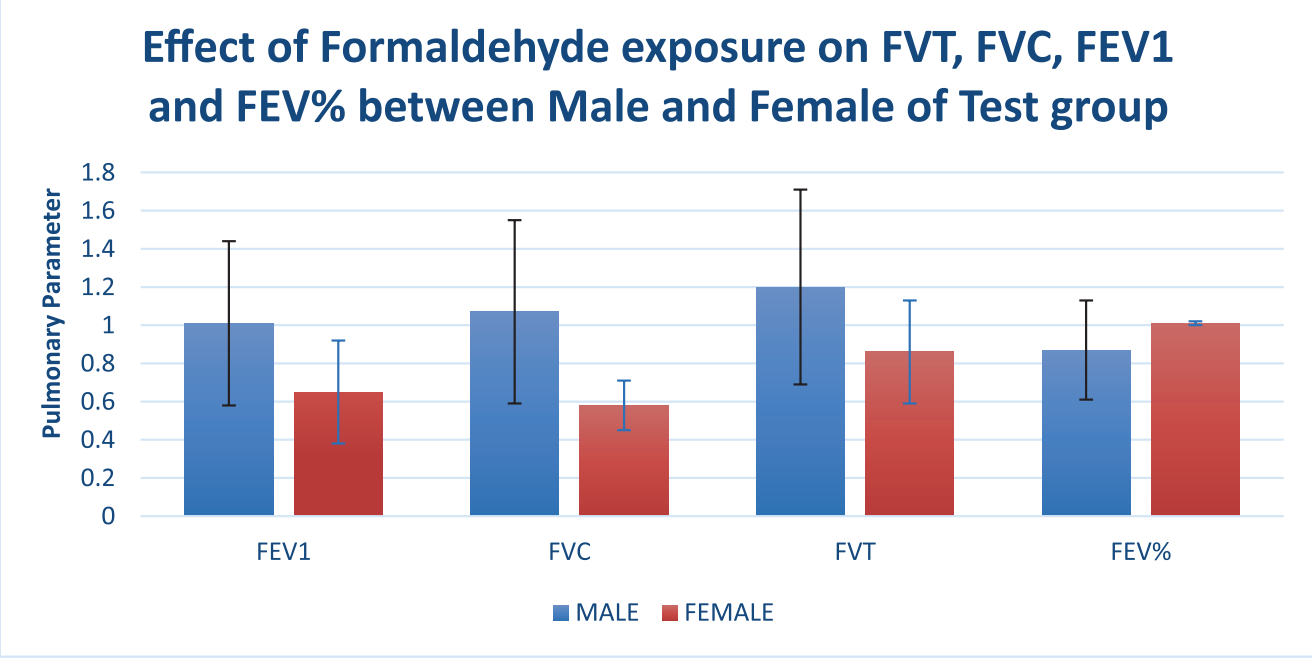

Figure 4. Bar chart shows the effects of FA exposure on FVT, FVC, FEV1, and FEV% between male and female of test groups.

the control group with test group and values were considered significant at $P < 0.05$. *$P < 0.05$ means significant and $P > 0.05$ means not significant. (These are represented in figures 3 and 4). Result from Table 4 showed that there was a significant decrease in FEV1 when comparing male (1.01 ± 0.43) to female (0.65 ± 0.27). For FVC, there was a significant decrease when comparing male (1.07 ± 0.48) to female (0.58 ± 0.13). For FVT, there was a significant decrease when comparing male (1.20 ± 0.51) to female (0.86 ± 0.27). For FEV%, there was an increase when comparing male

(0.87 ± 0.26) to female (113.3 ± 4.98), but was not significant. For SBP, there was a significant decrease when comparing male (124.60 ± 11.09) to female (113.3 ± 4.98). For DBP, there was an insignificant decrease when comparing male (74.40 ± 9.80) to female (72.80 ± 3.80). For HR, there was an insignificant increase when comparing male (76.86 ± 12.86) to female (80.86 ± 8.74). (See figure 3).

Discussion

FA (HCHO) is the gas produced by the oxidation of methyl alcohol. It is colorless and flammable with a strong pungent odor. FA is extremely soluble in water and the aqueous solution containing some 37% FA is called formalin. Commercially available formalin is generally a solution containing 37% FA together with some 10%–15% methanol to inhibit polymerization [33]. It is used for disinfection or sterilization of instruments used for medical purposes. It is also used as a preservative of biological specimens as well as cadavers. Medical students during their dissection course are exposed to FA, whose exposure is recently considered to be one of the causes of multiple chemical sensitivity.

The cardiopulmonary functions; SBP, DBP, FEV1, FVC, FVT, and FEV% were used to provide information on the cardiac and pulmonary state of students that volunteered in this study after an exposure of 6 hours per week for a period of 6 months. The present study was conducted to evaluate the effects of exposure to FA on the first year medical students in anatomy dissection laboratory. From this study, it showed a statistically significant increase ($P < 0.05$) in the SBP, significant decrease in FVC, FEV1, & FVT and insignificant increase ($P > 0.05$) in HR, insignificant decrease in DBP, and FEV% when compared to control group. (figures 1 and 2). The common clinical complaints recorded by the students after FA 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 FA which are caused due to bronchoconstriction attributed to the hypersensitivity reaction [34]. The binding of FA to endogenous proteins creates haptens that can elicit an immune response. Studies have shown that exposure to FA has been associated with immunological hypersensitivity leading to distinct acute and chronic effects. Chronic exposure to FA has been associated with immunological hypersensitivity as reflected by elevated circulating IgE and IgG auto antibodies to human serum albumin. In addition, a decrease in the proportion of *T* cells is observed indicating altered immunity [35]. A study done by Khaliq & Tripathi, reported decrease in FVC immediately after 2 hours of exposure to formalin, indicating bronchoconstriction on acute exposure to formalin. A decrease in values of FEV1 immediately after exposure was observed but it was not statistically significant [34].

A study showing evaluated acute pulmonary response in group of 34 workers exposed to FA in gross anatomy dissection hall; also reported decrease in FVC but FEV1/FVC ratio increased during exposure [36]. In another study, histology technicians were shown to have reduced pulmonary function, as measured by FVC, FEV1, and FEF25–75 compared with controls [37]. Contrary, to the present study, a study of 150 first-year medical students exposed to FA during the dissection of cadavers in a gross anatomy laboratory showed no significant differences in the pre- and post-exposure mean FEV1 and FVC [38]. 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 [39]. There have been an increasing number of reports of students suffering from various clinical symptoms including burning of eyes, lacrimation, and irritation of airways and dermatitis; which has a higher prevalence during gross anatomy dissection period [40].

The results of this study showed that respiratory function did not remain constant in the exposed group nor in the control group. It has been recognized that the variables in respiratory function are influenced by factors such as variabilities in the measurement, the observer, or the study subject [41]. In this study, the time of day during which the tests were performed was standardized, the instruments were maintained and calibrated properly, and the tests were carried out by a single observer. This procedure was expected to have minimized the influence of undesirable factors. Interestingly, changes in respiratory function are also related to circadian or diurnal variations [42,43]. The present study evaluated the respiratory function of subjects between 8:00 and 11:00 AM, between 1:00 and 3:00 PM, therefore, the increase in the respiratory function at 1 and 3 hours through the experiment in both the exposed and the control groups may be explained by the circadian variation.

A study found significant decrease in HR after exposure which could be due to direct effect of formalin on cardiac function [44]. These reflex reactions are derived from sympathetic nervous activity rather than parasympathetic nervous activity, and the reflex bradycardia could be caused by inhibiting the transmitter release at the adrenergic nerve [45]. A research using rat model concluded that the formalin caused cardiac failure possibly mediated by impaired calcium handling in excitation–contraction coupling mediated through the sarcoplasmic reticulum which could decrease cardiac contractility and reduced SBP [46]. It was speculated that as a result of this that there is increased end systolic volume which in turn increases back pressure and peripheral resistance leading to rise in DBP [44].

This study showed that FA fumes have cardiopulmonary effect on individuals. It also paves the way for further studies on chronic effects of FA especially understanding the adaptive compensatory changes taking place in the respiratory system. Those exposed to FA occupationally and non-occupationally are at the risks of FA adverse effects.

Recommendation

FA been a major environmental toxicant can lead to cardiopulmonary disturbances and dysfunction. Preventive measures should be taken for those who are occasionally exposed to FA. Also, research should be carried out to find out another alternative substance that can replace FA due to its effects.

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