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Effect of Periodic Exposure to Formaldehyde in the Anatomy Laboratory on some Plasma Protein Levels in Male Wistar Rats

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ABSTRACT: The objective of this paper is to evaluate the effect of periodic exposure to formaldehyde in the anatomy laboratory on some plasma protein levels in male Wistar rats using appropriate standard procedures. Data obtained showed that formaldehyde air level were 0.06±0.00 ppm (*parts per million*) at the control site, 0.47±0.02 ppm in the dissection hall on non-dissection days, and 1.95±0.02 ppm in the dissection hall on dissection days. Plasma levels of albumin, globulin and fibrinogen were 4.76±0.13 g/l, 3.12±0.07 g/l and 1.04±0.16 g/l respectively on non-dissection days and 5.06±0.07 g/l, 3.24±0.06 g/l and 1.18±0.18 g/l respectively on dissection days. Results revealed significant increase in the atmospheric levels of formaldehyde in the dissection hall but the plasma protein levels showed no significant difference. In conclusion, exposure to formaldehyde in the Anatomy laboratory may not affect plasma protein levels in Wistar rats.

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Formaldehyde is utilized in industrial applications like the manufacture of phenol-formaldehyde, melamine-formaldehyde, urea-formaldehyde and polyacetal resins (IARC, 2006). These resins can be used as adhesives when manufacturing particle board, plywood, furniture, fiber board and other products derived from wood (IARC, 2006; Gerberich and Seaman, 2004). One prominent use of formaldehyde is fixing of tissues which are relevant for microscopic and histological studies and it is also important in embalming human and animal remains thereby preventing them from undergoing decomposition. Thus, the use of formaldehyde finds relevance in the histopathology laboratories, mortuaries and Anatomy laboratories (IARC, 2006). Medical students are required to go through the Anatomy laboratory amongst other laboratories in the course of their training and the atmospheric levels of formaldehyde has been reported to be higher in the Anatomy laboratory when compared to other laboratories in a tertiary institution where medical students are trained (Ebojele and Iyawe, 2021). Formaldehyde has been reported to produce some undesirable effects especially in the respiratory system in humans (Patil *et al.,* 2012; Neginhal *et al.,* 2013; Shrivastava and Saxena, 2013; Ebojele and Iyawe, 2023). Available studies on acute occupational exposure in humans revealed clinical symptoms like skin irritation, eye soreness, nose irritation, throat irritation and rhinorrhea as well as reduction in pulmonary function like Forced Vital Capacity (FVC), Forced Expiratory Volume in one second (FEV_1), Peak Expiratory Flow

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Rate (PEFR) and FEV_1/FVC ratio (Khamgaonkar and Fulare, 1991; Kim *et al.,* 1999; Pourmahabadian *et al.,* 2006; Wei *et al.,* 2007). Some animal studies have reported oxidative stress in the liver and evidence of lipid peroxidation for exposures as high as 8 *part per million* (Petushok, 2000; Sogut *et al.,* 2004). Some researchers have tried to look at possible effects of formaldehyde on the central nervous system (Usanmaz *et al.,* 2002; Aslan *et al.,* 2006; Sarsilmaz *et al.,* 2007) as well as the reproductive system (Ozen *et al.,* 2005; Zhou *et al.,* 2006). Medical Students of a tertiary institution where this present study was carried out are usually exposed to the Anatomy laboratory where they carry out dissection for eight hours every week, that is, twice a week for a duration of four hours each. Will this periodic weekly exposure to the Anatomy laboratory have any effect on the plasma protein levels of the Medical Students? This periodic exposure to the Anatomy laboratory was mimicked in Wistar rats and they were exposed for five months to see if there will be any adverse effect of formaldehyde on plasma protein levels. Hence, the objective of this paper is to evaluate the effect of periodic exposure to formaldehyde in the anatomy laboratory on some plasma protein levels in male Wistar rats.

MATERIALS AND METHODS

Experimental animals: Fifteen male Wistar rats of comparable age weighing between 180-220g were procured from the animal house of the Department of Anatomy, University of Benin. The animals were kept in plastic cages with wire mesh floor and allowed to acclimatize for a period of two weeks on normal feeds and water before the commencement of the experiments. Animal management and experimental protocols were carried out in accordance with the recommendations of the 1996 Guide for the Care and Use of Laboratory Animals (Clark *et al.,* 1997).

Animal grouping: The rats were divided into three groups (A, B and C) with five animals in each group. Group A served as the control with nil exposure while groups B and C served as the test group. Group B animals were exposed to formaldehyde in the dissection room on non-dissection days for eight hours per week for a duration of five months while Group C animals were exposed to formaldehyde in the dissection room on dissection days for eight hours per week which was also equivalent to the period medical students spend in the anatomy laboratory during dissection and this was also carried out for a duration of five months.

Measurement of atmospheric levels of formaldehyde: Atmospheric levels of formaldehyde was measured using Formaldehyde Gas Meter (EXTECH FM200). The meter is automated, calibrated and has an external probe that detects the air levels of formaldehyde. Five measurements were taken on five different occasions at the control site and in the dissection hall on dissection days and non-dissection days and the average was calculated and taken as the air exposure level. Within the dissection hall, the measurements were taken around the dissection table to get an idea of the personal exposure, and three meters away from the dissection table to get an idea of the area exposure. Measurements were also taken at the different corners of the laboratory. The formaldehyde air levels were measured in *part per million* (ppm). The meter also gave measurement of the room temperature and the relative humidity.

Sample collection and analysis: Blood samples from the animals were collected through cardiac puncture as described by D'Armour *et al.* (1965). The blood samples were transferred into plain containers and were centrifuged at 2500rpm for five minutes to obtain the serum for biochemical analysis. Standardized diagnostic kits (Randox® by Randox laboratories Ltd, United Kingdom) were used for spectrophotometric (INICO® 1200 Spectrophotometer) determination of total protein and albumin as described by Tietz (1995).

Statistical analysis: Statistical analysis was done using Graph pad prism version 5.0. Results was presented as Mean ± SEM. Analysis of Variance was used to compare the means of test and control values while post hoc test was done using Student Newman Keul's test and a p-value of less than 0.05 was considered as statistically significant.

RESULTS AND DISCUSSION

Formaldehyde air level of control site and dissection room is shown in Table 1. There was a significant increase ($p<0.05$) in formaldehyde air level in the dissection room both on the dissection days and non-dissection days. Total protein, Albumin, Globulin and Fibrinogen concentrations showed no significant difference (Figures 1-4).

The atmospheric level of formaldehyde in the Anatomy laboratory measured in this present study was 1.95 *part per million* on dissection days and 0.47 *part per million* on non-dissection days (Table 1). This is a reflection of the amount of formaldehyde that the medical students are exposed to each week when they come into the Anatomy laboratory to carry out dissection..

Table 1: Formaldehyde air level, room temperature and relative humidity of control site and dissection room

Parameters	Control site	Dissection room on non-dissection days	Dissection room on dissection days	P-value
Formaldehyde air level (ppm)	0.06±0.00	0.47±0.02*	1.95±0.02*	0.0001
Room temperature (℃)	30.32±0.08	29.42±0.10*	30.06±0.23	0.0039
Relative humidity (%)	73.40±0.71	76.36±0.12	76.14±1.27	0.0518

Significant values are Mean ± SEM compared to control (* = P<0.05)

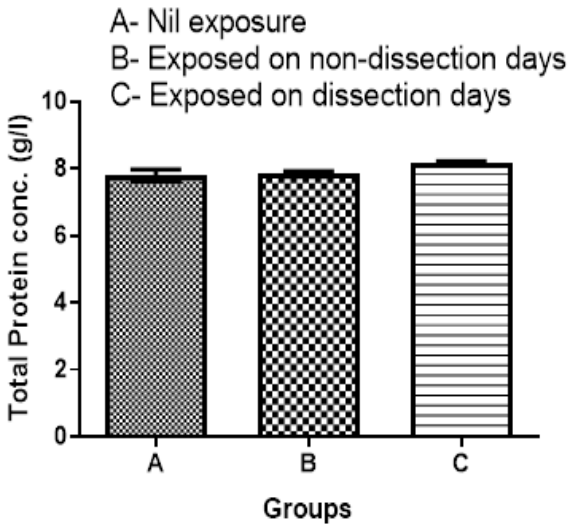

Figure 1 - Mean serum total protein concentration (g/l) of Wistar rats following periodic exposure to formaldehyde

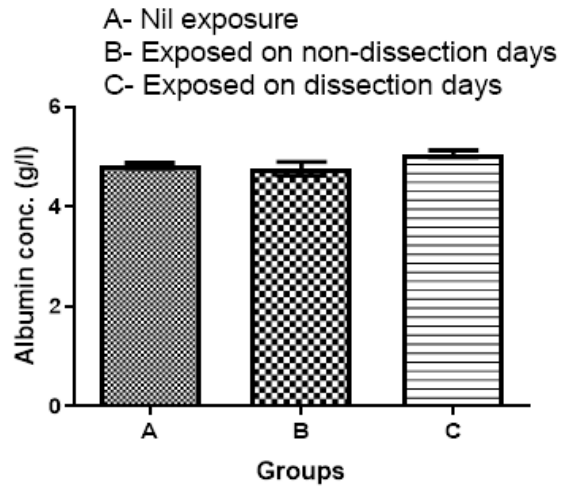

Fig 2: Mean serum albumin concentration (g/l) of Wistar rats following periodic exposure to formaldehyde

When Wistar rats were exposed to this same amount of formaldehyde that the medical students are exposed to we saw that Total protein, Albumin, Globulin, and Fibrinogen concentrations were not affected at this exposure level. This therefore suggests that periodic exposure to formaldehyde in the Anatomy laboratory may not have adverse effect on plasma protein levels in Wistar rats. In some studies carried out in rats formaldehyde was reported to produce oxidative stress in the liver (Petushok, 2000; Sogut *et al.,* 2004). The authors also reported evidence of lipid peroxidation among rats exposed to as high as 8 *part per million* of formaldehyde. In this present study, air exposure level to formaldehyde for group B rats exposed on non-dissection days was 0.47ppm while that of group C rats exposed on dissection days was 1.95ppm

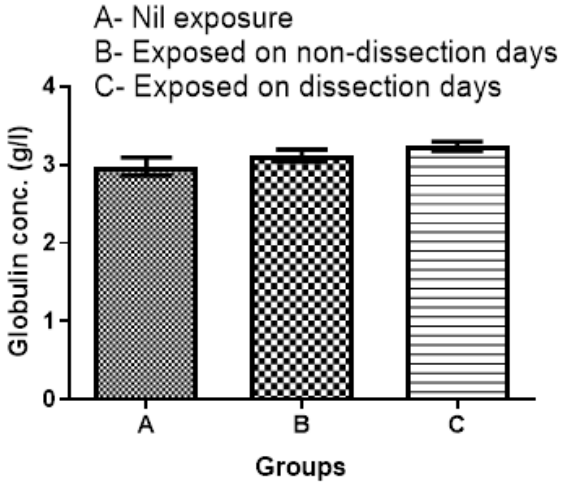

Fig 3: Mean serum globulin concentration (g/l) of Wistar rats following periodic exposure to formaldehyde

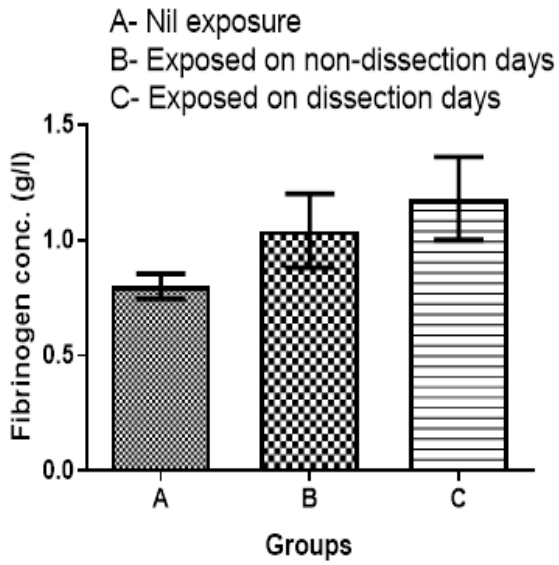

Fig 4: Mean serum fibrinogen concentration (g/l) of Wistar rats following periodic exposure to formaldehyde

The exposure level to formaldehyde in this present study is not up to the level that produced oxidative stress and lipid peroxidation in the study on rats earlier cited. Recall that this study carried out on wistar rats actually mimicked medical students attendance at the Anatomy laboratory for the purpose of dissection during the course of their training. Cilia destruction in the airways of wistar rats has been reported following chronic formaldehyde inhalation (Ebojele and Iyawe, 2022) and this revealed compromise in the respiratory system which is the first point of contact with formaldehyde. However, plasma protein levels were not affected in the Wistar rats at the exposure level in this present study. This could also imply that plasma protein levels may not be affected among medical students exposed to formaldehyde in the Anatomy laboratory, but this will be a subject of further study on the medical students themselves in order to substantiate the observations that have been made on Wistar rats.

Conclusion: We therefore conclude that periodic exposure to formaldehyde in the Anatomy laboratory may not have any adverse effect on plasma protein levels in Wistar rats but it seems to produce some inflammatory effects which can be linked to other systems within the rat.

Declaration of Conflict of Interest: The authors declare no conflict of interest.

Data Availability: Data are available upon request from the first author.

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