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Effect of Short-Term Exposure to Formalin on Male Reproductive Hormones of Students in Nnewi.

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***Abstract**: Formaldehyde is extensively used to preserve cadavers in departments of anatomy. This study investigated the effect of short-term exposure to formalin on male sex hormones levels of College of Health Sciences' students in Nnewi, Anambra State, Nigeria. There is paucity of information on this experimental design study in Nnewi hence the research. Forty (40) apparently healthy male students aged 18-30 years, were randomly recruited into the pre and post experimental design study. Five milliliters (5mls) each of baseline and post-formalin exposure blood samples were collected from each participant and used for the analysis of biochemical parameters. Serum Testosterone, Luteinizing hormone (LH), Follicle Stimulating hormone (FSH), Estradiol (E_2), and Prolactin (PRL) levels were determined using ELISA technique respectively. Data obtained were analyzed using paired Students t-test. Results showed a significant decrease in the mean serum testosterone level (11.21±5.13 vs 14.12±4.04; p=0.001) whereas, the mean serum follicle stimulating hormone (FSH) level was significantly increased (7.22±4.2 vs 6.46±4.67; p=0.025) post formalin exposure compared with pre-formalin exposure in the subjects. However, the mean serum Luteinizing hormone (LH), Estradiol, and Prolactin levels did not differ significantly after the subjects were exposed to formalin during dissection in the cadaver room when compared with their level before exposure to formalin (p>0.05). Therefore, findings in this study suggest that short term formalin exposure may predispose to hypogonadism and seminiferous tubular damage in males. Hence, adequate care is required to ensure reduction in subjects' exposure level to this carcinogen.*

***Keywords:** Formalin, Testosterone, Follicle stimulating hormone, Luteinizing hormone, Estradiol, Prolactin, Student, Dissection Laboratory.*

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I. Introduction

With more than 46 billion pounds of formaldehyde produced worldwide annually [1], most of which is widely used in the construction, textile, furniture, medical, chemical, and pharmaceutical industries, formaldehyde heavily impacts the everyday consumer. It is produced endogenously in all living organisms, including humans, but exposure to ubiquitous exogenous sources indoors, outdoors, at work, in residences, in food and medicine, poses a significant threat to public health [2]. Exposed populations include not only adult workers, who are exposed occupationally, but also the elderly, childbearing women, and young children. Emerging evidence supports an association between formaldehyde (FA) exposure and multiple adverse health effects [2].Formaldehyde (CH2O), the most simple and reactive ofall aldehydes, is a colorless, reactive and readily polymerizinggas at room temperature [3]. It has a pungentsuffocating odor that is recognized by most human subjectsat concentrations below 1 ppm [1]. Human studies have shown that chronic exposure toformaldehyde by inhalation is associated with eye, nose and throatirritation [4]. Most importantly, several studies report acarcinogenic effect in humans after chronic exposure toFA, in particular an increased risk for nasopharyngealcancer [5, 6, 7, 8, 9]. Since 2006, International Agency forResearch on Cancer (IARC) classifies FA as carcinogenicto humans (Group 1), based on sufficient evidence inhumans and in experimental animals [1]. Formaldehyde annual production rises up to 21 milliontons worldwide and it has increased in China, for

example,in the recent years, with 7,5 million tons producedin 2007. Given its economic importance and widespreaduse, many people are exposed to formaldehyde environmentallyand/or occupationally [10]. Occupational exposure involves not only workers indirect production of FA and products containing it, butalso in industries utilizing these products, such as thoserelated with construction and household [3]. The mostextensive use of Formaldehyde is in production of resins with urea,phenol and melamine, and also polyacetal resins. Theseproducts are used as adhesives in manufacture of particle-board, plywood, furniture and other wood products[1].Formaldehyde is also used in cosmetics composition and hasan important application as a disinfectant and preservative,reason why relevant workplace exposure may alsooccur in pathology and anatomy laboratories and inmortuaries [11, 1, 3].Exposure to toxic agents in various occupational environments is the most important issues in occupational health [12]. Formaldehyde as a single carbon compound with chemical formula of $O=C-H_2$ is a highly reactive and potent stimulus[13]. Exposure to low levels (0.1ppm) of formaldehyde irritates eyes; nose and upper respiratory airways[2, 14]. Exposure to high concentrations may result in nerve palsy, impairment of pulmonary function and asthma[15]. In prolonged exposures, cases of nasopharyngeal cancer (Pala *et al.*, 2008) as well as leukemia [16, 17]have been observed in humans.Moreover, exposure to formaldehyde vapor can destroy testicular structure and decrease percentages of sperm count and progressive motility. Males exposed to formalin have increased risk of sperm morphology [18].Therefore; this study is aimed at investigating the effect of short-term exposure to formalin on male reproductive hormones of students in Nnewi, Anambra State, Nigeria.

II. Materials And Methods

2.1 Study Site

This study was carried out at the dissection (cadaver room) laboratory of College of Health Sciences, Nnamdi Azikiwe University, Nnewi campus, Anambra State, Nigeria.

2.2Reseach Design

A total number of 40 students (males) of College Health Sciences, Nnamdi Azikiwe University, Nnewi Campus, Anambra State, Nigeria were randomly recruited for the experimental design study. The aim of the study was explained to the intending participants and thereafter, a structured questionnaire was used to obtain the demographic data of the subjects who gave their informed consent. Five milliliters (5mls) each of baseline and post-formalin exposure blood samples were collected from each participant. The blood samples were dispensed into plain container and allowed to clot; thereafter the serum was separated and used for biochemical assays. Biochemical parameters (Testosterone, LH, FSH, Estradiol, and Prolactin) levels were determined using ELISA technique respectively.

2.3Ethical Consideration

Ethics approval for the research was obtained from Faculty of Health Sciences and Technology Ethical Committee, Nnamdi Azikiwe University, Nnewi Campus, Anambra State, Nigeria.

2.4Inclusion criteria and Exclusion criteria

Apparently healthy students (males) who participated in anatomy dissection aged 18-30 years old who consented to the study were included for this study while those who were below 18 years or above 30 years old; who were sick or were non-students or not involved in the dissection were excluded from this study.

2.5Statistical Analysis

Statistical package for social science (SPSS; version 20) was employed in the analysis of the data collected. The results were expressed as Mean±SD and compared using paired Students t-test; with level of significance set at $p<0.05$.

III. Result

In the present study, the mean serum testosterone level was significantly decreased after the subjects were exposed to formalin during dissection in the cadaver room when compared with their level before exposure to formalin (11.21±5.13 vs 14.12±4.04; p=0.001); See table 1.However, the mean serum follicle stimulating hormone (FSH) level was significantly increased after formalin exposure compared with before formalin exposure in the subjects (7.22±4.2 vs 6.46±4.67; p=0.025); See table 1.Interestingly, the mean serum Luteinizing hormone (LH), Estradiol, and Prolactin levels did not differ significantly after the subjects were exposed to formalin during dissection in the cadaver room when compared with their level before exposure to formalin ($p>0.05$); See table 1.

Table 1: The mean serum levels of male sex hormones in subjects pre and post formalin exposure (Mean±SD; n=40).

Variables	Pre-formalin exposure	Post-formalin exposure	t-value	p-value
Testosterone	14.12±4.04	11.21±5.13	3.455	0.001*
Luteinizing hormone	5.50±3.54	4.81±3.41	1.021	0.313
Follicle stimulating hormone	6.46±4.67	7.22±4.2	-2.330	0.025*
Estradiol	71.32±17.71	68.93±19.53	0.627	0.534
Prolactin	16.8±7.64	18.83±8.81	-1.150	0.257

***Statistically significant at p<0.05.**

IV. Discussion

In the present study, the mean serum testosterone level was significantly decreased after the subjects were exposed to formalin during dissection in the cadaver room when compared with their level before exposure to formalin (11.21±5.13 vs 14.12±4.04; p=0.001). This is in consonance with the study of Zhi-Jun *et al.*who investigated the formaldehyde inhibitory effect on sexual behavior and expression of steroidogenic enzymes in the testes of mice and reported a significant decrease in testosterone level [19]. Other similar studies both in rats and mice also did report a decrease in testicular weight and levels of serum testosterone after formalin exposure when compared with their levels before formalin exposure in the subjects ([20, 21, 22, 23, 24]. This decrease in testosterone level may be due to the ability of formalin to induce genotoxicity, oxidative stress as well as disruption of the activity of proteins, enzymes and hormones important for the maturation of the male reproductive system, apoptosis and DNA methylation. Although formaldehyde is known to cause genotoxicity (DNA and chromosomal damage) and cytotoxicity (cell death or apoptosis), the mechanism is unclear. Limited evidence shows that oxidative DNA damage by reactive oxygen species (ROS) could play an important role. It is well known that excessive ROS production can cause developmental toxicity through oxidative damage to key cellular components such as DNA, proteins and lipids. More so, Leydig cell impairment may also be a contributory factor [20]. However, Lindbohm *et al.* has stated that exposure to formaldehyde vapor can destroy testicular structure and decrease percentages of sperm count and progressive motility and males exposed to formalin have increased risk of sperm morphology [18].Furthermore, the mean serum follicle stimulating hormone (FSH) level was significantly increased after formalin exposure compared with before formalin exposure in the subjects (7.22±4.2 vs 6.46±4.67; p=0.025). The mechanism for this increase is not quite clear to us. Again, the exact role of FSH in males is not yet clear; however, it is known that FSH acts on Sertoli cells to stimulate gametogenesis and the synthesis and release of inhibin [25]. Therefore, FSH may be elevated in disorders in which Sertoli cells numbers are reduced [25]. Besides, Mayne, (1994),has stated that a raised plasma FSH concentration indicates seminiferous tubular failure, irrespective of the plasma concentration and there is usually oligospermia [26].

Interestingly, the mean serum Luteinizing hormone (LH), Estradiol, and Prolactin levels did not differ significantly after the subjects were exposed to formalin during dissection in the cadaver room when compared with their levels before exposure to formalin (p>0.05). Meng *et al.* had earlier reported lowered estradiol level in birds exposed to formalin after they conducted a study to test the effectiveness of formalin-based avian influenza inactivated vaccines [27]. Therefore, findings in this study suggest that short term formalin exposure may predispose to hypogonadism and seminiferous tubular damage in males.

V. Conclusion

In conclusion, short term exposure to formalin caused a significant decrease in the mean serum level of testosterone and increased level of FSH whereas the mean serum LH, estradiol, and prolactin levels remained the same after a short-term exposure. Therefore, findings in this study suggest that short term formalin exposure may predispose to hypogonadism and seminiferous tubular damage in males.

VI. Recommendation

However, further studies using a larger sample size and including biometric data of the subjects might be necessary in elucidating the full mechanism of effect of formalin exposure on the male sex hormones.

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