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Oxidative Stress Markers and Liver Functions of Morticians Exposed to Formaldehyde in South-Eastern, Nigeria.

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Abstract: Background: *Human exposure to formaldehyde is associated with multiple adverse effects. Its exposure is known to cause oxidative stress in some vital organs like liver, kidney and lungs.*
AIM: *To investigate the toxicity and pathologyof inhaled chemicals in morticians occupationally exposed to embalmment chemicals(mainly formaldehyde) in Anambra state, Nigeria, using markers of cellular oxidative damage: super oxide dismutase (SOD), Glutathione peroxidase (GPx), Malondialdehyde (MDA), trace metals and liver markers (AST, ALT, ALP, Albumin, total protein , total and conjugated bilirubin) as biochemical indices.*
Materials/Methods: *The exposed group (n=45) comprised of male embalmers (morticians) who have had occupational exposure for a minimum of five years, while apparently healthy age-matched male subjects (n=45) without considerable exposure to formaldehyde served as control subjects. Informed consent was obtained from all enrolled subjects. A structured questionnaire was utilized to capture the bio-data and other pertinent information on work place exposure. Eight mls of blood samples obtained were used for assessment of oxidative stress and liver markers using standard methods.*
Results: *From the results obtained, SOD and GPxactivities of exposed group (0.6834±0.08555; 14.041±2.1253) were lower and significantly different from non-exposed subjects (0.82±0.080; 16.39±1.237) respectively ($P<0.05$). The trace metals (cofactors) of the anti-oxidants follow the same trend. MDA levels in exposed group were significantly higher in exposed when compared with unexposed ($P <0.05$). The mean levels of AST and ALT in exposed group were statistically significant when compared with the unexposed. The mean levels of AFP, total protein, albumin and conjugated bilirubin of the exposed were not significant when compared with the unexposed. However, the mean levels of total bilirubin of the exposed were significant when compared with the control unexposed group.*
Conclusion: *This study concludes that there was significant formaldehyde-induced depressive effect on antioxidant status and liver toxicity in chronic occupationally exposed morticians in Anambra State.*
Keywords: *Occupational exposure, formaldehyde, toxicity, oxidative stress, liver markers.*

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I. Introduction

Formaldehyde is a noxious, flammablegas colorless irritant which gives out pungent formaldehyde vapors and is widely used in the medical field as fungicide and preservative. It was discovered in 1867 by the British chemist, August WilheldVon Hofmann. It is the chemical most commonly used for preservation and embalment (Raja, 2012). The process of embalming a cadaver is by introducing a fixative into the body tissues. 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. Exposure occurs primarily by inhalation, where it is absorbed by the lungs and gastro intestinal tract. The Occupational Safety and Health Association (OSHA) recommendedpermissible exposure limit (PEL) of formaldehyde is0.75 ppm averaged over an eight-hour work shift and 2 ppm notto be exceeded during any 15-min work period (OSHA, 1998).

Amongst the groups who are at risk of the effects of formaldehydeexposure are medical students and staff members of Anatomy Department and Morticians. Studies have shown that evaporation offormaldehyde from formalin-treated cadavers in the anatomy dissection rooms and Mortuaries can produce high exposures (Emueet al, 2011). The poor ventilation of dissection rooms, poor working practices whichmay lead to spillage of formaldehyde during embalming, andignorance of consequences of formalin exposure are reasons for the high risk exposures. (Balmes, 2004; Dixit et al, 2005). In recent times, concerns have been raised on the standard of practice at mortuaries as it relates to occupational safety and health in developing countries including Nigeria (Okoth-Okellohet al., 2013; Ogunnowoet al., 2010). In the tropics, like Nigeria, the situation is usually worse due to the high temperature which favors the volatility of formaldehyde. Liver injury has long been associated with occupational exposure to a wide variety of chemicals. Its susceptibility to chemical injury is a result of its unique position within the circulatory system, and also because it is the primary organ for the biotransformation of chemicals within the body. Impaired liver function has been reported among such exposed professionals in South-western Nigeria (Olooto, 2010), and among exposed health professionals in Calabar, South-South Nigeria (Euphoria et al, 2014). Also exposures have been found to deplete some anti-oxidantsactivities in the body (Osadoloret al, 2014).

This present study is therefore aimed to assess the extent of oxidative stress if any by estimating the level of SOD, GPxincluding their cofactor Zinc and Selenium and MDA in Morticians exposed to formaldehyde and to evaluate the liver integrity of subjects exposed to formaldehyde by assessing levels of ALP, AST, ALT and Alpafeto-protein.

II. Materials and Methods.

The study was carried out in Anambra States, South Eastern Nigeria. It was of a cross sectionalstudy design. The morticians were identified from a list of registered Mortuaries and embalmment centers in Anambra State. They were identified from their association in the State. After verbal consent, detailed personal, and medical questionnaire was completed by morticians through personal interview. The questionnaires were pre-tested among twenty morticians in Imo State for validation. They contained questions on bio-data, medical history, knowledge of workplace hazards, attitude towards these hazards and preventive measures employed against the hazards. Each question was fully explained to the respondents to ensure adequate understanding of the issues being sought after.

2.1 Sample Size

The minimum sample size for the study was calculated using the formula when population is more than 10000. (Araoye, 2003).

$n = Z^2 pq/d^2$

where n = minimum sample size; Z = standard normal deviation at 95% confidence interval is 1.96; P = proportion of the population estimated to have the public health problem under study. Using 2.5% prevalence rate of occupational exposure to formaldehyde in Australia,
(Driscollet al., 2015).

P= 2.5/100 = 0.025

q = 1 – 0.025 =0.975

$$n = \frac{(1.96^2)\,(0.025)\,(0.975)}{(0.05)^2} = 37.6$$

Considering 10% atttrition rate = 4

Total population of study = 41

Forty one morticians occupationally exposed to formaldehyde for more than 5 years (workers group), and fortyunexposed white-collar workers (control group) were recruited for the study. The morticians were selected from both private and government hospitals Mortuaries in South East, Nigeria. All the included subjects in the two groups were from urban areas.

2.2 Sampling Method

The sampling technique employed was convenient sampling method and it involved the use of questionnaire which was personally administered.

2.3 Samples Collection and Assay

Eight milliliters (8 ml) of blood samples were collected from all subjects by sterile disposable syringes into a sterile plain container and allowed to clot, retracted and centrifuge at 3000 r.p.m for 10 minutes. Thereafter, serum were separated into two aliquots. One part of samples were stored at -20 ˚C until analysis of oxidative stress markers (GPx, SOD and MDA) within two weeks of collection, while the remaining aliquot were stored at -20 ˚C until analysis of other liver markers. The analysis were done at Chemical Pathology Department, NnamdiAzikiwe University teaching Hospital Nnewi

2.4 Statistical Analysis

The collected data and the laboratory results were computed. Statistical analysis was done using SPSS version 21. The quantitative results were expressed as means ± standard deviation (SD). Appropriate statistical tools which included independent t-test were employed in the analysis of data. P value < 0.05 will be considered significant.

III. Results and Discussion

Apart from the physical signs and symptoms like allergic reactions to formaldehyde exposures during work including; sneezing /airways-related symptoms, itching and watery eyes which are attributable to the high solubility of formaldehyde; such that even though it gains entry to the body as a gas, it easily solubilizes to liquid within the mucous membranes of the nasopharyngeal tract as well as the eyes resulting in irritation at these sites. This has been reported by many researchers (Binawara, et al, 2010; Jain, et al, 2012 and Onyijeet al, 2016). The effects of formaldehyde on the body mass index and fasting blood sugar (FBS) of Wistar albino rats exposed and non-exposed were presented in Table 1. The result indicates that there was a significant increase in BMI and FBS levels of the exposed group when compared to the control at p<0.05.

Table 1: A comparison of BMI and FBS of exposed and non-exposed group

Groups	BMI	FBS (mmol/L)
Control	21.583±2.069	6.118±1.857
Exposed to CH_2O	22.058±2.238	6.765±2.375
P Value	0.32	0.17

* Significant at 0.05 level of significance

Formaldehyde inhalation has been reported to deplete the activities of antioxidant enzymes, stimulate oxidative stress and thus promote hepatotoxicity and genotoxicity amongst others. From our findings(Table 2), the activities of anti-oxidant enzymes in the exposed group were significantly lower when compared with the unexposed control group (P< 0.05). This is in concordance with the study done in Benin City by Osadoloret al, (2014). From their findings, SOD and GPx activities were significantly reduced in exposedgroup when compared with non-exposed subjects. This could be as a result of generation of reactive oxygen species generatedduring the metabolism of excess exogenous formaldehyde leading to oxidative stress. The trace metals, Zinc which is a cofactor of the enzyme superoxide dismutase (SOD) and Selenium, a cofactor for Glutathione peroxidase follow the same trend as these trace metals are required for optimal function of the enzymes. The MDA which is and index of lipid peroxidation was significantly higher in exposed group than unexposed (P<0.05). However, Osadoloret al (2014) observed no significant change among the exposed and unexposed.

Table 2:A comparison of mean level oxidative stress markers among control and exposed group

Oxidative Stress markers/Trace elements	Control/non exposed group	Exposed Group	P Value
GPx(µmol/min)	0.82±0.080	0.6834±0.0850.01*	
SOD(µmol/min)	16.39±1.237	14.041±2.125 0.00*	
MDA(µmol/L)	1.78±0.330	2.276±0.560 0.021*	
Se(ppm)	2.05±0.419	1.2602±0.3040.01*	
Zn(ppm)	4.97±0.874	3.9729±0.953 0.00*	

* Significant at 0.05 level of significance

Formaldehyde metabolisms in the human body is carried out by theliver, incidentally it plays a central role in the body for intermediary metabolism of carbohydrates, proteins, lipids and xenobiotics. Chronic exposure to formaldehyde with the metabolic demands on the liver could affect general hepatic functions(Euphoria et al, 2015). Derangement in hepatic functions has been suggested following observed toxicity to the liver in morticians (Olooto, 2010) and several species of experimental animals (Teng et al., 2001; Cikmaz et al., 2010).

Our findings showed that Morticians occupationally-exposed to formaldehyde in south eastern Nigeria who were enrolled in this study have relatively increased valuesof AFP when compared with the controls. However, the mean values were not statistically significant. The values of AFP recorded in this study were similar to that observed by Euphoria,et al (2015). The values were below the cut-off point for establishing hepatocellular carcinoma.

In this study, we observed increased levels of AST and ALT among exposed workers which were statistically significant ($P<0.05$) when compared with the controls and such elevations are attributable to hepatic injury (Table 3).

Table 3. A comparison of Mean levels of Liver Markers of Control and Exposed Group

Liver Markers	Control	Exposed Group	P Value
AFP(ngl/dl)	2.288±1.4521	3.283±3.3951	0.85
ALT(U/L)	21.439±2.8727	41.780±8.9373 0.01*	
AST(U/L)	14.732±3.4061	34.707±6.93990.00*	
ALP(U/L)	51.049±6.9244	51.732±11.4215	0.74
ALB(g/dl)	44.659±5.9481	43.220±4.0652	0.20
PROT(g/dl)	**72.390±3.6802**	**69.927±4.2567**	**0.06**
Total. Bil. (μmol/L)	9.693±0.9106	10.893±1.0582 0.03*	
Conj. bil.(μmol/L)	2.52±1.2098	2.1756±0.3872	0.86

* Significant at 0.05 level of significance

Total Protein, Albumin and conjugated bilirubin were not statistically significant when compared with unexposed group (Table 3). The mean level of total bilirubin of the exposed group was significantly higher than those of the unexposed group. This showed that the synthetic functions of the liver were not affected but the excretory functions were affected. This result however differs from the study done by Euphoria et al (2015) who observed significant changes in both synthetic and excretory functions of the liver of exposed group when compared with the unexposed.

IV. Conclusion

The current study highlighted the adverse health effects of formalintreatedcadavers on morticians, which necessitate re-evaluationof the concentration of formalin, proper ventilation inthe embalming rooms, and assessment of working practices conditionsinMortuaries.Enlightenment campaigns should be advocated to sensitize the embalmers on the adverse health effects of formaldehyde.

Limitations of the study. The study did not include measurement of air concentrationof formalin at the Anatomy department. Measuring Nmethylenvalinein blood, as biomarker, was not included.

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