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EFFECT OF SHORT-TERM EXPOSURE TO FORMALIN ON KIDNEY FUNCTION TESTS 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 kidney function tests of students in Nnewi. There is paucity of information on this study in Nnewi hence the research. A total number of 50 students (male and female) 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 creatinine was determined by Jaffe Slot Alkaline Picrate method; urea by Berthelot method; uric acid by uricase method; Albumin by Bromocresol Green method; Total protein by Biuret method and electrolytes (Na^+, K^+, Cl^-, and $HCO3^-$) were determined using Ion Selective Electrode. Data obtained were analyzed using paired Students t-test. Results showed a significant increase in the mean serum urea (5.41±1.23 vs 4.49±1.17), uric acid (356.24±55.09 vs 306.96±57.90) , serum albumin, total protein and electrolytes (Na^+, K^+, Cl^-, and $HCO3^-$) levels post formalin exposure when compared with pre formalin exposure ($p< 0.05$) whereas, the mean serum creatinine level did not differ significantly post formalin exposure ($p>0.05$). In conclusion, short term exposure to formalin caused a significant increase in the mean serum levels of urea, uric acid, albumin, total protein as well as the electrolytes levels.

KEYWORDS: Formalin, Creatinine, Urea, Uric acid, Albumin, Total protein, Electrolytes, Student, Dissection Laboratory.

INTRODUCTION
Formaldehyde was discovered in 1856 by the British Chemist, August Wilheld Von Hofmann (Dixit, 2008). Formaldehyde is a colorless and odorless gas that is extensively used for its tissue embalming properties, which is why it is commonly found in anatomy laboratories and funeral homes (Viegas *et al.*, 2010). Formaldehyde (FA) is a highly water-soluble aldehyde that exists in the natural structures of organisms and is widely used due to its chemical properties. CH_2O (FA) is a highly reactive substance due to its strong electrophilic properties, and it can change from a solid or liquid into the gaseous form at room temperature. Its pure form has a characteristic pungent odor and is an irritant to the respiratory tract. A 37% solution of formaldehyde in water is known as formalin, whereas the polymerized solid form is called paraformaldehyde. The liquid form of formaldehyde, which is produced by the oxidation of methanol, is generally expressed in milliliters (mL), whereas the gas form is expressed in parts per million (ppm) (RFPOF, 1982; Feron *et al*., 1991; Zararsiz *et al*., 2011). Formaldehyde, which is inevitably taken into organisms in an exogenous manner, is also endogenously present in organisms. Exogenous intake commonly occurs through the skin and digestive system and mostly via the respiratory system. Orally, it is ingested in fresh water, sugar, coffee, fruits and vegetables, drugs and the protective additives in some foods. It can be inhaled in

cigarette smoke, in smoke due to the combustion of wood or liquid-based fuels, in the exhaust of vehicles with burning fossil fuels and in the fumes of paints used for surfaces and furniture. In the medical field, employees in anatomy, histology and pathology laboratories are affected by formaldehyde, which is used especially as a solution for embalming and fixation (Restani and Galli, 1991; Cheney and Collins, 1995). In humans, glycine and serine are the most important sources of endogenous Formaldehyde. Additionally, N-methyl amino acids and sarcosine can be converted into formaldehyde via oxidative demethylation by specific enzymes. Endogenous tissue levels range from 3 to 12 ng/g and, of this proportion, 40% occurs in the free form (National Toxicology Program, 2010). Formaldehyde, which has a very short half-life (t1/2=1.5 min), is metabolized into formic acid in the liver and erythrocytes, with a reaction catalyzed by formaldehyde dehydrogenase (FDH) enzymes after formaldehyde is taken into body, regardless of the manner (respiratory, oral, i.p. or i.v.) of intake. Formaldehyde is a hapten and formaldehyde-protein complex may be immunogenic (Maibach, 1983). The chemical is extensively used to preserve cadavers in departments of anatomy. The primary route of exposure to formaldehyde is by inhalation, where it is absorbed by the lungs and gastro-intestinal tract and to a much lesser extent through the skin (Maibach, 1983). The literature on formaldehyde contains reports on dermatitis and asthma (Hendrick and Lane, 1977; Owen and Beck, 2001). Formaldehyde can cause skin and respiratory irritations along with other adverse symptoms to individuals who are exposed to this chemical. Potential health effects include sore throat, coughing, shortness of breath, headache, vomiting, blurred vision, and diarrhea (Tang *et al.,* 2009). On industrial exposure to formaldehyde, however only few reports have mentioned the effect of formaldehyde on medical students during dissection (Chia *et al.,* 1992; Kim *et al.,* 1999). Recently, the International Agency for Research on Cancer (IARC) classified formaldehyde as a known human carcinogen (Group 1) based on "sufficient epidemiological evidence that formaldehyde causes nasopharyngeal cancer in humans "(IARC, 2006).

The process of embalming a cadaver is by introducing a fixative into the body tissues 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. The embalming fluid is made up of a combination of chemi-cals that include fixatives, preservatives, germicides, buffers, wetting agents, anticoagulants, dyes, perfuming agents, *etc* (Dixit, 2008). Biochemical markers play an important role in accurate diagnosis and in assessing risk and adopting therapy to improve clinical outcome, serum analysis of renal function markers like urea, creatinine, uric acid and electrolytes are used routinely (Gowda *et al*., 2010). Blood tests for Blood Urea Nitrogen (BUN) (Kamal, 2014) which is a major nitrogenous end product of protein and amino acid catabolism (Gowda *et al.,* 2010) and creatinine (Kamal, 2014) which is a breakdown product of creatine phosphate in muscle (Gowda *et al.,* 2010) are excreted by kidneys. BUN is an indirect and rough measurement of renal function that measures the amount of urea nitrogen in blood and is directly related to excretory function of kidney. Creatinine tests diagnose impaired renal function and measure the amount of creatinine phosphate in blood. Urea and creatinine are good indicators of a normal functioning kidney and increase in the serum are indications of kidney dysfunction (Kamal, 2014). BUN and serum creatinine are widely accepted as the most common parameters to assess renal functions (Kamal, 2014; Suresh *et al.,* 2014). This study is therefore designed to investigate the effect of short-term exposure to formalin on kidney function tests, of students of Nnamdi Azikiwe University, Nnewi Campus, Anambra State, Nigeria.

MATERIALS AND METHODS

Study Site

This study was carried out at the Anatomy Laboratory of Department of Anatomy, Faculty of Basic Medicine, College Health Sciences, Nnamdi Azikiwe University, Nnewi Campus, Anambra State, Nigeria.

Reseach Design

A total number of 50 students (males and females) 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. Serum creatinine was determined using Jaffe Slot Alkaline Picric Acid method as described by Ochei and Kolhatkar, (2007); serum urea was estimated using Berthelot method as described by Taylor, (1989); serum uric acid was assayed using uricase method as described by Trivedi *et al.,* (1978); serum Albumin and Total protein were assayed using Bromocresol Green and Biuret methods as described by (Carl *et al*., 2008; and Gornal *et al*., 1949) while serum electrolytes (Na^+, K^+, Cl^-, and $HCO3^-$) were determined using Ion Selective Electrode Method.

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.

Ethical Consideration

Ethical approval for the research was obtained from Faculty of Health Sciences and Technology Ethical

Committee, Nnamdi Azikiwe University, Nnewi Campus, Anambra State, Nigeria.

Inclusion criteria and Exclusion criteria

Apparently healthy students (males and females) 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.

Statistical 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 $p<0.05$.

RESULT

The mean serum creatinine level 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 (96.98±24.81 vs 96.34±21.35; p>0.05); See table 1.

However, the mean serum urea level was significantly increased after formalin exposure compared with before formalin exposure in the subjects (5.41±1.23 vs 4.49±1.17; p=0.000); See table 1.

Again, the mean serum uric acid level of the subjects was significantly increased after their exposure to formalin when compared with their values before formalin exposure (356.24±55.09 vs 306.96±57.90; p=0.000). See table 1.

Interestingly, there were significant increases in the mean serum albumin (4.13±0.77 vs 3.60±0.58; p=0.001) and total protein (80.56±5.04 vs 74.52±5.11; p=0.000) levels in subjects after formalin exposure when compared with before formalin exposure in the subjects. See table 1.

Furthermore, there were significant increases in mean serum electrolyte (Na^+, K^+, Cl^-, and $HCO3^-$) profile levels in subjects after formalin exposure when compared with before formalin exposure in the subjects (P<0.05). See table 1.

Table 1: The mean serum levels of Renal function parameters in subjects pre and post formalin exposure (Mean±SD; n=50).

Variables	Pre-formalin exposure	Post-formalin exposure	t-value	p-value
Creatinine (µmol/L)	96.34±21.35	96.98±24.81	0.233	0.816
Urea (mmol/L)	4.49±1.17	5.41±1.23	-8.392	0.000*
Uric acid (µmol/L)	306.96±57.90	356.24±55.09	-7.167	0.000*
Albumin (g/dl)	3.60±0.58	4.13±0.77	-3.529	0.001*
Total protein (g/L)	74.52±5.11	80.56±5.04	-7.830	0.000*
Sodium (Mmol/L)	136.05±2.31	139.15±3.45	-7.468	0.000*
Potassium (Mmol/L)	3.55±1.35	3.65±1.81	-5.548	0.000*
Chloride (Mmol/L)	97.88 ± 2.63	101.26 ± 1.87	-9.967	0.000*
Bicarbonate(Mmol/L)	21.42 ±2.14	24.32 ±2.46	-6.548	0.000*

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

DISCUSSION

In the present study, the mean serum levels of urea (5.41±1.23 vs 4.49±1.17; p=0.000) and uric acid (356.24±55.09 vs 306.96±57.90; p=0.000), were significantly increased in the subjects after formalin exposure when compared with their mean values before formalin exposure whereas, the mean serum creatinine level did not differ significantly in the subjects after formalin exposure when compared with their level before formalin exposure (p>0.05). This result is in line with the report of Kum *et al*. (2007) who found that the serum urea concentration was increased in rats exposed to 6ppm formaldehyde 8hours/day for 6weeks whereas no changes was observed in serum creatinine concentration in comparison to the control animals (Kum *et al.*, 2007). This increase in the mean serum urea level may be as a result of dehydration effect of formalin exposure (Carl *et al*., 2008). However, urea has a limiting value as a test of kidney function because serum urea level might be increased due to a high-protein dietary intake by the subjects (Carl *et al*., 2008). Hence, formalin being a dehydrating agent induces a temporary hemoconcentration in subjects resulting in the elevation of urea level in the serum.

However, the mean serum creatinine level is much less affected by these extra-renal factors as it depends majorly on the muscle mass and body weight (Carl *et al*., 2008) and this perhaps explains why its level remained the same in the phase of an increasing urea and uric acid levels. Importantly, in situations where pre-renal factors affect the level of serum urea; the serum creatinine level may be normal (Carl *et al.*, 2008; Kamal, 2014; Suresh *et al*., 2014). Other similar studies in animals did show no formaldehyde-induced kidney effects in acute/intermediate duration inhalation studies (Pitten *et al*., 2000; Malek *et al*., 2003C) as well as in chronic inhalation studies with rats and mice (Kerns *et al*., 1983; Kamata *et al*., 1997). Furthermore, there were significant increases in the mean serum albumin (4.13±0.77 vs 3.60±0.58; p=0.001) and total protein (80.56±5.04 vs 74.52±5.11; p=0.000) levels in subjects after formalin exposure when compared with before formalin exposure

in the subjects. This is contrary to the study of Kum *et al*., (2007) which reported no significant differences in the mean serum albumin (4.13±0.77 vs 3.60±0.58; p=0.001) and total protein (80.56±5.04 vs 74.52±5.11; p=0.000) levels in subjects after formaldehyde exposure. Again, this increase may be due to haemoconcentration experienced by the subjects after formalin exposure.

Interestingly, there was significant increases in mean serum electrolytes (Na^+, K^+, Cl^-, and $HCO3^-$) levels post formalin exposure when compared with pre formalin exposure ($P<0.05$). However, the mechanism behind these increases in the mean serum electrolyte levels post formalin exposure remains unclear to us; moreover, the dehydration effect due to formalin inhalation might have caused an increase in osmolarity which resulted in antidiuretic hormone release hence the increase in serum electrolyte levels due to inability to restore plasma osmolarity by rehydration.

CONCLUSION

In conclusion, short term exposure to formalin caused a significant increase in the mean serum levels of urea, uric acid, albumin, and total protein as well as the electrolytes levels (Na^+, K^+, Cl^-, and $HCO3^-$) whereas the mean serum creatinine level remained the same after a short-term exposure.

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 kidney functions.

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