

## MICRONUTRIENT LEVELS IN WORKERS OCCUPATIONALLY EXPOSED TO FORMALDEHYDE

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### ABSTRACT

**Aim:** The aim of the work was to determine the levels of some micronutrients in the serum of persons occupationally exposed to formalin in Benin City, Nigeria.

**Methods:** The exposed group (n=36) comprised male embalmers (morticians) who have had occupational exposure for a minimum of five years, while apparently healthy age-matched male subjects (n=34) without considerable exposure to formaldehyde served as control subjects. The levels of zinc, copper, selenium, iron and chromium in their blood samples were determined using Atomic Absorption Spectrophotometer.

**Results:** Statistically significant findings were observed in micronutrient status in the exposed group. Zinc ( $90.39 \pm 1.24$  ug/dl), Copper ( $106.49 \pm 4.56$  ug/dl), Chromium ( $1.5 \times 10^{-3} \pm 0.00$  ug/dl) and Iron ( $117.79 \pm 3.42$  ug/dl) when compared with the non-exposed group, Zinc ( $106.15 \pm 1.47$  ug/dl), Copper ( $165.08 \pm 3.64$  ug/dl), Chromium ( $2.2 \times 10^{-3} \pm 0.00$  ug/dl) and Iron ( $158.10 \pm 2.57$  ug/dl). Selenium level in the exposed group ( $4.6 \times 10^{-3} \pm 0.00$  Unit/ml) was exceptionally higher than in the non-exposed group ( $1.4 \times 10^{-3} \pm 0.00$  ug/dl).

**Conclusion:** Formaldehyde contributes to depression of some micronutrients in plasma in occupationally exposed subjects.

**Keywords:** Occupational exposure, Formaldehyde, Toxicity, Micronutrients.

### INTRODUCTION

Minerals are present in up to tens of thousands of grams in the human body whilst only a few

grams of trace elements are required by the body. The recommended dietary allowance of minerals is usually greater than 200 mg/day whilst that for trace elements is less than 200

mg/day and this can be used to classify the difference between minerals and trace elements. The human body needs about 72 trace elements for normal functioning. About eight of the trace elements are commonly found in agricultural soils, though all 72 can be found in many types of seafood. Trace elements are vital for the human body to maintain complex physiological functions related to body's growth and development. Essential trace elements are iron, zinc, copper, cobalt, chromium, fluorine, iodine, manganese, molybdenum and selenium. Probably essential trace elements include nickel, tin, vanadium, silicon and boron while aluminum, arsenic, barium, bismuth, bromine, cadmium, germanium, gold, lead, lithium, mercury, rubidium, silver, strontium, titanium and zirconium are classified as non-essential elements (Megan and Veldee, 2001). Various studies have demonstrated the toxic effects of formaldehyde on some human organs such as the urinary, respiratory and cardiac tissues. It has been reported that sub acute and sub chronic formaldehyde inhalation may stimulate oxidative stress and thus, cause some secondary toxic effects in cellular activities. This increase in the oxidative stress could cause various damages to cells and their activities (Gulec et al., 2006). Oxidative damage to DNA, proteins, and other macromolecules has been implicated in the pathogenesis of a wide variety of diseases notably heart disease and cancer (Halliwell, 1994). It has been shown that formaldehyde dehydrogenase requires glutathione as a co-factor during the reaction where formaldehyde is metabolized into formic acid in the liver and erythrocyte. Thus, as the formaldehyde concentration increases, the blood glutathione level decreases. This depletion in the level of glutathione; an anti-oxidant, increases the toxicity of formaldehyde (Usanmaz *et al.*, 2002). In another study, it was found that formaldehyde exposure led to glomerular and tubular degeneration, tubular dilatation and congestion. These histopathological changes, observed in renal tissue, clearly demonstrate that formaldehyde exposure has severe nephrotoxic effects (Gulec et al., 2006). Also, it was demonstrated that the activities of superoxide dismutase which is an antioxidant enzyme and malon dialdehyde, a biomarker for lipid peroxidation were significantly increased in

some rats. This suggests that formaldehyde toxicity can lead to oxidative damage in tissues (Gulec et al., 2006). In this study, we investigated the effect of occupational exposure to formaldehyde on micronutrients metabolism in morticians.

## MATERIALS AND METHODS

### Study Area and Subjects Recruitment

This work was conducted in the Benin metropolis, Nigeria, with a total of seventy (70) subjects between the ages of 25 and 65 years. The exposed group (morticians; n=36) were subjects occupationally exposed to histological and embalment chemicals (mainly formaldehyde) for up to five years. Apparently healthy age-matched males (n=34) with minimal or no occupational contact with histological and embalment chemicals served as non-exposed group.

### Sample Collection

5.0 ml of blood was collected from each participant with a sterile syringe. The blood sample collected was thereafter transferred to a plain container. The serum was later separated and transferred into another plain container for further analytical procedures.

### Estimation of Essential Trace Elements

#### Assay of Trace Element Levels

Blood samples obtained from exposed and non-exposed subjects were analyzed for selenium, zinc, copper, iron and chromium using Atomic Absorption Spectrophotometer (AAS) model 210VGP, manufactured by BUCK SCIENTIFIC England. All analytical procedures were carried out at the analytical laboratory of the International Institute for Tropical Agriculture (IITA), Ibadan, Nigeria.

#### Statistical Analysis

Data collected were analyzed using the computer package Statistical Package for Social Sciences (SPSS) version 16.0 and values were given in mean and standard error of the mean. Student's t-test was applied and the level of significance at 95% confidence interval.

## RESULTS

**Table 1: Comparison of Micronutrients levels in Exposed and Non-exposed Groups**

Variables	Non-exposed Group Mean±SEM	Exposed Group Mean±SEM	P-Value	Significance
Zn (ug/dl)	106.15±1.47	90.39±1.24	0.000	**P<0.01
Cu (ug/dl)	165.08±3.64	106.49±4.56	0.000	**P<0.01
Se (ug/dl)	1.4 x 10 <sup>-3</sup> ±0.00	4.6 x 10 <sup>-3</sup> ±0.00	0.000	**P<0.01
Cr (ug/dl)	2.2 x 10 <sup>-3</sup> ±0.00	1.5 x 10 <sup>-3</sup> ±0.00	0.000	**P<0.01
Fe (ug/dl)	158.10±2.57	117.79±3.42	0.000	**P<0.01

\*\*P<0.01-Highly Significant, P>0.05- Not Significant

Mean± SEM of serum zinc level in exposed subjects (90.39±1.24) was reduced and significantly different compared with non-exposed group (106.15±1.47); p<0.01. Similarly, Mean± SEM of copper, chromium and iron were comparatively lower in exposed group compared with non-exposed subjects; and the difference were statistically significant, p<0.01. In exception, serum selenium level was higher in the exposed group (4.6 x 10<sup>-3</sup> ±0.00) than in non-exposed group (1.4 x 10<sup>-3</sup> ±0.00) and the difference was significant, p<0.01.

## DISCUSSION

A number of chemicals used in the histology laboratories as well as chemicals used in the embalment of dead bodies have been found to cause adverse pathophysiologic effects on systemic functions resulting from either acute or chronic occupational exposure (Gulec *et al.*, 2006). Formaldehyde is widely used in the industrial and medical fields, and employees in these sectors are frequently exposed to it (Cheney and Collins, 1995). Formaldehyde has been used extensively in various laboratories for decades. It is obviously known that it has some adverse effects on human health. Formaldehyde has been found to induce rhinitis, degeneration, frank necrosis, hyperplasia and squamous metaplasia of ciliated and non-ciliated nasal respiratory epithelium (Gurel *et al.*, 2005). Furthermore, epidemiological studies of industrial workers, embalmers and pathology anatomists have associated formaldehyde exposure to elevated risk for cancer at various sites including the brain, nasal cavities, lung, pancreas and lymphohaematopoetic system (Gulec *et al.*, 2006; Gurel *et al.*, 2005; Mehmet 2013; Morgan 1997; OSHA, 1992). According to the United States National Toxicological Programme (US-NTP), European Union (EU) and International Agency for Research on Cancer (IARC), formaldehyde is classified as a weak genotoxic, probable carcinogenic agent for

humans (category 3)(NTP, 2010). In the present study, we investigated micronutrients metabolism and status in workers occupationally exposed to embalment and histological chemicals, of which formaldehyde was of higher percentage. Though, serum level of selenium (Se) in the exposed group was slightly higher compared with non-exposed subjects, remarkably, there was a significant decrease in the levels of zinc (Zn), copper (Cu), chromium (Cr), and iron (Fe) in the exposed groups compared with non-exposed group. This markedly indicates depressed micronutrient status in occupationally exposed subjects. This marked decrease in the activities of essential trace element (as seen in zinc, copper, chromium and iron) in the exposed group as compared with the non-exposed can imply that formaldehyde exposure/toxicity depletes serum trace minerals which may as well results in several pathophysiological development such as cancer and inflammation. Various studies on the role of zinc in cancer have received increasing attention as a link between zinc deficiency and cancer has now been established in human studies. It is now reported that zinc status is compromised in cancer patients compared to healthy people. Zinc has been ascribed roles in the metabolic functions and interaction of malignant cells. The zinc content of leukaemic

leukocytes has been found to be reduced, and it has also been reported that zinc deficiency enhances the carcinogenic effects of nitroso methyl benzylamine (Morgan, 1997;NTP,2010; Collins et al.,2001). It was found an increase in serum copper/zinc ratios in patients with cancers of the lung, breast, gastrointestinal tract and gynecological malignancy. Nutritional zinc deficiency in rats increases oesophageal cell proliferation and the incidence of N-nitroso methyl benzylamine induced oesophageal tumours. Zinc deficiency in humans is associated with an increased risk of developing esophageal squamous cell carcinoma (Gurel et al., 2005;Cohen et al.,1998). In another report zinc has been affirmed as an essential mineral that is integral to many proteins and transcription factors that regulate key cellular functions such as the response to oxidative stress, DNA replication, DNA damage repair, cell cycle progression, and apoptosis. In particular, several proteins involved in DNA damage signalling and repair, replicative enzymes, such as DNA and RNA polymerases, and transcription factors, such as tumour protein p53 (p53), require zinc for proper function (Cheng et al., 2003). Zinc deficiency has also been shown to upregulate expression of the tumour suppressor protein, p53, but impairs the DNA binding abilities of p53, nuclear factor  $\kappa$  B (NF $\kappa$ B), and AP-1 transcription factors in rat glioma C6 cells (Cheng et al., 2003). These studies suggest that a decrease in cellular zinc alone causes DNA damage and impairs DNA damage response mechanisms, resulting in a loss of DNA integrity and potential for increased cancer risk. As regards iron, it is an essential metal for all living organisms participating in cellular processes, such as DNA synthesis, enzyme functions, and oxygen transport has also been implicated in cancer development as a result of its deficiency. Cellular iron metabolism is homologous among most cell types; cellular iron homeostasis is primarily mediated by transferrin (Tf), transferrin receptor-1 (TfR1), and ferritin (Megan and Veldee, 2001). Copper on the other

hand has been previously linked to conditions involving copper deficiency which include osteoporosis, osteoarthritis, rheumatoid arthritis, cardiovascular disease, colon cancer, and chronic conditions involving bone, connective tissue, heart, and blood vessels (Cohen et al., 1998; Collins et al.,2001;Halliwell 1997;Filiz et al., 2005). Based on our data, we infer that depressed micronutrients level constitute a risk factor for formalin-mediated medical conditions and therefore conclude that formaldehyde contributes to depressed micronutrients in plasma in occupationally exposed morticians.

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