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Full Length Research Paper

Micronutrient levels in the plasma of Nigerian females with breast cancer

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The levels of heavy and essential metals in the serum of breast cancer patients were determined, in order to find out which of them could be of importance in the treatment and prognosis of the cancer. Serum copper, zinc, iron, magnesium, manganese, chromium, cadmium, lead and selenium were measured using atomic absorption spectrophotometer in 29 newly diagnosed breast cancer patients and compared with 30 healthy control subjects. The mean serum zinc and manganese levels were insignificantly low in breast cancer patients compared with the controls. The mean serum zinc and manganese levels were insignificantly lowered in with breast cancer compared to controls. However, the levels of magnesium, iron, chromium, cadmium lead and selenium were not significantly raised in breast cancer patients compared with the controls. The exact mechanism responsible for the alterations in trace metals in patients with breast cancer is largely unclear and requires further evaluation. However, the serum copper level may be of value in determining the prognosis of these patients.

Key word: Breast cancer, essential trace metals, prognosis.

INTRODUCTION

Breast cancer is the most common malignancy in women and is considered to be the leading cancer-related cause of death among women in most developed countries (Adebamowo et al., 2005). Unfortunately, till now, there is no effective therapy that is able to cure or prevent the disease. Given this, a large number of epidemiological studies have been undertaken to identify potential risk factors for cancer, but trace elements or heavy metals have received little attention (Adebamowo et al., 2005; Becker et al., 2007). Trace elements, such as selenium, zinc, iron, magnesium, manganese, cadmium, chromium and lead are found naturally in the environment, and human exposure derives from a variety of sources, including air, drinking water, and food (Becker et al., 2007). In this study, we focus largely on the levels of elements noted above in breast cancer patients.

Trace elements and heavy metals have been studied in recent years to assess whether they have any modifying effects in the etiology of cancers (Verougstratte et al., 2003; Fletcher and Zlotta, 2007; Navarro and Rohan, 2007; Cui et al., 2007). Overall, the evidence currently available supports an inverse association between selenium exposure and prostate cancer risk, and possibly also a reduction in risk with respect to lung cancer, although additional prospective studies are needed (Fletcher and Zlotta, 2007). There is also limited evidence for an inverse association between zinc and breast cancer (Navarro and Rohan, 2007). Most studies have reported no association between selenium and risk of breast cancer (Cui et al., 2007). There is compelling evidence in support of positive associations between arsenic and risk of both lung and bladder cancers, and between cadmium and lung cancer risk (Verougstratte et al., 2003).

Copper, iron and selenium are essential for numerous enzymes and therefore it is reasonable to assume that variations in serum level of these biochemical markers may be associated with the pathogenesis of cancer. Biochemical alterations of these metals in the serum of cancer patients can help in appropriate treatment and also as indicators of prognosis as the disease progresses. To this end, the present study determined the serum levels of Fe, Zn, Pb, Cr, Cd, Mn, Mg, Se and Cu in

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Table 1. Mean (SE) of demographic and anthropometric measurements in breast cancer patients and healthy controls.

Index	Cases (n = 29)	Controls (n = 30)	t	P
Body mass index	27.36 (1.25)	24.36 (1.09)	1.80	0.08
Waist to hip ratio	1.38 (0.48)	0.80 (1.31)	1.21	0.23
Age at menarche (years)	14.31 (0.33)	14.30 (0.40)	0.02	0.98
Age at menopause (years)	48.73 (1.13)	49.67 (1.23)	0.47	0.64
Age at first pregnancy (years)	26.50 (1.04)	24.56 (1.20)	1.18	0.24
Parity	3.67 (041)	3.87 (0.43)	0.31	0.75
Miscarriage/abortion	4.60 (1.75)	2.20 (0.51)	1.31	0.20

Nigerian breast cancer patients.

MATERIALS AND METHODS

Participants

Twenty nine (29) newly diagnosed breast cancer patients were recruited from the Surgery Clinics of the Lagos University Teaching Hospital (LUTH), Idi-Araba and the Lagos State University Teaching Hospital (LASUTH), Ikeja, Lagos State, Nigeria. The control subjects included thirty (30) apparently healthy women which were recruited mostly from members of staff of the University College Hospital, Ibadan, Nigeria. This study excluded patients or controls with inflammations, diabetes mellitus, hypertension, hepatitis, tuberculosis, jaundice, pregnancy or breast-feeding subjects and subjects on hormonal therapy. These were based on responses to questionnaires and clinical investigations.

Height

This was measured using a weighting scale and the readings were recorded to the nearest meter.

Weight

This was taken with Salter bathroom scale placed on a flat surface and the readings were recorded to the nearest 0.5 kg.

Body Mass Index (BMI)

This was calculated from the height and weight of subjects using the formula:

BMI (kg/m^2) = Weight (kg) / $Height^2$ (m^2)

Collection of blood and measurement of trace element levels

10 ml of venous blood was obtained from antecubital fossa into sample bottle. The blood sample was allowed to clot, retracted and centrifuged in Centaur MSE centrifuge machine (Fisons, England) at 3,500 rpm for 5 min after which the serum was separated and stored at -20°C until ready for assay. Serum levels of Cu, Mg, Fe, Zn, Mn, Cr, Cd, Pb and Se were determined using atomic absorption spectrophotometer as previously described (Olaniyi and Arinola, 2007).

The data was subjected to statistical analysis using the mean, standard error and student's unpaired t-test. P value < 0.05 was accepted as significant.

RESULTS AND DISCUSSION

A total of twenty nine (29) breast cancer patients and thirty (30) healthy controls were recruited for the investigation. The mean age of the breast cancer patients was 47.17(± 2.68) years and that of controls was 46.07(± 2.24) years. Table 1 compares the demographic and anthropometric measurement of breast cancer patients with healthy controls. The mean BMI, WHR, age at menarche, age at menopause, age at first pregnancy, parity, and number of miscarriages/abortions of cases were not significantly different from the controls. Table 2 shows the mean levels of trace elements in cases and controls. There were no statistically significant differences in the mean values of serum zinc, manganese, magnesium, iron, chromium, cadmium, lead and selenium in breast cancer patients compared with the controls. However, mean serum level of copper was significantly reduced in breast cancer patients compared with the controls

The rate at which breast cancer is spreading like an epidemic is alarming and there is large number of case reported in the recent years particularly in the younger generation because of its obscure etiology (Adebamowo et al., 2003). This observation call for urgent control and management of this cancer. Gowal et al. (2007) reported that a decline in the cell mediated immunity predisposes to oncogenesis, and a close association has been found between immune responses and macro- or micronutrient status (Wintergerst et al., 2007). This implied that it may be possible to monitor the prognosis of cancers using the levels of trace metals.

The present study showed that anthropometric and demographic indices are similar in breast cancers patients and controls, thus indicating that lifestyles, diets and socio-cultural exposures are the same in the two groups of subjects.

Filomeni et al. (2007) suggested that the copper ions and copper complexes react with hydrogen peroxide to

Table 2. Mean (SE) of trace elements in breast cancer patients compared with healthy controls.

Metals	Experiment	n	Mean	S.E	t	p
Mg (mg/L)	Test	29	5.081	0.23	0.42	0.67
	Control	30	4.930	0.27		
Fe (ug/L)	Test	29	59.62	2.53	0.15	0.87
	Control	30	59.05	2.50		
Zn (mg/L)	Test	29	143.27	6.62	0.01	0.99
	Control	30	143.38	7.54		
Mn (ug/L)	Test	29	59.04	2.45	1.65	0.10
	Control	30	65.35	2.96		
Cu (ug/L)	Test	29	55.35	2.20	2.2	0.03
	Control	30	63.05	2.74		
Cr (ug/L)	Test	29	52.65	2.11	0.13	0.89
	Control	30	52.25	2.17		
Cd (ug/L)	Test	29	54.65	2.11	0.13	0.89
	Control	30	54.25	2.17		
Pb (ug/L)	Test	29	53.15	2.03	0.42	0.67
	Control	30	51.90	2.11		
Se (ug/L)	Test	29	57.62	2.53	0.15	0.87
	Control	30	57.05	2.50		

form hydroxyl radicals that cause damage to protein, RNA and DNA. The damages are not repairable by cellular mechanisms thus initiating the malignant process. In this study, serum levels of copper showed a significant decrease in the cancer group when compared to controls, thus supporting the uptake of Cu from the blood by cancer cells. Clinical anaemia and haematological abnormalities are reported in breast cancer cases (Boehm et al., 2007). These may lead to the release of Fe from its store, thus the slight increase of Fe in our breast cancer patients.

Selenium forms the integral part of the enzyme glutathione peroxidase, type I iodothyronine deiodinase, metalloprotein, fatty acid binding protein and seleno-protein P. Therefore selenium is considered as an antioxidant nutrient and the diseases where low selenium is implicated range from nutritional disorders like protein energy malnutrition to degenerative diseases such as cancer (Alexander, 2007). Our study reported a non-significant increase in serum selenium in cancer, thus implicating selenium as a cancer protective agent. This is support of a previous study indicating that higher dietary intake of selenium in humans may be protective against cancers (Alexander, 2007).

Cadmium and cadmium compounds are known to be human carcinogens based on findings of increased risk to lung cancer and pancreatic cancer among exposed workers (Kolodiazgnaia et al., 2007). Parenteral adminis-tration or oral exposure to cadmium can result in proliferate lesions and tumors of the prostate in rats. The pathogenesis of cadmium-induced carcinogenesis was found to include aberrant gene expression resulting in stimulation of cell proliferation or blockage of apoptosis, or activation of transcription factors such as the metallo-thionein gene (Kolodiazgnaia et al., 2007). Tobacco is a significant source of Cd (Kiziler et al., 2007) and raised level of Cd may cause renal tabular dysfunction, osteomalacia, osteoporosis, lung cancer and prostate cancer (Kiziler et al., 2007). Thus the local effect of Cd increase might have contributed to the pathogenesis of breast cancer.

Chronic occupational and environmental exposure to Pb has lead to increase in serum Pb level which causes anaemia, peripheral neuropathy and venal tubular dys-function (Olife et al., 2007). Also, there is strong evidence that hexavalent Cr causes cancer in laboratory animals when it is consumed in drinking water. Previous studies have shown that hexavalent chromium causes lung cancer in humans in certain occupational settings as a result of inhalation exposure (McConnell, 2006). Also, diabetes mellitus has been found to be associated with Cr because Cr is known to potential insulin action (Sahin et al., 2007). Therefore we suggested that increased level of toxic elements (Pb and Cd) might have contributed to development of breast cancer.

Magnesium deficiency can paradoxically increase the risk of, or protect against oncogenesis (Cortes and Moses, 2007). It has been proposed that Mg is central in the cell cycle, and that its deficiency is an important conditioner in precancerous cell transformation (Cortes and Moses, 2007). In addition, immunocompetence (that eliminates transformed cells) is Mg-dependent (Son et al., 2007). The increase in the level of Mg in breast cancer patients is an indication of its protective effects against cancer.

Manganese is a trace element which is ingested with food or water and it is needed to stay healthy. At high levels, it can cause damage to the brain, liver, kidneys, and the developing fetus (Smith et al., 2007). There are no data available relating cancers and manganese (Smith et al., 2007). But incidence of pancreatic tumors in male rats and thyroid tumors in male and female mice were reported due to excessive exposure (Morello et al., 2007). Low Mn in breast cancer patients may be due to its consumption by cancerous cells during the development of the breast cancer.

The present study shows that only copper level was significantly reduced in patients with breast cancer compared with the controls. This may be an indication that Cu is associated with the pathogenesis of breast cancer. Concerted efforts toward the use of this element in monitoring the efficacy of or supplementing breast cancer treatment may be attempted.

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