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Evaluation of Mg, Cu, Zn, Cr and Mn Concentrations in Iraqi patients' female with Breast Cancer.

Zohair I. AL-Mashhadani
Abdul Jabbar A. Mukhlis
Dept. of Chemistry/ College of Education for Pure Science (Ibn AL-Haitham)/ University of Baghdad.
Aliaá S. AL-Faraji
Center for Market Research and Consumer Protection/ University of Baghdad

Abstract

To investigate the concentration and role of certain important elements in 30 patients women with breast cancer (without treatment, with treatment, and treated but recancer) by using statistical analysis. The serum concentration of some important elements (Mg, Cu, Zn, Cr, and Mn) of the patients with breast cancer, and (7) healthy control women it is found that: there is a significant increase in the concentration of (Mg, Zn, and Mn), but significant decrease in Cu concentration in all breast cancer patients compared with the healthy control. And significantly higher in Cr concentration in notreated and treated with recancer, but lower in treated patients as compared with healthy control.

Key words: trace elements, breast cancer.

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Introduction

Breast Cancer
Cancer is a disease in which cells become abnormal and form more cells in an uncontrolled way[1]. With breast cancer, the cancer begins in cells that make up the breast (usually in the tubes that carry milk to nipple or the glands that make milk). The cancerous cells form a mass of tissue called a malignant tumor that starts from cells in the breast. Sometimes, the cancer spreads to other parts of the body[1,2].

The disease occurs mostly in women, but men can get breast cancer as well. Breast cancer is the most common cancer among women, other than skin cancer. It is the second leading cause of cancer death in women, after lung cancer[1-4]. About one in eight women will be diagnosed with breast cancer during their lifetime. Breast cancer also strikes men but in much lower numbers (1 in 100)[4]. There are several types of breast cancer, although some of them are quite rare. In some cases a single breast tumor can have a combination of these types or have a mixture of invasive and in situ cancer which are[5]:

1- Ductal carcinoma in situ. (DCIS).
2- Lobular carcinoma in situ. (LCIS).
3- Invasive (or infiltrating) ductal carcinoma. (IDC).
4- Invasive (or infiltrating) lobular carcinoma. (ILC).

Minerals Biochemical Background[6,7]:
Minerals are required for both physiological and biochemical function, they may be divided into two groups:

1. Macrominerals (Important Minerals):
Macrominerals which are required in amount greater than 100 mg/day including:

Calcium, Phosphorus, Sodium, Potassium, Chloride and Magnesium[6,7].

Magnesium (Mg):

There are two major roles for magnesium in biological system:
1. It can compete with calcium for binding sites on protein and membrane.
2. It can form chelates with important intracellular anionic ligands, notably adenosine tri-phosphate (ATP)[8].

The kidneys are the main organs of Mg homeostasis in maintaining plasma concentration, during periods of Mg depletion, kidney Mg excretion can be markedly reduced. Approximately 25% of filtered Mg is reabsorbed in the proximal tubule and 50% to 60% in the ascending limb of the loop of Henle[9].

The major part of Mg in plasma about (60-70)% exists as free ions or in the form of various diffusible complexes, the remainder is bound to protein. Reference Value = 0.63-1.0 mmol/L (1.26-2.10 m Eq/L)[10].

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2. Microminerals (Trace Elements):

Microminerals which are required in amount less than 100 mg/day including: Copper, Iodine, Iron, Zinc, Chromium, and Manganese [11,12].

Copper (Cu):

Copper is an essential trace element that is an integral component of certain metalloenzymes and protein [13]. Copper is necessary for the formation of blood cells and connective tissue. It is also involved in the producing of the skin pigment melanin[14].

Abnormalities in copper metabolism have come a hall marks for diagnosing many diseases states[15]. The highest concentration of copper is found in liver, brain, kidney and heart, while intermediate copper concentration is found in the lung, intestine and spleen[16]. Generally, serum copper level has been found to be anon specific indicator of disease activity in many malignant and non malignant diseases. It was found that serum copper level is elevated in a variety of malignant lymphoproliferative disorders, such as leukemia[17], Hodgkin's disease[18] and non-Hodgkin's lymphoma[19-21]. Reference Value = 700-1500 µg/L [10].

Zinc (Zn):

Zinc is an essential component of many important enzymes, such as ALP, SOD, RNA and DNA polymerase [22]. Zinc plays an important role in protein synthesis regulation of gene expression [23]. Moreover, zinc stabilizes the structure of proteins and nucleic acid [24].

Zinc presents in higher concentration in the liver, pancreas, kidney, heart and leukocytes, where it shows a rapid deposition and turnover in these tissues. Other tissues, show slower kinetic rates including muscle, red blood cell, brain and bone[25]. 98% of the total body zinc is intracellular [26], therefore the plasma might be only a transport medium. Abnormalities of serum zinc level has been observed in association with certain malignancies [27]. Reference Value = 70-120 µg/dL[10].

Chromium (Cr):

Trivalent chromium is a nutritional component for a large class of organisms[28]. Trivalent chromium (Cr(III) or Cr^{3+}) in trace amounts influences sugar and lipid metabolism in humans and its deficiency is suspected to cause a disease called chromium deficiency[29]. However, chromium deficiency is thought to be extremely rare in the general population and has only ever been confirmed in three people on parenteral nutrition, which is when a patient is fed a liquid diet through intravenous drips[30]. In contrast, hexavalent chromium (Cr (VI) or Cr^{6+}) is very toxic and mutagenic when inhaled Cr(VI) has not been established as a carcinogen when in solution, though it may cause allergic contact dermatitis (ACD)[31]. Reference Value = < 0.05-0.5 µg/L [10].

Manganese (Mn):

Manganese is an essential trace nutrient in all forms of life[32]. The classes of enzymes that have manganese cofactors are very broad and include oxidoreductases, transferases, hydrolases, lyases, isomerases, ligases, lectins, and integrins. The reverse transcriptases of many retroviruses (Though not lentiviruses such as HIV) contain manganese[33]. The human body contains about 10 mg of manganese, which is stored mainly in the liver and kidneys. In the human brain the manganese is bound to manganese metalloproteins most notably glutamine synthetase in astrocytes[34]. Reference Value = 0.43-0.76 µg/L[10].

The aim of our study is to evaluate some biochemical parameters like minerals (i.e. Mg, Cu, Zn, Cr, and Mn). In Iraqi patients suffering from Breast cancer and compared that with the same parameters in normal healthy Iraqi control.

Subjects, Material and Methods

Patients:

Blood samples were collected from a thirty women with breast cancer (without treatment (8) women, treatment (12) women , treatment and recancer (10) women), with age range (19-60) years at the Medical City Hospital in Baghdad. Seven apparently healthy women were selected with age range (20-43) years.

Ten milliliters (ml) of venous blood were collected into plain tubes from each patient and healthy individuals after 12 hours fasting. The blood samples were allowed to stand for 15 minutes (min) then centrifuged at 3500 rpm for 10 min. Serum was frozen at $-20°C$ till used for the estimation of Mg, Cu, Zn, Cr, and Mn by atomic absorption technique.

Results and Discussion

Results

Serum Magnesium (Mg) Concentration:

The results showed that there is no significant difference ($P \geq 0.05$) in serum Mg^{2+} concentration of breast cancer patients compared with healthy control as shown in table (1).

Serum Copper (Cu) Concentration:

Data presented in Table (2) showed a non-significant difference ($P \geq 0.05$) in serum copper (Cu^{2+}) concentration of all breast cancer patients compared with healthy control and showed that the case without treatment is less in Cu concentration three times and half than the control, while the treated and recancer group is less in concentration of Cu five times compared with healthy control.

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Serum Zinc (Zn) Concentration:

The results showed that, there are no significant difference ($P \geq 0.05$) between the concentrations of Zn^{2+} in serum of all breast cancer patients compared with healthy control group as shown in table (3).

Serum Chromium (Cr) Concentration:

The results showed a non-significant difference ($P \geq 0.05$) in serum Cr^{3+} concentration of all breast cancer patients compared with healthy control as shown in table (4).

Serum Manganese (Mn) Concentration:

Data presented in Table (5) showed a non-significant difference ($P \geq 0.05$) in serum Manganese concentration of total breast cancer patients compared with healthy control group.

Discussions

Serum Magnesium (Mg) Concentration:

Serum and tumor magnesium concentrations were determined in patients with breast cancer using atomic absorption spectrophotometry. Serum values were found to be within normal limits of control. The cancerous tissues were found to contain significantly more magnesium than the control tissues. There was no correlation between the serum and tissue values and neither of these correlated with axillary lymph node metastasis[35]. Magnesium (Mg) deficiency can paradoxically increase the risk of, or protect against cancer yet we will find that just as severe dehydration or asphyxiation can cause death, magnesium deficiency can directly lead to cancer. We can see that magnesium deficiency would lead to physiological decline in cells setting the stage for cancer. An thing that weakness cell physiology will lead to the infections that surround and penetrate tumor tissues. These infections are proving to be an integral part of cancer[35].

Serum Copper (Cu) Concentration:

Cu blood level show low concentration than controls. A sharp different values in cases and controls. These mean known risk factors and related variables. We suggest that the low level incorporation of Cu in cancer cases and that the same mineral might play a role in breast cancer risk[36].

In the human and other mammals, the first observable evidence of copper deficiency is a drop in the level of blood ceruloplasmin (Cp). Cp is a copper-containing protein secreted by the liver into the blood. The copper in Cp accounts for about 90% of the total plasma copper. As copper availability to the liver decreases, the liver decreases production and secretion of Cp. Thus, plasma Cp is a good surrogate marker of body copper status[36].

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Serum Zinc (Zn) Concentration:

Previous studies that have assessed breast cancer in relation to Zinc have yielded inconsistent results. Our data raise the possibility that relatively low levels of Zinc in breast tissue may be associated with a modest increase in risk of subsequent breast cancer[37].

Deficiency of Zinc may contribute to mammary carcinogenesis due to the roles of this element in regulating cell proliferation differentiation. Additionally, Zinc have immune-enhancing and antioxidant effect[37].

In conclusion, our data do not support the hypothesis that decrease in breast cancer risk, and indeed, raise the possibility that Zinc may be associated with a modest increase in risk of subsequent breast cancer among women with breast disease[37].

Serum Chromium (Cr) Concentration:

A large accumulation of Cr in the breast cancer. These findings may have an implication for the pathogenesis of breast cancer. The etiology of human breast cancer is still controversial, although hormonal influences, toxic compounds, oxidative stress, and lipid peroxidation have been suggested to play a role in breast cancerogenesis[38]. Cr has been recognized as mutagens and carcinogens because of their ability to inhibit the repair of damaged DNA. In addition, they can enhance the mutagenicity and carcinogenicity of directly-acting genotoxic agents[39].

Serum Manganese (Mn) Concentration:

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.

High conc. Mn in breast cancer patients may be due to its consumption by cancerous cells during the development of the breast cancer[40]. Many, if not all, *in vivo* as well as *in vitro* studies demonstrate the importance of Mn for cellular defense in hypoxy as well as against cytotoxic drugs[41,42]. It was shown that following Mn gene transfection, tumor cells overexpressing Mn have a lower mitotic speed[41,42]. For this reason,it was asserted that Mn has a tumor suppressor role for human breast cancer[43].

Conclusion

Results of the present study suggest that Mg, Cu, Zn, Cr, and Mn may play an important role in breast cancer. A significant elevation in the concentration of Mg, Cu, Zn, Cr, and Mn in female breast cancer.

Recommendation

Although, some of the present data were statistically non-significant, our interpretation from these results indicate that the chemotherapy are unusefull in treatment of breastcancer.

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Table (1): Magnesium (Mg) concentration (ppm) in serum of patients with breast cancer (no treatment, treatment, and treatment & recancer) and healthy control.

Groups	N	Mean	SD	t-test
without treatment	8	21.6983	11.5446	$P \geq 0.05$
With Treatment	12	38.4175	17.4881	$P \geq 0.05$
With Treatment & recancer	10	31.4700	2.5880	$P \geq 0.05$
Control	7	20.7900	2.4325	$P < 0.05$

Table (2): Copper (Cu) concentration (ppm) in serum of patients with breast cancer (no treatment, treatment, and treatment & recancer) and healthy control.

Groups	N	Mean	SD	t-test
without treatment	8	1.7648	0.0010	$P \geq 0.05$
With Treatment	12	4.7725	0.0002	$P \geq 0.05$
With Treatment & recancer	10	0.2500	0.0001	$P \geq 0.05$
Control	7	5.5660	0.0011	$P < 0.05$

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Table (3): Zinc (Zn) concentration (ppm) in serum of patients with breast cancer (no treatment, treatment, and treatment & recancer) and healthy control.

Groups	N	Mean	SD	t-test
Withou treatment	8	0.1850	0.0004	P ≥ 0.05
With Treatment	12	0.2000	0.0001	P ≥ 0.05
With Treatment & recancer	10	0.1950	0.0011	P ≥ 0.05
Control	7	0.1850	0.0012	P<0.05

Table (4): Chromium (Cr) concentration (ppm) in serum of patients with breast cancer (no treatment, treatment, and treatment & recancer) and healthy control.

Groups	N	Mean	SD	t-test
without treatment	8	14.9967	5.6089	P ≥ 0.05
With Treatment	12	11.2825	5.3397	P ≥ 0.05
With Treatment & reccancer	10	19.4050	11.7309	P ≥ 0.05
Control	7	14.7550	7.1206	P<0.05

Table (5): Manganese (Mn) concentration (ppm) in serum of patients with breast cancer (no treatment, treatment, and treatment & recancer) and healthy control.

Groups	N	Mean	SD	t-test
withouttreatment	8	0.0105	0.0002	P ≥ 0.05
With Treatment	12	0.0079	0.0001	P ≥ 0.05
With Treatment & recancer	10	0.0065	0.0002	P ≥ 0.05
Control	7	0.0032	0.0001	P<0.05

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تقييم تراكيز المغنسيوم والنحاس والزنك والكروم والمنغنيز في المريضات العراقيات المصابات بمرض سرطان الثدي

زهير ابراهيم المشهداني
عبد الجبار عبد القادر مخلص
قسم الكيمياء / كلية التربية للعلوم الصرفة (ابن الهيثم) / جامعة بغداد
علياء سعدون عبد الرزاق الفراجي
مركز بحوث السوق وحماية المستهلك / جامعة بغداد

الخلاصة

تم أخذ عينات   لغرض بيان تركيز ودور بعض العناصر المهمة الأساسية في المرضى المصابين بسرطان الثدي. تتألف من (30) مصابة بالمرض (بدون علاج، بعلاج، بعلاج مع رجوع المرض) وتم قياس تراكيز (المغنسيوم والنحاس والزنك والكروم والمنغنيز) في مصل (30) مريضة و (7) نساء تطوعن كمجموعة سيطرة خالية من أي مرض. كانت نتائج البحث للمجاميع المذكورة باستخدام التحليل الإحصائي كما يأتي: حدوث ارتفاع معنوي باستعمال تراكيز العناصر المهمة الأساسية (المغنسيوم و الزنك و المنغنيز) ولكن حدوث انخفاض معنوي في تركيز النحاس بين جميع المرضى مقارنة بالأصحاء. وارتفاع معنوي في تركيز الكروم في المرضى الذين لم يأخذوا العلاج وفي الذين اخذوا العلاج مع رجوع المرض ولكن مع حدوث انخفاض معنوي في المرضى الذين اخذوا العلاج مقارنة بالأصحاء.

الكلمات المفتاحية: العناصر النزرة، سرطان الثدي.