Effect of Some Antioxidant Parameters in Breast Cancer

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(Received 14 / 1 / 2008 , Accepted 11 / 9 / 2008)

Abstract
This research has been done to determine the effects of some biochemical parameters in women with breast cancer. Seventy three blood samples of women with breast cancer and other twenty blood samples of healthy women as control group at ages ranging from 45-70 years, living in Mosul city. Some vitamins, trace elements and electrolytes were measured in these women. The results showed a significant decrease in vitamins A, C and E (as antioxidants) of breast cancer women as compared with the control group, while sodium and chloride levels were significantly increased, but there was no change in potassium level in those patient. This study showed a significant decrease in zinc level, while there was a significant increase in calcium level, and the magnesium level has no change in breast cancer women compared with control group.

Introduction
Antioxidants are substances that may protect cells from the damage caused by unstable molecules known as free radicals which may cause cancer (21). Antioxidants interact with the stabilized free radicals and may prevent some of the damage free radical otherwise might cause. Examples of antioxidants include beta-carotene, lycopene, vitamins C, E and A and other substance (20).
In analysis of beta carotene and vitamin C were significantly associated findings suggest that antioxidant vitamins such as beta-carotene and vitamin C intake could lower the breast cancer risk in Korean women, the researchers concluded (19).
One of the important vitamins is ascorbic acid is an important vitamin which participates in a great variety of biological events concerning electron-transport reaction, the oxidative catabolism of aromatic amino acid, and scavenging the ROS and may thereby prevent oxidative damage to important biological macromolecules such as DNA, lipid and protein (34).
Vitamin C acts as antioxidants by reacting directly with ROS or regenerating vitamin E from α-tocopheroxyl radical (14). Thus, it protects cell membranes from external oxidants and has a glutathione-sparing effect (7). Also Alta'ee found a significant decrease in vitamin C levels in serum of patients with different types of cancer (6).
Vitamin A is another important vitamin, it is considered as antioxidant because of its capacity to relieve oxidative stress. Vitamin A prevents lipid peroxidation by scavenging free radical and other oxygen species. Moreover, the vitamin A has been implicated as a biological factor in reducing the incidence with cancer (28).
Vitamin E is also has a strong antioxidant action, preventing oxidation of polyunsaturated fatty acid in cell membranes by free radicals. The important antioxidant function of vitamin E appears to be the inhibition of lipid peroxidation, scavenging lipid peroxy radicals to yield lipid hydroperoxides and tocopheroxyl radical (31).
Breast cancer is a major public-health problem in many countries. It is the most common malignancy and the most frequent cause of cancer death among females (1). One of the risk factor for breast cancer is dietary factors.
Breast cancer this is the most common type of cancer women in the world. There is an increased risk of breast with factors including rapid early growth, greater adult high and weight gain in adulthood. Diets high in monounsaturated fat, high in vegetables, fruits may reduce the risk (19).
Trace elements are essential elements which are required for growth or for the maintenance of life. Zinc (Zn) is one of the most abundant trace elements in human body. It is an essential cofactor for enzymes, which control many cell processes including DNA synthesis, membrane stability, breast development and protection from free radical damage (7). Low concentration of Zn was found in the serum of patients with carcinoma of the larger and with different types of cancer (6, 30). Other study showed low level of Zn in patients with breast cancer (2).
Magnesium (Mg) is the second most abundant intracellular ion. Mg is essential for the function of more that (300) cellular enzymes, including those related to the transfer of phosphate group, all reaction that require ATP. These contains are required for cellular energy metabolism (18)
Electrolytes are ions carrying an electric charge. They are classified as anions or cations based on the type of charge they carry. They regulate important physiological function. Electrolyte imbalance causes a variety of symptoms that can be severe, the imbalance is commonly caused by lose of body fluids through prolonged vomiting, diarrhea, sweating and high fever. The most serious from of electrolyte imbalance in cancer patients include disorder called tumor lysis syndrome that results in electrolyte imbalance from the killing of cancer cells. Both of these can be life-threatening if not managed appropriately (17).

Materials And Methods
Five milliliters of venous blood was taken from each patient and leave it for (15) minutes at room temperature for coagulation, then serum can be separated by centrifugation at (3000 Kg) for (10) minutes. Serum was kept frozen at (- 20 °C) for some biochemical tests (33). Seventy three blood samples of women with breast cancer and other twenty blood samples of healthy women as control group at ages ranging from 45-70 years, living in Mosul city.
Vitamin C in serum can be determined photometrically with 2,4-dinitrophenyl hydrazine (DNPH) to form the red bis-hydrazone (19).
The chemical methods for determination of vitamin E in serum are based on oxidation reduction reaction.

Following specific elution techniques, fractions are commonly subjected to the Emmerie-Engel procedure in which tocopherol is oxidized to tocopherol quinone by $FeCl_3$, and the Fe^{++} in the resultant $FeCl_2$ is complexed with α,α-dipyridyle to produce a red colour with absorbance at (520 nm). Interfering lipid soluble substance were extracted into xylene after precipitation of serum protein with ethanol (31). To determine carotene interference α,α-dipyridyl was added to an aliquot of the xylebe layer and the absorbance was measured at (460 nm). Ferric chloride was then added to yield a coloured compound whose absorbance at (520 nm) was proportional to the tocopherol concentration. This absorbance was corrected for carotene interference when the absorbance measured at (460 nm) was subtracted (15).

Vitamin A has a strong absorption in the ultraviolet region with a maximum level at (327 nm). It is destroyed by ultraviolet light. The optical density differences between irradiated and non-irradiated serum extracts can therefore be used to measure the vitamin A content (35).

Zinc in serum was assayed by using atomic absorption spectrophotometry.

Serum magnesium was determined by colorimetric method using manufactured kit by Syrbio (France).

Serum calcium was determined by colorimetric method using manufactured kit by Biocon (Germany).

Sodium, potassium and chloride in serum were determined using flame emission spectrometry.

Statistical analysis

The results are expressed as mean ± SD our date were analyzed statistically using paired t-test to compare subjects result for various parameters among different groups tested in the work. The difference is considered significant at $p \leq 0.05$ (23).

Results

Vitamin concentration in blood serum of breast cancer women

The results in Table (1) showed that there was a significant decrease ($p < 0.001$, $p < 0.001$, $p < 0.001$) in serum vitamins A, E, C concentration in breast cancer women compared to the control group. Similar results have been reported by other investigators (8,29,36).

The increased risk of breast cancer in vitamin A deficiency is thought to be the result of a depletion in β-carotin, this compound is a vary effective antioxidant and is suspected to reduce the risk of breast cancer known to be initiated by production of free radicals. This result is in conformable with several studies which observe low levels in vitamin A in patients with brain tumors (29) and in lung and gastric cancer (4,5).

In present study, our results is in corresponding with (29) in which they noted that low levels of vitamin E concentrations may facilitate oxidative damage in patients with breast cancer. The major site of vitamin E is to act as a natural antioxidant by scavenging free radicals and molecular oxygen (27).

It has other roles, unrelated to antioxidant activity, including the maintenance of cell membrane structure and effects on DNA synthesis and cell signaling. There is a lot of evidence from tissue cultures and experimental animals studies indicating that antioxidant decrease oxidative DNA damage, thereby decreasing mutagenesis and carcinogenesis (21).

Furthermore, vitamin E plays a crucial role in the maintenance of the immune system, because immune function is linked to the release of O_2 radicals that participate in macrophages. Thus linked to the release of O_2 radicals that participate in macrophages. Thus the immune system has been shown to be more sensitive than other systems to antioxidant deficiencies in the diet (11).

The decrease in vitamin C level in malignant cases was higher than that in benign tumors which may due to free radical formed in body fluids. Patients with breast cancer are detoxified by antioxidant including vitamin C that is the consumption of vitamin C will be higher which leads to the decrease of its concentration in the blood (36). High intake of vitamin C has been shown to inhibit carcinogenic activities of certain substances (25).

Finally, the results of several studies suggest that increased antioxidant vitamins are associated with a decreased risk of certain types of cancer (8, 13, and 29).

Table (1): comparison between the patient with breast cancer women and control group for vitamins.

parameters	Mean ±S.D.		P-value
	patients	Control group	
Vitamin A µmol/L	0.56±0.057	1.37±0.063	<0.001
Vitamin C µmol/L	15.54±1.22	31.29±0.084	<0.001
Vitamin E µmol/L	5.87±1.08	16.53±1.13	<0.001

Trace elements concentration in blood serum of breast cancer women

The results in Table (2) show that there was significant decrease ($p < 0.001$) in zinc concentration in serum of breast cancer women compared to the control group. Similar results have been reported by other investigators (2, 3).

The reduction in concentration of zinc in biomembranes underlines some of the disorder associated with zinc deficiency with a loss of zinc from the membrane resulting in an increase susceptibility of oxidative damage, structural strains, and alteration in specific receptor sites and transport systems (26).

The antioxidant properties of zinc have been demonstrated in vitro. Zinc may exert its antioxidant effect by decreasing the susceptibility of essential sulfhydryl group of proteins to oxidation and by competing with pro-oxidant metals, such as iron and copper for biological binding sites (18).

The results of the present study suggest that zinc concentration may be considered a biochemical marker of oxidative stress associated with cancer (16).

Magnesium concentration in serum of breast cancer women was no significant difference ($p > 0.05$) compared with control group agreement with (5).

The level of calcium in serum of breast cancer women and found to be significantly increased ($p < 0.001$), when compared with control group. Similar results have been reported by other investigators (10, 32).

Decreased level of ascorbate in blood should result in increased ionized Ca levels, as Ca complexes with ascorbate. There is evidence that, ascorbated blood clots a little more slowly than normal blood. However, that increased ascorbate intake can increase mobilization of freshly deposited Ca in bone and this would tend to oppose decreased Ca levels (25).

Table (2): comparison between the patient with breast cancer women and control group for trace elements.

parameters	mean±S.D.		P-value
	patient	Control group	
Magnesium mmol/L	0.81±0.05	0.83±0.04	>0.05
Calcium mmol/L	2.78±0.53	2.46±0.18	<0.001
Zinc mmol/L	13.23±2.98	20.47±5.64	<0.001

Electrolytes concentration in blood serum of breast cancer women

Table (3) shows that there was a significant increase ($p < 0.001$) in sodium concentration of blood serum in breast cancer women when compared with control group.

Potassium concentration has a non-significant difference between patients and control group, Table (3). On the other hand a significant increase ($p < 0.05$) of chloride concentration was observed on serum of breast cancer when compared with control group.

The patients with different types of cancer are usually presented with prolonged vomiting due to the increase in the intractional pressure which is in agreement with (12, 22). The vomiting will lead to dehydration and hypernatremia (increased serum sodium concentration) results from excess loss of water relative to sodium loss, decreased water intake or retention or increased sodium and fluoride intake due to an excessive intravenous infusion (24).

These symptoms are commonly attributed either to the cancer treatment or to cancer itself. Other causes included tumor lysis syndrome when cancer cells are killed by therapy, they spill their inner (intracellular) contents, which accumulate in the body faster than can be eliminated. These excess intracellular contents cause the metabolic and electrolyte disturbances that result in tumor lysis syndrome (17).

Table (3): comparison between the patient with breast cancer women and control group for electrolyte.

parameters	Mean±S.D.		P-value
	patients	Control group	
Sodium mmol/L	145.±1.29	137.45±1.93	<0.001
potassium mmol/L	3.65±0.075	3.19±0.11	<0.005
chloride mmol/L	94.67±4.24	88.78±2.63	<0.005

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تاثير بعض مضادات الاكسدة في مرضى سرطان الثدي

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(تاريخ الاستلام: ١٤ / ١ /٢٠٠٨ ، تاريخ القبول: ١١ / ٩ / ٢٠٠٨)

الملخص

لغرض معرفة تاثير بعض المتغيرات الكيموحيوية في مرضى سرطان الثدي. تم قياس مستويات فيتامين كل من A و E و C وبعض العناصر النادرة والالكتروليتات في (٧٣) امراة مصابة بسرطان الثدي و (٢٠) امراة سليمة (كمجموعة سيطرة)، تراوحت اعمارهن من (٤٥-٧٠) سنة ومن سكنة مدينة الموصل. وقد اظهرت النتائج وجود انخفاض معنوي في مستوى فيتامين A و C و E في مرضى سرطان الثدي مقارنة مع مجموعة السيطرة، ومن ناحية اخرى لوحظ وجود زيادة معنوية في مستويات كل من الصوديوم والكلورايد في حين لم يلاحظ أي تغير معنوي في مستوى البوتاسيوم، كذلك اظهرت النتائج انخفاض معنوي في مستوى الزنك وزيادة معنوية في مستوى الكالسيوم في حين لم يلاحظ أي تغير معنوي في مستوى المغنسيوم عند مقارنتهم مع مجموعة السيطرة.