Estimation of Some Trace Elements and Antioxidant Status in Breast Cancer Patients Undergoing Radiotherapy

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Abstract

Breast cancer (BC) is the most prevalent tract cancer in the world, including Iraq. The classified breast tumors to benign, malignant, and radiotherapy. Cancer treatment depends on certain stages such as mastectomy then chemotherapy alone or with radiation therapy or endocrine therapy according to the prognostic features obtained from the pathology report. The present study included 100 females. The women were split into two groups, control group that consisted of 50 apparently healthy females and 50 patients with BC group who undergo the radiotherapy. The current study highlighted on some of the anthropometric measurements, including the oxidative stress index malondialdehyde (MDA), the concentrations of total antioxidant capacity (TAC), serum albumin (Alb), serum uric acid (UA), and finally the concentrations of copper (Cu) and zinc (Zn) as trace elements were measured as well. The results were compared to control. There was a significant variation in MDA and albumin when comparing patient group with control, while uric acid was statistically insignificant when comparing control group with patients group. Cu concentration was statistically high when compared with control group. On the other side, a significant decrease of Zn concentration of patients was observed compared to control group .In this study, the evaluation of these parameters maybe used as a helpful tool in treatment of breast cancer.

Keywords: *Breast Cancer, Malondialdehyde, Total antioxidant capacity, Copper, Zinc.*

Introduction

Breast cancer is the major cause of death among women worldwide. Benign breast tumors are the most famous kinds of breast tumors that usually do not turn into cancers but they can be connected with a higher risk of creating breast cancer growth in the future [1]. Malignant tumors are the growth of abnormal cells that lead to the formation of mass clusters where cells divide and grow abnormally and quickly in uncontrollable way then float to many parts of the body and may spread cancer to far parts of the body during the lymphatic system or blood stream · Women, who are taking radiation to treat other cancers ,have a tenfold increased danger, of breast cancer.

The risk from breast cancer varies if the radiation is given before the menstruation. However, the danger is not increasing after the age of 45 years [2]. Malondialdehyde, is one of α, β-unsaturated aldehydes. These aldehydes have the structure C=C−C=O.Malondialdehyde is indicator of lipid peroxidation. The estimation of malondialdehyde became use extensively, because it seems to provide a good way of assessing lipid peroxidation in biological materials. Malondialdehyde happen in biologics materials in Free State and in diverse covalently bound forms [3].

Antioxidants are compounds that can help preventing the harmful reactions of the chemical chain with oxygen and/or with nitric oxide. This process is called oxidation reactions. The mechanism of the antioxidants includes a reaction with the free radicals that react with certain molecules, providing a protection against oxidation reaction. In addition, antioxidants may enhance the immunity system and as a result, reduce the

chance of cancer formation and infection. Antioxidants help balancing the beneficial oxidant generation, frequently acts as cell signaling that damages oxidative stress [4].

The albumin is a negative protein and a multi posts plasma protein, which is a non-glycosylated that regulates the structure of a heart shaped protein with 67% of the alpha snail. The albumin is made primarily in the liver. The synthesis of the albumin inhibits inflammation and a decrease in the serum concentration of this protein is a fixed sign of a poor diagnosis in various diseases that describe the albumin serum as an independent indicator of survival in several cancers including breast cancer that lowers serum albumin to be an independent index of cancer patients[5].

Uric acid is a chemical created when the body breaks down purines. . Uric acids have antioxidant characteristics and in human serum have a role in 60% of free radical scavenging action when it is in the normal level. Most uric acid dissolves in blood and travels to the kidneys [6]. Copper produces the reactive oxygen species which in turn may attack deoxyribonucleic acid (DNA) creating a DNA mutation. Cu can also play as an element in the pathological process of cancer. Cu can be concerned in the activation of many organic peroxides and can make them more carcinogenic [7].

Zn had an important function by establishing the building of DNA, ribonucleic acid (RNA) and ribosome so that; it was considered an anti-carcinogenic agent. Zn is important to the functions of many duplication factors, proteins that distinguish certain DNA series and transcription of the control gene. Zn prevents the damage of free radicals and may influence immune response [8]. The aim of this study is to measure the serum levels of MDA, Cu, Zn and antioxidants levels in BC patients undergoing radiotherapy against the serum of healthy individuals.

Materials and Methods

Samples were obtained from 50 females patients undergoing radiotherapy, in Oncology Teaching Hospital/Baghdad during 2017. The complete physical examination was done to each patient.

The final diagnosis was established by aspiration of cysts fine needle aspirate (FNA) to check cytology, histology (biopsy) and mammography. As control, 50 females were chosen as healthy subjects. All blood samples were gotten from the patients and control. Patients and control were aged between 30 and 65 years. Blood samples of 5ml were collected in small vials, centrifuged at 3000 rpm for 10 min, after allowing the blood to clot at room temperature.

The serum of the blood samples was liquated and frozen ready to use. MDA calculate by using Buege & Aust enzymology method .Thiobarbituric acid (TBA) method of Buege & Aust was used to measure the MDA which reacts with thiobarbituric acid and gives pink color .The concentration of malondialdehyde measured with λ_{max} of 535 nm [9]. On the other hand, serum TAC was determined. The antioxidant in the sample reacts with special quantity of hydrogen peroxide .A certain quantity of the generated hydrogen peroxide deleted by the antioxidants.

By using colorimetric ally through an enzymatic reaction, the remnant of hydrogen peroxide was determined [10] Serum albumin was measured by spectrophotometric method. The methode is based on the specific bonding of bromocresol green (BCG), an anionic dye, and the protein at acid pH with outcomes shift in the absorption wavelength of the complex. The density of the color established is proportional to the concentration of albumin in the sample. Absorbance was read at 630 nm [11].

Also serum uric acid measured by spectrophotometric method. Uricase acts on uric acid to produced allantoin, carbon dioxide and hydrogen peroxide. Hydrogen peroxidase reacts with a chromogen (amino – antipyrine and dichloro-hydroxybenzensulfonate) to yield quinoneimine, a red colored complex. The absorbance measured at 520nm [12]. Copper and zinc were determination by using Varian Spectra AA 220 flame atomic absorption spectrometer. The spectral lines used for determination were324.7 nm for copperand213.9 nm for zinc [13].

Statistical Analysis

The results that expressed as means ±SD Student's t-test were applied to match the

magnitude of variation in the average values between the two groups, and (p< 0.05) was considered statistically significant.

Results and Discussion

MDA is an important biological marker of lipid peroxide having the ability to interact mainly with deoxyguanosine and deoxyadenosine DNA which can cause mutations[14]. The mean value ± SD of MDA radiotherapy breast cancer and the control subjects are illustrated in table (1). The results show a significant increase between the patients and control groups (P<0.05).

Table 1: Levels of Serum MDA, TAC, Albumin and Uric Acid in Sera of Patients with Breast Cancer Undergoing Radiotherapy and Healthy Subjects

Parameters	Control(mean ±SD)	Patients(mean ±SD)	P-value
MDA (μmol/L)	47.30±2.60	68.50±2.50	P <0.05
TAC (mmol/L)	01.30±0.36	0.41±0.23	P <0.05
Albumin(g/dl)	4.40±0.39	3.52±0.32	P <0.05
Uric acid(mg/dl)	3.90±0.60	4.00±0.13	P>0.05

The rise of MDA in cancer has been shown to be linked with the body's oxidative stress which leads to the loss of PUFA in the plasma membrane and asserts that oxidative stress leads to dysfunction in the mitochondria and even regulates important factors such as the nuclear respiratory agent. Increasing in the peroxidation level of lipids in the serum of BC patients when compared to the normal is consistent with few studies. In the case of radiation therapy, a noticeable increase is observed in MDA because radiotherapy increases oxidative stress of patients[15].

TAC in serum shows significant decrease between two groups (P<0.05). Studies have indicated raised oxidative stress in patients with BC undergoing radiotherapy[16] .This can be ascribed to the increase in the free radical production and/or the decrease in the antioxidants intake. According to some studies, radiotherapy for breast cancer patients is linked to increased reactive oxygen and nitrogen and decrease antioxidant concentration.

The damaged tissue can lead to the formation of ROS generated by the increased efficiency of phagocytes or the release of the ions of the transitional elements of the carcinogenic cells [17]. Determination of TAC may not always represent the true antioxidant activities. It may be useful in diagnosis because its steps are easy and fast [18].The mean value ±SD of serum albumin in sera of control and patient with breast cancer undergoing radiotherapy are respectively shown in Table (1). The results illustrate that there is a distinguishable difference between two the groups (P<0.05). There are many studies that have confirmed that low serum albumin levels are a sign of low survival for many types of cancer such as lung cancer, ovarian cancer, and breast cancer [19] .

Decrease albumin concentration can be due to pro inflammatory cytokines like tumor necrosis factor (TNF-α) and interleukin 6 (IL-6) which are known to down regulate albumin synthesis and increased acute-phase protein production in isolated hepatocyte [20]. UA is derived exclusively from xanthine and hypoxanthine by xanthine oxidoreductase (XOR). It is also observed that there is non-significant increase in control and patient groups (P>0.05).

Uric acid is one of the important antioxidants that play a role in the prevention of cancer by preventing the formation of free radicals especially the roots of oxygen, but its anti-inflammatory properties play an important role in causing cancer. One of the most important foundations of early diagnosis of breast cancer is the measurement of uric acid [21]. Table (2) illustrates the concentration of trace elements. Copper shows a high concentration in cancer tissue, possibly due to the angiogenesis increase. Cu deficiency is considered as an anticancer strategy [22].

Table 2: Levels of Cu and Zn in Sera of Patients with Breast Cancer Undergoing Radiotherapy and   Healthy Subjects

Parameters	Control(mean ±SD)	Patients(mean ±SD)	P-value
Cu (g/dl)	105.90±2.75	143.63±1.10	P <0.05
Zn (g/dl)	70.01±0.90	59.80±2.10	P <0.05

The concentration of Cu in breast cancer serum samples in our study was increased significantly compared to the healthy individuals (P<0.05) which is in a full agreement with the findings of many researchers in breast cancer. This study supports the previous studies, which also showed that Cu can be concerned in the activation of several organic peroxides and can produce the hydroxyl groups, which are the radicals that cause the mutation in DNA, which may be one of the causes of cancer development [23].

As demonstrated by previous researchers, Zn concentration in cancer patients was decreased as compared to healthy individuals which seem in accordance with the results of our study where serum concentration of Zn was significantly lower in serum samples of BC patients as compared to serum samples of healthy subjects (P<0.05) [24]. Zn shows an influenced role in the stabilization of DNA, RNA and ribosome structures, it is also necessary for the function of many transcription factors, where it plays an important role for many transcription factors [25].

Conclusion

In summary, we found serum level of MDA in patients with cancer undergoing radiotherapy is high, whereas low status of antioxidants and albumin comparing the control, while we did not see a significant change in the level of uric acid between two groups. We also noticed the high-level of copper in serum of patients and low-level of zinc compared to healthy subjects.

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