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Research Article

Assessment of lipid peroxidation status in breast cancer patients receiving radiotherapy: an in-vivo human study

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ABSTRACT

Introduction: Cancer is a group of diseases characterized by uncontrolled growth and spread of abnormal cells. If the spread is not controlled, it can result in death. Cancer is caused by both external factors (tobacco, infectious organisms, chemicals, and radiation) and internal factors (inherited mutations, hormones, immune conditions, and mutations that occur from metabolism).

Objectives of the study: This study aim to investigate the level of lipid peroxidation in breast cancer patients who receives cancer therapies.

Material and Methods: The whole experimental work was conducted at the Jinnah post graduate medical Centre and THQ hospital sabzazar and multiple Basic Health Units under Primary & Secondary Healthcare Department. Those breast cancer patients who receiving radiotherapy, chemotherapy and adjuvant radiotherapy were selected to study the lipid peroxidation status in the diseased condition. **Results:** The data explains the levels of MDA in breast cancer females. The data suggest that lipid peroxidation is increases in breast cancer. The reason is due to high damage of membrane and lipid peroxidation poducts. **Conclusion:**By reducing oxidative stress, antioxidants counteract the effects of chemotherapy-induced oxidative stress on the cell cycle and enhance the cytotoxicity of antineoplastic agents.

Keywords: Cancer, Antioxidants, Therapies

INTRODUCTION

Cancer is a group of diseases characterized by uncontrolled growth and spread of abnormal cells. If the spread is not controlled, it can result in death. Cancer is caused by both external factors (tobacco, infectious organisms, chemicals, and radiation) and internal factors (inherited mutations, hormones, immune conditions, and mutations that occur from metabolism). These contributory factors may act collectively or in sequence to initiate or promote carcinogenesis.[1]Cancer is a leading cause of mortality and morbidity worldwide, counting for 7 million deaths per year. It is the second most common cause of death in developing countries. Cancer is the second leading cause of death worldwide, surpassed only by cardiovascular disease.[2]Therefore, fighting cancer is measured to be one of the most significant areas of research in medicine and which possibly contributes to increased interest in chemoprevention as an alternative approach to the control of cancer. Natural or dietary factors have attracted a great deal of interest because of their safe efficacy and perceived ability to act as highly effective chemo preventive agents.[3]

Cancer is due to failure of the mechanisms that usually control the growth and proliferation of the cell. Normally, in an adult tissue many cells do

not proliferate except during healing process. Cancer occurs when normal mechanism of cell is disturbed and cells produced or divide excessively. The loss of normal mechanism of cell is may be genetics or may be due to the influence of tumor-promoting chemicals, hormones and sometime viruses.[4] There are two major lines of investigations in cancer biochemistry; the metabolism of cancer cell and the effect of cancer on the host metabolism. The cancer cell presents at least three abnormal behavior patterns, involving proliferation, differentiation and its social relationship with neighboring cells.

Cancer development is a multistage process that requires the collective action of manifold events that occur in one cell alone.[5]Cancertreatment by radiation and anticancer drugs reduces inherent antioxidants and induces oxidative stress, which increases with disease succession. The possible causes of cancer include, damage to DNA by reactive oxygen species, which are at highest rank in the development and onset of cancer.[6]

OBJECTIVES OF THE STUDY

This study aim to investigate the level of lipid peroxidation in breast cancer patients who receives cancer therapies.

MATERIALS AND METHODS

The whole experimental work was conducted at the Jinnah post graduate medical Centre and THQ hospital sabzazar. Those breast cancer patients who receiving radiotherapy, chemotherapy and adjuvant radiotherapy were selected to study the lipid peroxidation status in the diseased condition.

Groups	Treatment
A	Control
B	Breast cancer (before and after radiotherapy)

Blood collection

5.0 ml blood sample was taken from vein. Blood was further processed for the estimation of MDA. Commercially available enzymatic kits of Randox were used. Blood was centrifuged at 4000 rpm for 10 minutes and serum was separated. Blood samples will be collected into EDTA tubes from fasting proteins. The blood will be centrifuged and indomethacin and butylatedhydroxytoluene will be added into the plasma samples before they will be stored at -80°C until analysis**.**

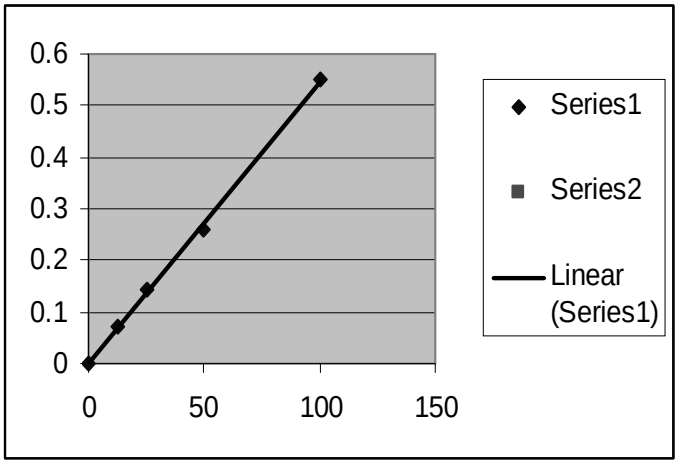
Determination of thiobarbituric acid reactive substances (MDA) in tissues:

TBARS in tissue was estimated by the method of Ohkawa et al. (1979). 0.2 ml tissue homogenate of each group was taken in test tubes and add 200 µl of 8.1% sodium dodecyl sulfate (SDS), Then add 1.5 mL of 20% acetic acid solution (pH 3.5) and 1.5 mL of 0.8% TBA. The mixture was made up to 4.0mL with distilled water and heated in a water bath at 90◦C for 60 min.

After cooling with tap water, 1.0mL of distilled water and 5.0 mL of n-butanol were added and shaken vigorously and centrifuged at 4000 rpm for 10 minute upper butanol layer was taken and its absorbance at 532 nm was read.

Concentration nmol/ml	Absorbance
100	0.550
50	0.260
25	0.145
12.5	0.070
0	0.000

Standard curve



Y= -0.129X + 0.592

R^2= 0.8952

X=Concentration

Y= Absorbance of sample

RESULTS

The data present in this table explains the levels of MDA in breast cancer females. The data suggest that lipid peroxidation is increases in breast cancer. The reason is due to high damage of membrane and lipid peroxidation poducts.

Table 01: MDA values of all therapies and control group

BREAST	CONTROL	MDA(moles/ml)			
		MALES (n=00)		FEMALES (n=15)	
	2.35	BEFORE	AFTER	BEFORE	AFTER
0	0.00	0.00	0.00	4.26±0.00	5.24±0.00
R1	0.00	0.00	0.00	2.99±0.38	4.95±0.97
R2	0.00	0.00	0.00	2.95±1.02	5.13±1.06
R1+B	0.00	0.00	0.00	3.76±0.70	5.89±0.91
R2+B	0.00	0.00	0.00	3.26±0.00	6.58±0.00
B	0.00	0.00	0.00	0.00±0.00	0.00±0.00
Total	2.35	0.00	0.00	3.16±0.80	5.27±0.98

Means±SD

R1=Received Radio Therapy Single Time

R2=Received Radio Therapy Two Times

R1+C=Received Radio Therapy Single Time + Chemotherapy

R2=Received Radio Therapy Two Times + Chemotherapy

C=Only Received Chemotherapy

0=received no therapy

DISCUSSION

Cancer therapy, such as chemotherapy, can result in the generation of excess ROS/RNS. Thus cancer therapy and the resulting production of excess oxidative stress can damage biological systems other than tumors. During chemotherapy the highest known levels of oxidative stress are generated by anthracycline antibiotics, followed in no particular order by alkylating agents, platinum-coordination complexes, epipodophyllotoxins, and camptothecins. The primary site of ROS/RNS generation during cancer chemotherapy is the cytochrome P450 monooxygenase system within liver microsomes. Enzyme systems, such as the xanthine-xanthine oxidase system, and non-enzymatic mechanisms also play a role in creating excess oxidative stress during chemotherapy.The very high levels of oxidative stress caused by anthracyclines is also related to their ability to displace coenzyme Q10 (CoQ10) from the electron transport system of cardiac mitochondria, resulting in diversion of electrons directly to molecular oxygen with the formation of superoxide radicals.[7]

Anthracyclines and other chemotherapeutic agents cause generation of high levels of ROS/RNS, but not all chemotherapeutic agents generate excess oxidative stress. Some agents generate only modest amounts of ROS/RNS. Examples of this are: platinum-coordination complexes and camptothecins, taxanes, vinca alkaloids, anti-metabolites, such as the anti-folates, and nucleoside and nucleotide analogues.[8]However, most chemotherapeutic agents generate some oxidative stress, as do all anti-neoplastic agents when they induce apoptosis in cancer cells. Drug-induced apoptosis is usually triggered by the release of cytochrome c from the mitochondrial electron transport chain. When this occurs, electrons are diverted from NADH dehydrogenase and reduced CoQ10 to oxygen, resulting in the formation of superoxide. Chemotherapeutic agents used to treat cancer cause oxidative stress, which produces side effects, and among the most common side effects is chronic fatigue. Chronic fatigue caused by cancer therapy can reduce therapeutic efficacy.[8] Although many anti-neoplastic agents have clearly established

mechanisms of action that are not dependent upon the generation of ROS/RNS, these drugs can only mediate their anticancer effects on cancer cells that are exhibiting unrestricted progression through the cell cycle. They must also have intact apoptotic pathways. Thus oxidative stress interferes with cell cycle progression by inhibiting the transition of cells from the G0 to G1 phase, slowing progression through S phase by inhibition of DNA synthesis. This results in inhibition of cell cycle progression of the G1 to S phase, and it also results in inhibition by checkpoint arrest.[9]

Chemotherapeutic agents can also activate DNA repair systems. DNA repair of damage caused by alkylating agents and platinum complexes results in resistance to these drugs, and checkpoint arrest during oxidative stress can enhance the repair processes and diminish the efficacy of treatment. Abolishing checkpoint arrest produces the opposite effect and enhances the cytotoxicity of anti-neoplastic agents.[10]

CONCLUSION

By reducing oxidative stress, antioxidants counteract the effects of chemotherapy-induced oxidative stress on the cell cycle and enhance the cytotoxicity of antineoplastic agents.

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