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Lipid Peroxidation Status in Different Stages of Breast Cancer Women Treated by Chemotherapy

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Abstract:

In the scenario of increasing evidence of cancers, the aim of the study was to evaluate the role of oxidative stress in breast cancer. For that purpose, histopathologically positive proved cases were selected for the present study. 97 healthy subjects attending camps organized by Cancer Hospital & Research Institute and 157 confirmed cases coming from the Cancer Hospital for treatment were considered for the study. The blood samples of above control and patients were collected for assay. The subjects were divided into groups on the basis of disorder. MDA levels as an index of lipid peroxidation. In our present study, the levels of MDA in serum were increased significantly in patients suffering from breast cancer. The normal blood level of MDA, which was 7.24 μg/ml, was increased to 7.5 μg/ml in patients of first stage cancer registering no significant change in MDA level. In the second stage cancer patients, the MDA level was further increased to 9.32 μg/ml, showing 28.7 % increase when compared with control. In the third stage cancer patients, the level of MDA was found to be 10.83 μg/ml showing 49.5 % increase when compared with control. The effect of chemotherapy on MDA level was show significant change in different stages of breast cancer. Before chemotherapy the conc. of MDA was 7.24 μg/ml, which was increased to 13.06 μg/ml after

chemotherapy, showing the 80.39 % increase. The high levels of serum MDA indicate increased lipid peroxidation in breast cancer.

Key words: lipid peroxidation, MDA, chemotherapy.

Introduction

Breast cancer is a malignant tumor that has developed from cells of the breast. A malignant tumor is a group of cancer cells that may invade surrounding tissues or spread to distant areas of the body. Breast cancer is the second most common cancer in women. Experimental investigations as well as clinical and epidemiological evidence reveal that reactive oxygen metabolites (ROM) are involved in initiation, promotion and progression of carcinogenesis, where inactivation or loss of certain tumor-suppressor genes have occurred (Haris , 1989).

Free radicals are formed in both physiological and pathological conditions in mammalian tissues. In healthy conditions at cellular level, a subtle balance exists between the free radical generation and the antioxidant defense. Reactive Oxygen species (ROS) are essential for multiple normal physiological processes like cell differentiation (Abe *et al*., 2000), apoptosis (Ghosh, 1998), cell immunity and cellular defense against microorganisms (Lajarin *et al*., 1999) at low concentrations. Excess generation of these oxygen free radicals and oxidants generate a phenomenon called oxidative stress which cause oxidative damage to biomolecules resulting in lipid peroxidation, mutagenesis and carcinogenesis. There is accumulating evidence from animal and human systems implicating a role of oxidative stress and lipid peroxidation in the development of breast cancer (Mianying Wang *et al*., 1996). Several studies reported that malonoaldehyde; the end product of lipid peroxidation can cause cross-linking in lipids, proteins and nucleic acids (Freeman BA 1982). It is also evident that overproduction of ROS/RNS (Kang, 2002) plays an important

role in the promotion and progression of human cancers, including breast cancer (Aghvami *et al*., 2006, Yeh, 2005). The human body is equipped with certain enzymatic and non-enzymatic antioxidant systems (Faruk Tas *et al*., 2005*).*

Most patients with breast cancer are treated with a combination of the anticancer chemotherapy drugs. These antineoplastic agents cause a reduction in antioxidant levels because their toxicity increases the peroxidation of the unsaturated fatty acids of membrane phospholipids (Conklin KA. 2004). Their main adverse effects may be heart damage (cardio toxicity) and vomiting which considerably limits their usefulness. (Simůnek T. 2009).

Therefore the current study aimed to investigate the effect and association of breast cancer on lipid peroxidation, as well as effect of chemotherapy treatment on breast cancer patients.

Material and method

Histopathologically positive proved cases were selected for the present study. 97 healthy subjects attending camps organized by Cancer Hospital & Research Institute and 157 confirmed cases coming from the Cancer Hospital for treatment were considered for above study. The blood samples of above control and patients were collected for assay.

The subjects were divided into following groups on the basis of disorder:

- Normal healthy subjects
- Stage I subjects
- Stage II subjects
- Stage III subjects

Lipidperoxidation

Lipidperoxidation in haemolyasate was measured by method of Ohkawa *et al.,* (1979).

Result and discussion

Lipid peroxidation plays an important role in the control of cell division. Low concentration of oxygen free radicals has been reported to stimulate cell proliferation; whereas high levels induce mutagenecity, cytotoxicity and cell death (Kang, 2002). Cellular fatty acids are readily oxidized by ROS to produce lipid peroxyl radicals and lipid hydro peroxides. Lipid peroxyl radicals can subsequently propagate into MDA. (Rice et al, 1993). These lipid radicals can diffuse through membranes, thus modifying the structure and function of membrane and resulting in a loss of cell homeostasis (Chaudhary et al, 1994). The products of lipid peroxidation are easily detected in blood plasma and have been used as a measure of oxidative stress. The most commonly measured product is MDA. In addition the unsaturated aldehydes produced from these reactions have been implicated in modification of cellular proteins and other materials (Packer 1994, Weir et al 1996).

In our present study MDA levels were found to be significantly changed in different stages of breast cancer patients. The levels of MDA in serum were increased significantly in patients suffering from breast cancer. The normal blood level of MDA, which was 7.24 μg/ml, was increased to 7.5 μg/ml in patients of first stage cancer registering no significant change in MDA level. In the second stage cancer patients, the MDA level was further increased to 9.32 μg/ml, showing 28.7 % increase when compared with control. In the third stage cancer patients, the level of MDA was found to be 10.83 μg/ml showing 49.5 % increase when compared with control. The effect of chemotherapy on conc. MDA level were show significant change in different stages of breast cancer. The conc. of MDA was significantly increased in patients suffering from breast cancer. Before chemotherapy the conc. of MDA was 7.24 μg/ml, which was increased to 13.06 μg/ml after chemotherapy, showing the 80.39 % increase.

Our results are in accordance with the finding of various workers like Kumaraguruparan et al (2002), and Khanzode (2004) shows that level of MDA increased gradually as compared to control groups and the maximum rise occurs at stage III. The enhanced LPO may also be due to depletion of the activities of enzymes SOD, GST, GPx, and catalase which are the free radical scavenging enzymes or higher production of O_2^- and H_2O_2 and subsequent increase in the MDA level. There is a possibility of the accumulation of both the ROMs which may result in significantly higher LPO at cellular and molecular levels. However some contradictory reports indicating lower lipid peroxidation measured by plasma TBA has also been reported in breast cancer patients (Seven et al, 1998).

Changes in the state of lipid peroxidation seem to be a great feature of cancer cells and may be a prerequisite to cell division (Brawn *et al*, 1981). The increased lipid peroxidation in chemotherapy treated cancer patients may also be due to a poor antioxidant system (Szatrowski *et al*, 1991).

Table 1: Comparison of lipid peroxidation in different stages of breast cancer

Parameter	Control Group (n=97)	Stage I (n=37)	Stage II (n=50)	Stage III (n=46)
TBARS	7.24±0.07	7.50±0.11	9.32±0.16 [a,b]	10.83±0.21 [a,b,c]

Table 2: Effect of chemotherapy on lipid peroxidation in breast cancer patients

Parameter	TBARS
Before chemotherapy	7.24±0.074
After chemotherapy	13.06±0.92 [abc]

Values are expressed mean ± SE

Units: TBARS: µg/ml

[a]p< 0.05 values are significant vs control group; [b]p < 0.05 values are significant vs stage I ; [c]p < values are significant vs stage II group.

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