

Research Article

**Analysis of level of antioxidants in cancer patients
 after receiving radiotherapy**

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ABSTRACT

Introduction: The involvement of the reactive oxygen species (ROS) is well documented in various disease processes, including cancers. Under normal circumstances, the redox status of cells is maintained by a balance between ROS production and its sequestration by antioxidants. **Aims and objectives:** The main objective of the study is to analyse the level of antioxidants in cancer patients after receiving radiotherapy. **Material and methods:** This cross sectional study was conducted in DHQ Hospital, Shangla during March 2018 to December 2018. This study was done with the permission of ethical committee of hospital. The data was collected from 100 cancer patients of both genders. We include breast cancer patients who receives radiotherapy. Those patients who receiving radiotherapy were selected to study the antioxidant status in the diseased condition. **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 products. No significant association was observed between breast cancer risk and the highest quartiles of these antioxidant intakes from dietary sources compared with the lowest quartiles of intake, either for premenopausal or for postmenopausal breast cancer. **Conclusion:** It is concluded that antioxidants such as beta-carotene, vitamin C, vitamin E and zinc may reduce the risk of breast cancer. By reducing oxidative stress, lipid peroxidation, antioxidants counteract the effects of chemotherapy-induced oxidative stress on the cell cycle and enhance the cytotoxicity of antineoplastic agents.

Key words: Antioxidants, Cancer, Female, Lipid peroxidation

INTRODUCTION

The involvement of the reactive oxygen species (ROS) is well documented in various disease processes, including cancers. Under normal circumstances, the redox status of cells is maintained by a balance between ROS production and its sequestration by antioxidants. While ROS is used as an innate mechanism of host immunity to fight against extracellular pathogens, including bacterial and viral infections, an exacerbated generation causes imbalance in cellular redox potential leading to alterations in signalling pathways and

neocarcinogenesis. ROS release can be affected by several cellular compartments¹.

Cancer is the leading cause of death worldwide. Although outcomes of cancer therapy have improved, cancer becomes a systemic disease beyond a particular point. Because complete recovery of cancer patients following a single treatment is quite difficult, a multidisciplinary approach combined with surgery, chemotherapy, radiotherapy, and immunotherapy is usually utilized². Other approaches using complementary and alternative medicine (CAM) modalities are

an important choice among cancer patients. Hyodo et al reported that 44.6% of cancer patients use CAM treatments in Japan. Patients undergoing chemotherapy tend to prefer CAM, particularly dietary supplements³. However, it is not common for clinicians to use CAM as a general therapy in Japan because of the uncertainty regarding the safety and effects of CAM therapies.

The development of cancer has been linked to an inability of the host immune system to respond appropriately to tumor antigens, which leads to tumor immune evasion⁴. The recognition and eradication of cancer cells by the immune system are categorized as elimination, equilibrium, and escape phases, referred to as the 3Es of immunoediting, which are governed by various factors⁵. Briefly, in elimination phase, the host immune cells via the surveillance process recognize and try to eliminate nascent tumors⁶. Whereas the equilibrium phase starts when a few tumor cells become resistant enough to sustain immune surveillance mechanisms and enter into the dormant stage, where equilibrium exists between tumor cell proliferation and immune cell mediated apoptosis⁷.

Theoretical background

Oxidative stress is a key component in the carcinogenesis process. Stimulated by endogenous and exogenous factors, reactive oxygen species (ROS) induce cellular damage. Although radiation certainly produces ROS, some anticancer agents such as alkylating agents and platinum and antitumor antibiotics exert cytotoxicity by generating free radicals. Some endogenous antioxidant defense mechanisms, such as superoxide dismutase, glutathione peroxidase, and catalase, can counterbalance oxidative microenvironments. Nonenzymatic exogenous antioxidants such as vitamins, minerals, and polyphenols also have the ability to quench ROS activity⁸. Therefore, antioxidant therapies may alleviate the adverse effects of chemotherapy and/or radiotherapy but may antagonize antitumor effects by reducing oxidative damage³.

AIMS AND OBJECTIVES

The main objective of the study is to analyse the level of antioxidants in cancer patients after receiving radiotherapy.

MATERIAL AND METHODS

This cross sectional study was conducted in DHQ hospital, Shangladuring March 2018 to December 2018. This study was done with the permission of ethical committee of hospital. The data was collected from 100 cancer patients of both genders. We include breast cancer patients who receives radiotherapy. Those patients who receiving radiotherapy were selected to study the antioxidant status in the diseased condition.

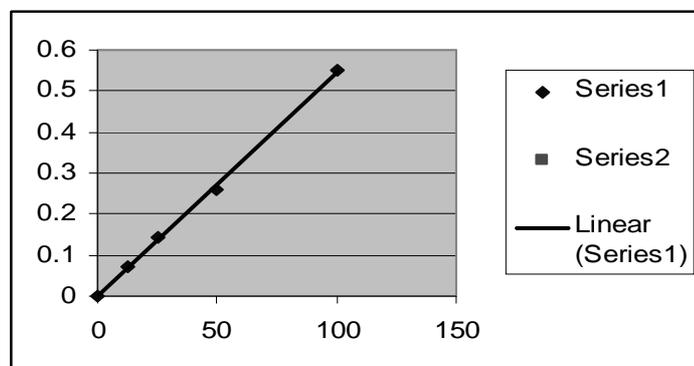
Exclusion criteria

- Patients who suffer from cardiac diseases were excluded from this study.
- Patients at TNM stage-III were excluded.

Data collection

5.0 ml blood sample was taken from vein. Blood was further processed for the estimation of antioxidants (Lipid peroxidation). 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.

Standard curve for lipid peroxidation



$$Y = -0.129X + 0.592$$

$$R^2 = 0.8952$$

X = Concentration

Y = Absorbance of sample

Statistical analysis

A chi-square test was used to examine the difference in the distribution of the fracture modes (SPSS 19.0 for Windows, SPSS Inc., USA). Two-way ANOVA was performed to study the contributions.

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 (table 01, figure 01). The reason is due to high damage of membrane and lipid peroxidation products. No significant association was observed between breast cancer risk and the highest quartiles of these antioxidant intakes from dietary sources compared with the lowest quartiles of intake, either for premenopausal or for postmenopausal breast cancer (table 02).

Table 01: MDA values of all therapies and control group

BREAST	CONTROL	MDA(moles/ml)	
		BEFORE	AFTER
	2.35		
0	0.00	4.26±0.00	5.24±0.00
R1	0.00	2.99±0.38	4.95±0.97
R2	0.00	2.95±1.02	5.13±1.06
R1+B	0.00	3.76±0.70	5.89±0.91
R2+B	0.00	3.26±0.00	6.58±0.00
B	0.00	0.00±0.00	0.00±0.00
Total	2.35	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

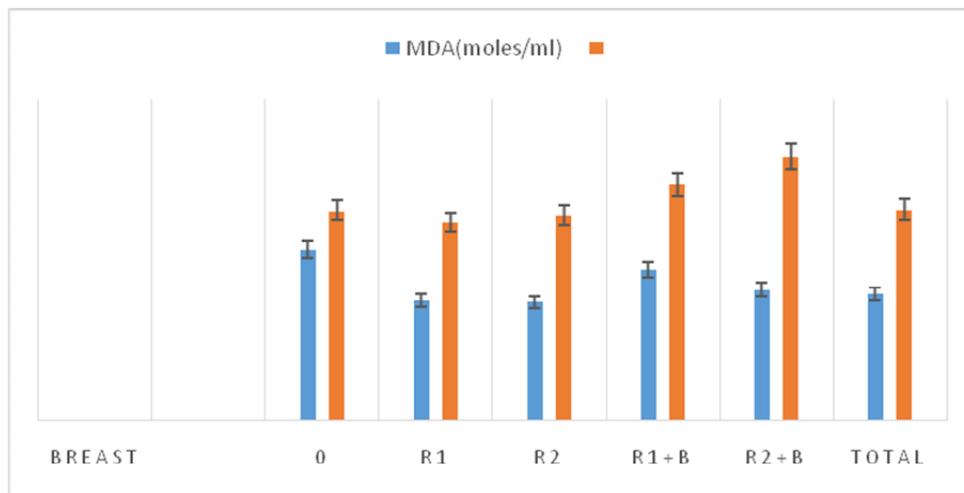


Table 02: Antioxidant status in control and selected cases

Characteristic	Cases	Controls	p
	Mean	Mean	
Beta-carotene (µg/wk)	31643.6	32369.8	0.55
Vitamin E (mg/wk)	56.4	56.8	0.82
Vitamin C (mg/wk)	1101.2	1137.1	0.38
Selenium (µg/wk)	660.2	651.6	0.54
Zinc (mg/wk)	65.7	64.9	0.52
From supplement (years)			
Vitamin A	0.88	1.02	0.38

Beta-carotene	0.59	0.77	0.16
Vitamin C	3.22	3.53	0.24
Vitamin E	1.53	1.80	0.16
Zinc	0.60	0.83	0.09
Selenium	0.37	0.47	0.33

DISCUSSION

Despite recent advances in local and systemic treatment modalities, chemotherapy, radiation therapy and immunotherapy are widely considered either alone or in combinations for a variety of cancers. In chemotherapy, cancer cells are targeted by chemically modified agents/compounds with cytotoxic properties; radiation therapy uses high-energy particles/waves, including x-rays and gamma rays, to kill tumor cells; and immunotherapy treatments are designed to stimulate the host's own immune system to attack cancer cells⁷. One of the consequences of chemotherapy and radiation therapy is the generation of ROS which via its direct and indirect effects on tumor cells, induces DNA damage and/or affects DNA replication machinery, leading to aberrations in several cellular signaling pathways resulting in chemotherapy- or radiation therapy-induced cell death⁹.

Most of these therapies are not considered a good option as a single agent to treat advanced-stage/metastatic cancers, in part due to the development of therapy-induced innate and/or acquired tumor resistance or local/systemic toxicities leading to either reduced response, non-responsiveness or tumor relapse after an initial antitumor response¹⁰.

Therefore, potentially new therapeutic approaches with agents that exhibit anticancer properties and can potentiate chemotherapy- or radiation therapy mediated antitumor responses are required for inducing optimal and long-term benefits in cancer patients¹¹.

Although studies in cell cultures and animals showed that vitamin E and C prevent transformation of normal cells to cancer cells and selectively induce apoptosis in cancer cells, the results of epidemiologic studies have been inconsistent¹².

CONCLUSION

It is concluded that antioxidants such as beta-carotene, vitamin C, vitamin E and zinc may reduce the risk of breast cancer. By reducing oxidative stress, lipid peroxidation, antioxidants counteract the effects of chemotherapy-induced oxidative stress on the cell cycle and enhance the cytotoxicity of antineoplastic agents.

REFERENCES

1. Marinescu, S, Anghel, R, Gruia, MI, Beuran, M. Involvement of reactive oxygen species in the mechanisms associated with cervical cancer specific treatment. *Chirurgia (Bucur)*. 2014;109:806-811.
2. Cui, J, Chen, Y, Wang, HY, Wang, RF. Mechanisms and pathways of innate immune activation and regulation in health and cancer. *Hum Vaccin Immunother*. 2014; 10:3270-3285.
3. Panieri, E, Gogvadze, V, Norberg, E, Venkatesh, R, Orrenius, S, Zhivotovsky, B. Reactive oxygen species generated in different compartments induce cell death, survival, or senescence. *Free Radic Biol Med*. 2013;57:176-187
4. Sena, LA, Chandel, NS. Physiological roles of mitochondrial reactive oxygen species. *Mol Cell*. 2012;48:158-167
5. Bernardes, SS, de Souza-Neto, FP, Ramalho, LN. Systemic oxidative profile after tumor removal and the tumor microenvironment in melanoma patients. *Cancer Lett*. 2015;361:226-232
6. Vences-Catalán, F, Rajapaksa, R, Srivastava, MK. Tetraspanin CD81 promotes tumor growth and metastasis by modulating the functions of T regulatory and myeloid-derived suppressor cells. *Cancer Res*. 2015;75:4517-4526.
7. Jones, LM, Broz, ML, Ranger, JJ. STAT3 establishes an immunosuppressive microenvironment during the early stages

- of breast carcinogenesis to promote tumor growth and metastasis. *Cancer Res.* 2016;76:1416-1428.
8. Koebel, CM, Vermi, W, Swann, JB. Adaptive immunity maintains occult cancer in an equilibrium state. *Nature.* 2007;450:903-907.
 9. Lee-Chang, C, Bodogai, M, Martin-Montalvo, A. Inhibition of breast cancer metastasis by resveratrol-mediated inactivation of tumor-evoked regulatory B cells. *J Immunol.* 2013;191:4141-4151.
 10. Earnest CP, Wood KA, Church TS. Complex multivitamin supplementation improves homocysteine and resistance to LDL-C oxidation. *J Am Coll Nutr.* 2003;22:400-407. [
 11. Prakash P, Krinsky NI, Russell RM. Retinoids, carotenoids, and human breast cancer cell cultures: a review of differential effects. *Nutr Rev.* 2000;58:170-176
 12. Block G, Hartman AM, Dresser CM, Carroll MD, Gannon J, Gardner L. A data-based approach to diet questionnaire design and testing. *Am J Epidemiol.* 1986;124:453-469.