Indian Journal of Pharmacy Practice | Association of Pharmaceutical Teachers of India

Effect of Antioxidant Supplementation in Cancer Patients on Radiotherapy

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ABSTRACT

Submitted: 15/06/2013 Accepted: 21/06/2013

Introduction: Cancer and its treatment by radiotherapy are believed to be associated with oxidative stress. A study was carried out to assess the oxidant and antioxidant status and the beneficial effects if any of the antioxidant supplementation in cancer patients undergoing radiotherapy. **Objectives:** Since, antioxidants are known to detoxify Reactive oxygen species (ROS), the effect of antioxidant supplementation was studied in these patients. **Methodology:** Blood samples were drawn before and after the radiotherapy with or without antioxidant supplementation to estimate malondialdehyde (MDA) as an index of lipid peroxidation; the nitric oxide, Vitamin E and total antioxidant capacity (TAC) were estimated to assess the antioxidant status in these patients. **Results:** As compared to control, the MDA levels were significantly increased while the levels of TAC, nitric oxide, Vitamin E were significantly reduced in these patients and more significantly in the patients after radiotherapy. While on supplementation with antioxidant therapy the levels of MDA were significantly reduced and the levels of nitric oxide, Vitamin E and TAC were significantly elevated as compared to the group without antioxidant supplementation. **Conclusion:** Thus our findings confirm the presence of oxidative stress in cancer patients as well as the increase in oxidative stress by radiotherapy and suggest the possible preventive role of antioxidant supplementation in cancer patients undergoing radiotherapy.

Keywords: Antioxidant, Cancer, Radiotherapy, Oxidative stress, ROS.

INTRODUCTION

Cancer is the leading cause of death in developed countries and second leading cause of death in Developing countries. The global burden of cancer continues to increase largely because of the aging, increased life expectancy, growth of the world population and the increasing adoption of cancer-causing behaviors, such as tobacco usage[1] especially in economically developing countries. Since cancer is more common in population with the advanced age, the increase in life expectancy appears to have contributed for the increased number of cancer patients.

Although there has been a remarkable progress in cancer treatment, in reality the progress has been very poor because still one in three of the population (at least in the West) develops cancer at some time in their lives and many die out of it. Radiotherapy, Chemotherapy and Surgical therapy are the most accepted treatments for cancer. There has been tremendous advancement in cancer radiotherapy. The radiation therapy generates reactive oxygen species (ROS)[2] and these ROS are neutralized in vivo by the antioxidants for the homeostasis.[3] Oxidative stress may result when there is imbalance in favor of the ROS. This Oxidative stress is known to damage biological structures by reactive oxygen species[4] due to their excessive generation and impaired efficiency of endogenous antioxidant defense mechanisms. There comes a point of protection from this damage by supplementation with antioxidants. The consideration of whether to use antioxidants concomitantly with chemotherapy and radiation therapy has evolved into a heated debate.[5] The findings on the role of Antioxidants in Cancer are with many controversies[6] and there appears to be a need for reassessment of the role of antioxidants at each of the cancer hospitals and research centers for establishment of the facts at local levels.

In light of the above facts the present study was planned to explore the possible alterations of oxidant – antioxidant status in cancer patients undergoing radiotherapy and effect of antioxidant supplementation. Although this work has global implications, we aimed at one cancer hospital, Sri Siddheshwar Cancer Hospital and Research Centre, located in Solapur, Maharashtra, India. The effort we would consider worthwhile even if it extends the life of an extremely small number of patients even marginally or even if it serves in improving the quality of their 'life survived'.

MATERIALS AND METHODS

This study included 30 proven cases of cancer undergoing radiotherapy in Shri Siddheshwar cancer hospital and research centre, Solapur, Maharashtra, India. The patients were treated with external telecobalt (Co 60) therapy. The patients were given 20 to 30 radiation doses of 200 cGy per day, 5 days a week. They were given 20-30 doses depending upon the purpose of radiation i.e. for palliative or

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for cure respectively based on the clinical evaluation. Equal number of controls was also included in the study. Solapur being the border district of Maharashtra, the patient input to this hospital is not only from Maharashtra but also from Karnataka and Andhra Pradesh. Cervical cancer and breast cancer formed majority of cases in female patients while in males cancer of tongue, cheek, esophagus, larynx and lungs, was most common owing to the rampant use of tobacco in and around this region. Of the thirty cases, 15 patients were prescribed one tablet per day of "A to Z" tablets containing antioxidants with multivitamin and minerals viz. Vitamin C 40mg, Vitamin B3 16 mg, Vitamin E 15mg, Vitamin B5 5mg, Vitamin B6 - 1mg, Vitamin B2-1.4mg., Vitamin B1-1.2mg., Vitamin A-600mcg, Folic Acid 100mcg, Methylcobalamin 1mcg, Zinc Oxide equivalent to elemental zinc 10mg, Manganese Chloride equivalent to elemental Manganese 2mg, Copper gluconate eq. to elemental Copper 0.9mg, Sodium Selenate equivalent to elemental Selenium 55mcg.

The study was cleared by institutional ethical committee. Informed consent was obtained from each participant in the study. Blood sample of 10ml was collected from the patients who have given the written informed consent. The collection was done while collecting for routine pathological investigations without additional prick to the patients. The sample was collected partly in heparinised bulb and partly in plain bulb. The plasma and serum were separated by centrifugation at 3000 rpm for 10 minutes at room temperature and samples were analysed. Serum MDA levels were measured by thiobarbituric acid method as described by Satoh[7], Nitric oxide was determined by Cortas and Wakid method[8], Vitamin E was measured by the reduction of ferric to ferrous ion which then forms a red colored complex with α- α'-bipyridyl as in Baker and Frank method[9] and the TAC was estimated by FRAP method[10]. The follow up collection in only 22 patients was possible after 1 month; hence they were only included in the present study for the post radiotherapy investigations. All patients were given the antioxidant AtoZ tablets for one month and the repeat analysis of the parameters was done. The statistical analysis was done using "students t" test. The values are expressed as Mean ± SD.

RESULTS

The values of various biochemical parameters in table:1 are the differences in the values of MDA & antioxidant levels in Control and cancer patients before radiotherapy. The values are expressed as Mean ± SD. Statistical significance was assessed by "students t" test. Compared to control, the values in cancer cases were found to be significant for MDA $p < 0.05$, Nitric oxide ($p<0.005$), Vit E ($p<0.001$) and TAC ($p<0.001$).

The values of various biochemical parameters in Table: 2 are the differences in MDA & antioxidant levels in cancer patients before and 1 month after radiotherapy with & without antioxidant supplementation.

Table 1: MDA & antioxidant levels in Control and cancer patients before radiotherapy.

Parameter	Control n=30	Cancer patients n=30
MDA (nmol/dl)	43.27±13.6	72.11±43.31*
Vit E (mg/l)	1.16±0.27	0.57±0.22 #
Nitric Oxide (nmol/l)	374.81±95.1	236.84±50.01 $
TAC (nmol/l)	2.82±0.74	1.75±0.54 #

All values are expressed as mean±SD. * p<0.05, $p<0.005, #p<0.001

Table 2: MDA & antioxidant levels in cancer patients before and 1 month after radiotherapy with & without antioxidant supplementation.

Parameter	Before radiation n=30	After 1 month on radiation without antioxidant n=12	After 1 month on radiation with antioxidant n=12
MDA (nmol/dl)	72.11±43.31	153.84±47.10$	115.38±44.41*
Vit E (mg/l)0.	57±0.22	0.39±0.14*	0.86±0.23*
Nitric Oxide (nmol/l)	236.84±50.01	181.58±71.01	221.64±49.26
TAC (nmol/l)	1.75±0.54	1.18±0.63*	2.38±0.43*

All values are expressed as mean±SD. * p<0.05, $p<0.005, #p<0.001

The difference in the values before and after radiation were significant for MDA ($p<0.005$) and on on antioxidant supplementation in patients on radiotherapy the reversal was also significant ($p<0.05$). The levels of antioxidants, Vit E and the TAC were significantly reduced ($p<0.05$) after radiotherapy while the reduction was not significant in case of nitric oxide. The supplementation with antioxidant tablets AtoZ has significantly enhanced the levels of antioxidants, Vit E and TAC ($p<0.05$) in comparison with the group without supplementation.

DISCUSSION

Significantly elevated levels of serum total lipid peroxide (MDA $P<0.001$) were observed in cancer patients as compared to controls and the difference was further widened on radiotherapy. Significantly decreased levels of serum nitric oxide ($p<0.002$), serum vitamin E ($p<0.01$) and TAC ($p<0.05$) were observed in cancer patients and widened difference in the radiotherapy cases was also observed here as compared to controls. There was further elevation of MDA, reduction in nitric oxide, and TAC in patients on radiotherapy. A moderate reversal in serum levels of MDA and antioxidants was observed with the present antioxidant (AtoZ tablets) supplementation. The toxic effects of radiotherapy such as nausea, vomiting, anemia however were not appreciably reversed by administration of these tablets. The supplementation with a still stronger and solely

antioxidant agent would have resulted better reversal but was not possible since the clinicians consent was for the milder one.

Since beta carotene is reported to reduce radiation toxicity without reduction in antitumor efficacy, the elevation in Vit E level is beneficial.[11] Thus the present study showed significant elevation of ROS in cancer patients which was further aggravated by radiotherapy. Beneficial effects of antioxidant administration during radiotherapy were observed in management of oxidative stress and thus reducing toxic effects of ROS.

ACKNOWLEDGEMENTS

The authors are grateful to the management and entire clinical and other team members of Shri Siddheshwar Cancer Hospital and Research Centre for the permission and assistance. Authors are also thankful to the Head and all the staff Dept of Biochemistry Dr. V M Govt. Medical College, Solapur for their kind support in the biochemical estimations.

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