ASSESSMENT OF OXIDATIVE STRESS AND EFFECT OF ANTIOXIDANT SUPPLEMENTATION DURING RADIOTHERAPY IN CARCINOMA OF UPPER DIGESTIVE TRACT

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ABSTRACT

Oxidative stress was studied by estimating plasma levels of malondialdehyde (MDA), beta carotene, vitamin E and erythrocytic superoxide dismutase (E-SOD) activity in 50 cases of carcinoma of upper digestive tract which included carcinoma of oral cavity, pharynx and oesophagus. While plasma MDA level was found to be increased (3.5 ± 1.0 nmole/ml), a significant decrease in beta carotene (81.2 ± 14.5 mg%), vitamin E (8.5 ± 1.1 mg/L) level and E-SOD activity (657.0 ± 80.6 U/G Hb) were observed in carcinoma of upper digestive tract. Patients were treated with radiotherapy which itself was toxic enough and produced its deleterious effects by generation of reactive oxygen species (ROS). As antioxidants can detoxify ROS, beneficial effect if any, of antioxidant administration during radiotherapy was studied in two groups of patients, group A (n=5, supplemented with antioxidants) and group B (n=5, without antioxidant supplementation). Plasma MDA level was found to be elevated in both the groups but the increase in group B was significant, compared to pretreatment level. Further, body weight was found to be significantly decreased in group B patients, which was maintained in group A patients. Moreover, group A patients showed significant elevation in beta carotene concentration, thus showing beneficial effect of administration of antioxidants during radiotherapy without disturbing the desirable therapeutic effect of radiotherapy.

KEY WORDS : Antioxidant, Carcinoma, Radiotherapy, ROS.

INTRODUCTION

Reactive oxygen species (ROS) or prooxidants, generated *in vivo* are known to be consumed by cellular and extracellular antioxidants to maintain homeostasis. An imbalance in this equilibrium in favour of prooxidants leads to oxidative stress which contributes to many disease processes including cancer (1). In the present study, ROS related changes were assessed in cancer of upper digestive tract which

included oral cavity, pharynx and oesophagus by determining plasma MDA, a lipid peroxidation product, beta carotene and vitamin E, the nutrient antioxidants and E-SOD activity reflecting enzymatic antioxidant status of the body. Radiotherapy, an accepted treatment modality of carcinoma is known to produce its deleterious effects by generation of ROS (2). Antioxidants, especially beta carotene was found to act against the undesirable effects of radiotherapy. Radioprotective role of beta carotene against genotoxic damage was observed (3). SOD was found to protect radiation induced cystitis in bladder carcinoma (4). In this study, patients with carcinoma of oral cavity were followed up to assess the effect of antioxidant supplementation during cobalt 60 radiotherapy both clinically and biochemically.

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MATERIALS AND METHODS

A total of 50 histopathologically proved cases of carcinoma of upper digestive tract (oral cavity & pharynx, n=29, oesophagus, n=21) alongwith equal number of age and sex matched healthy controls chosen randomly were included in the study. About 5ml of blood was collected in EDTA vial. Plasma was separated and used to estimate MDA(5); beta carotene and vitamin E (6). Washed RBC was used to estimate SOD activity(7). It was possible to follow up 10 of the patients suffering from carcinoma of oral cavity. All of them were treated with external telecobalt (Co 60) therapy. The total dose given was 6,600 CGy in 33 fractions, each fraction containing 200 CGy.

Five of the patients undergoing radiotherapy were given additional antioxidant supplementation by administering "antoxid" tablets containing beta carotene 50mg, vitamin A palmitate 2500 IU, vitamin E acetate, 10 IU alongwith vitamin C, zinc, manganese and copper, being manufactured by American Remedies Soft Caps Pvt. Ltd, (the dose being 1 tablet thrice daily for 33 days) and were grouped as group A. The other group (group B, n=5) received same schedule of radiotherapy but no antioxidant supplementation was advised.

The blood samples of these patients were collected on 33rd day and were analysed for ROS related parameters. Radiation induced toxicities were evaluated in terms of anaemia, leukopenia, nausea, vomiting and oral mucositis (8). Weights of the patients were also recorded.

All results were expressed in mean $\pm$ SD values. Mean plasma levels of all biochemical parameters of cases & controls were compared by Student's t test. The difference in plasma levels of biochemical parameters and body weight before and after treatment was tested by Wilcoxon rank sum test.

RESULTS AND DISCUSSION

The study group with carcinoma of upper digestive tract was found to be associated with significantly elevated level of plasma MDA ($P < 0.001$) and significantly decreased level of plasma beta carotene, vitamin E and E-SOD activity, ($p < 0.001$) (Table1).

No significant difference in radiotherapy induced toxicity regarding anaemia, leukopenia, nausea, vomiting and oral mucositis was observed by administration of antioxidants to group A during radiotherapy. It was observed that both the groups

Table 1 . The levels of different biochemical parameters in cases with carcinoma of upper digestive tract and controls.

Variates	Control n=50	Carcinoma of upper digestive tract n=50
Malondialdehyde (n mole/ml)	2.4 $\pm$ 0.5	3.5 $\pm$ 1.0 *
Beta carotene (mg %)	99.0 $\pm$ 7.2	81.2 $\pm$ 14.5 *
Vitamin E (mg/L)	10.1 $\pm$ 1.1	8.5 $\pm$ 1.1 *
Erythrocytic superoxide dismutase activity (U/G Hb)	763.4 $\pm$ 38.1	657 $\pm$ 80.6 *

All values are expressed as mean $\pm$ SD

* Difference statistically significant when compared with the control group ($p < 0.001$)

showed increased concentration of plasma MDA, however the increase was significant in group B patients compared to pretreatment levels. No significant change was observed in mean vitamin E level. E-SOD activity was comparably high in both the groups which might be due to the inducible nature of the enzyme (9). The plasma beta carotene concentration was significantly higher in group A cases. As beta carotene can reduce radiation toxicity without reduction in antitumour efficacy(10), this elevation is an important observation. In this study body weight which was found to be decreased in group B patients, was found to be maintained in group A (Table 2). Weight loss results from direct tissue destruction by radiotherapy and increased catabolism due to stress condition. In animal studies radiation sickness was found to cause reduced appetite and poor intake of food which was counteracted by the supplemented antioxidants (11).

Thus the present study showed significant elevation of ROS in carcinoma of upper digestive tract which was further aggravated by radiotherapy. Beneficial effects of antioxidant administration during radiotherapy was observed in management of oxidative stress and thus reducing toxic effects of ROS. Further, this preliminary study showed that weight loss was prevented by antioxidant administration during radiotherapy without affecting therapeutic efficacy.

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Table 2. Mean values of body weight and different biochemical parameters before and after radiotherapy in group A (antioxidant supplemented) and group B (antioxidant not supplemented)

Variates	Radiotherapy (with antioxidant, n=5)		Radiotherapy (without antioxidant, n=5)	
	Before a	After b	Before c	After d
Body wt (kg)	43	43	35	31*
Malondialdehyde (n mole/ml)	3.5	4.8	3.6	5.7*
Beta carotene (mg%)	88	116*	76	72
Vitamin E (mg/L)	7.7	8.1	7.1	7.1
Erythrocytic superoxide dismutase activity (U/G Hb)	634	737*	634	830*

* The difference in pre and post treatment values were found to be significant at $p < 0.05$ for body weight (c vs d), malondialdehyde (c vs d), beta carotene (a vs b), erythrocytic superoxide dismutase activity (a vs b and c vs d).

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