SOME OXIDATIVE STRESS RELATED PARAMETERS IN PATIENTS WITH HEAD AND NECK CARCINOMA

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ABSTRACT

Forty cases of head and neck cancer were studied for plasma superoxide dismutase, malondialdehyde and thiol levels and results were compared with a group of forty normal healthy volunteers. Mean plasma superoxide dismutase activity was not found to be altered while malondialdehyde concentration was significantly higher when compared with the control group. On the other hand, mean thiol level was significantly lowered. The data suggests increased level of oxidative stress in patients with head and neck cancer.

KEY WORDS

Head and neck carcinoma, Oxidative stress, Antioxidants, Superoxide dismutase, Malondialdehyde, Thiol.

INTRODUCTION

Incidence of the carcinoma of head and neck region varies considerably through out the world, with about 1% of all cancers in Europe to nearly 36% in India (1). It is relatively common in India due to certain geographical, social, and socioeconomic factors as well as some professional hazards. Various etiological factors include tobacco, alcohol, Epstein-Barr virus (particularly responsible for nasopharyngeal carcinoma) besides certain dietary factors (2).

It is well known that all carcinogens are highly reactive electrophiles, which may attack electron rich sites on the macromolecules (particularly DNA) in the target cell. Many defense mechanisms, within the organism, evolve to limit the level of reactive oxygen species and the damage they induce. These biochemical defenses include both, the complex systems, e.g. catalase, glutathione peroxidase (GSH-Px), glutathione-S-transferase (GST), superoxide dismutase (SOD) etc. as well as various low molecular weight free radical scavengers such as vitamin C, tocopherols, carotenoids, reduced glutathione (GSH) and other thiol. Several workers have reported that enzymatic free radical system is significantly

impaired and lipid peroxidation is increased in cancer (3-5).

Recent studies from this laboratory have shown altered levels of some of the intracellular as well as extracellular components of the antioxidant defense system even in head and neck cancer. For example, GSH, vitamin E, and vitamin C levels were significantly reduced whereas ceruloplasmin, GST and γ -glutamyltranspeptidase activities were increased in such patients (6-9). The present study was planned to evaluate some oxidative stress related parameters such as SOD activity, Malondialdehyde (MDA) level and thiol content in patients with head and neck cancer. The changes were correlated with the type of lesion, histopathology and TNM stage of cancer. Further the effect of radiotherapy was also studied on these parameters.

MATERIALS AND METHODS

Forty histopathologically proved cases of head and neck cancer, all males (age 35- 80 Years), attending the Department of ENT, PGIMS, Rohtak, were selected for the study. Results were compared with a group of forty normal healthy, age and sex matched volunteers. Patients with cancer of any other regions who have already received treatment in any form and those having acute infections, hepatobiliary diseases, respiratory diseases or renal diseases were excluded.

Each patient was subjected to detailed clinical history, general physical examination, ENT examination and examination of lymph nodes draining the areas. Thirtyfive out of 40 (nearly

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88%) patients were smokers. Among them 30 (75%) were also alcoholics. Radiological investigations included X-ray soft tissue neck (in case of growth larynx or hypopharynx) or X-ray nasopharynx and base of the skull (in case of growth nasopharynx). Besides, all the patients were also subjected to routine laboratory investigations. Five ml heparinised blood was collected and plasma was separated by centrifugation at 5000 rpm. Plasma SOD activity was measured according to Misra and Fridovich (10), where one enzyme unit (EU) has been defined as the amount of protein required to inhibit autooxidation of epinephrine by 50% under standard assay conditions. MDA level was estimated using TBA (11) while thiol content was determined using dithiobisnitrobenzoic acid (12). Data were statistically analyzed by Student's 't'-test.

RESULTS AND DISCUSSION

The results of the present study demonstrate that mean plasma SOD activity in patients with head and neck cancer was comparable with the controls ($p>0.05$; Table 1). Only one patient had abnormal level of SOD. On the other hand, the mean value for plasma MDA concentration was found to be increased by nearly two-folds, in patients as compared to controls ($P<0.05$). Thirtyeight out of 40 (95%) patients had abnormal MDA levels. There was no significant difference in SOD activity as well as MDA level when compared with the type of lesion, histopathology or TNM stage of cancer. Our findings are in agreement with Seven et al (3) who evaluated oxidative stress in blood of patients with laryngeal carcinoma. They revealed the presence of increased lipoxidative damage, but no changes with respect to endogenous antioxidant components such as GSH, GSH-Px, and Cu-Zn SOD. Guven et al (4), reported significantly higher activities of SOD in erythrocytes of cancer patients with metastasis, and suggested an impairment in antioxidant system. Devi et al (5) reported increased activity of Cu-Zn SOD and GSH-Px in patients with leukemia and suggested that the controversial findings in

literature, related to antioxidant status in cancer patients, may arise from the type of cancer studied. They suggested that an adaptive antioxidant response against oxidative stress is tissue specific since the constitutive levels as well as inducibility of some antioxidant enzymes (SOD, GSH-Px and catalase) vary from tissue to tissue.

In present study also no significant change in plasma SOD was observed even after radiotherapy. The values of SOD though should have increased after radiotherapy as an adaptive response to combat free radicals generated by ionizing radiations, however reduction in the tumor mass, might have overcome the induction of SOD, hence explaining its unaltered levels.

Increased levels of MDA further confirm increased oxidative stress in these patients. Increased generation of oxygen derived free radicals in such patients could also be due to their increased production in vivo and/or a result of tobacco smoke since majority of these patients were smokers as well as alcoholics. The SOD/MDA ratio was significantly reduced, which further suggests an increased oxidative stress in these patients. The ratio however, remained nearly same even after radiotherapy.

Reactive oxygen species also oxidize thiol, which include GSH as well as the -SH groups of proteins (P-SH). Thiol levels were found to be significantly reduced in patents as compared to controls. Fifteen out of 40 (about 38%) patients had abnormal thiol levels. Oxidative stress causes depletion of thiol levels. The levels remained significantly unaltered even after radiotherapy. Reduced thiol levels are in agreement with the reduced levels of various low molecular weight antioxidants such as GSH, Vitamin E and Vitamin C, which are known to scavenge free radicals (6-7).

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Table 1: Plasma SOD, MDA and Thiol levels in patient with head and neck cancer and effect of radiotherapy on these parameters (Values are Mean $\pm$ SEM for 40 subjects in each group)

Group	SOD (EU/ml)	MDA (nmol/ml)	SOD/MDA	Total thiols (nmol/ml)
Controls	3.64 $\pm$ 0.14	5.60 $\pm$ 0.24	0.75 $\pm$ 0.06	2.56 $\pm$ 0.22
Patients				
Pre RT	3.63 $\pm$ 0.17	10.95 $\pm$ 0.47*	0.35 $\pm$ 0.03*	1.90 $\pm$ 0.18*
Post RT	3.77 $\pm$ 0.16	11.48 $\pm$ 0.61*	0.38 $\pm$ 0.03*	1.52 $\pm$ 0.19*

*Difference statistically significant when compared with the control group ($p<0.05$).

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