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A preliminary study of antioxidants in oral cancer prognosis

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ABSTRACT

Background: Free radicals and antioxidants have been implicated in initiation and progression of various epithelial malignancies. But their role in overall prognosis, drug resistance and cancer recurrence is not clearly understood. Hence, the role of erythrocytic glutathione (GSH) and malondialdehyde (MDA) and plasma ceruloplasmin (CP) and total glutathione-S-transferase (GST) were evaluated to assess the prognosis and survival of patients with oral cancer. **Materials and methods:** Biopsy proven oral cancer patients (n=17) stage IV who underwent same mode of treatment were chosen for this study. Erythrocytic GSH and MDA, plasma CP and total GST levels of above patients which were measured before onset of any treatment were compared with their prognosis. **Statistical analysis:** Mann-Whitney test and Independent Sample T Test. **Results and dicussion:** We observed that patients who had recurrence of cancer within 2 years of onset of treatment, had higher levels of GSH, GST and CP as compared to their respective levels in patients who had no evidence of recurrence. This indicates there may be a role for these antioxidant parameters namely GST, GSH, CP in assessment of long term survival of oral cancer patients.
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KEYWORDS

Oral cancer;
Prognosis;
Antioxidants;
Recurrence;
Survival.

INTRODUCTION

Oxidative challenge due to generation of free radicals is implicated in triggering or transforming non-malignant cells to malignant ones either by DNA damage or by modulating gene expression. Furthermore, lipid peroxidation is a significant characteristic of free radical reactivity which results in deleterious effect on cells leading to their damage[1].

Antioxidants like glutathione (GSH)[2,3] ceruloplasmin (CP)[4-7] antioxidant enzymes like glutathione-S-transferase (GST)[8,9] and lipid peroxidation product malondialdehyde (MDA)[3,10] have been implicated in pathogenesis and prognosis of various epithelial malignancies including oral cancer. But their role in overall prognosis and cancer recurrence is not clearly understood. Therefore, we compared erythrocytic MDA and GSH, plasma CP and total GST (estimated before the onset of treatment) in biopsy proven stage IV oral squamous cell carcinoma patients (n=17) with their prognosis in 2 years.

MATERIALS AND METHODS

Approval for the study was given by the Institutional Ethics Committee. Informed consent was obtained

TABLE 1: Comparison of variables in patients who had cancer recurrence (Mean±SD)

Parameter	Recurrent (64%) (n = 9) #	Non-recurrent (36%) (n = 5) #	Significance *
GSH mg/grHb	5.51±3.76	5.26±2.63	p < 0.920**
CP mg/dl	38.88±26.70	32.05±21.55	p < 0.697 **
MDA M/grHb	4.53±2.22	3.97±1.51	p < 0.745 **
GST IU/L	6.45±3.97	3.30±2.2	p < 0.792 **

***Independent sample't' test, ** = Not significant, #= only 14 out of 17 came for follow up**

from each patient before withdrawal of blood sample.

Seventeen oral cancer patients who were clinically and histologically diagnosed as squamous cell carcinoma of oral cavity (stage IV) who underwent same mode of treatment were chosen for this study. Patients with oral carcinoma were staged using International Union against Cancer (UICC) TNM classification (1974) in the study. None of the patients with oral cancer had any habit of smoking, tobacco, and alcohol consumption. All the cases were treated with combination of surgery followed by a course of radiotherapy of around 23 fractions over 4 to 5 weeks.

Blood samples were taken from oral cancer patients using aseptic precautions. Blood was collected into ethylenediamine tetraacetate (EDTA) bottles and immediately centrifuged under refrigeration at 3000×g for 10 minutes. Plasma was carefully removed and separated cells washed thrice with cold phosphate buffer containing 0.15mol/L NaCl, pH 7.4. The erythrocytes were suspended in an equal volume of physiological saline as 50% cell suspension[11]. Hemolysate was prepared from erythrocyte suspension by addition of distilled water and was used in the estimation of GSH[12] and MDA[13]. Hemoglobin content of erythrocytes was measured by cyanmethhemoglobin method[14]. Plasma was used for the estimation of CP[15] and total GST[16].

Statistical analysis was carried out using Independent Sample t test.

RESULTS

Since all the patients were in stage IV cancer, only 36% of patients had no recurrence. All the above parameters namely erythrocytic GSH and MDA and plasma CP and total GST were higher in patients who had recurrence of cancer compared to their respective levels in patients who had no evidence of recurrence. (TABLE 1).

DISCUSSION

The generation of reactive oxygen radicals in mammalian cells profoundly affects numerous critical cellular functions, and the absence of efficient cellular detoxification mechanisms which remove these free radicals can result in several diseases. ROS are tumorogenic by virtue of their ability to increase cell proliferation, survival, cellular migration, and also by inducing DNA damage leading to genetic lesions that initiate tumorogenicity and sustain subsequent tumor progression[1].

Enhanced antioxidant capacity of tumor tissues make them less susceptible to oxidative stress conferring specific growth advantage[17] which has also been implicated in radio/chemo resistance leading to tumor recurrence[8,9]. In this study even though all the patients were in stage IV cancer, some had no recurrence of cancer. Then we grouped them into good and bad responders. We observed that patients with higher pretreatment levels of GST, GSH, and CP had recurrence within 2 years of onset of treatment. This means high levels of these antioxidants produced in these cancer patients as an adaptive response to combat the free radicals generated as a consequence of high metabolic rate protected these cells against the cytotoxic effects of radio/chemotherapy and hence leading to recurrence.

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