

## EFFECT OF VITAMIN E ON PROTEIN BOUND CARBOHYDRATE COMPLEXES IN RADIATION TREATED ORAL SQUAMOUS CELL CARCINOMA PATIENTS

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### ABSTRACT

Serum glycoproteins were evaluated in oral squamous cell carcinoma patients treated with radiotherapy and also the effect of vitamin E was studied. Cell surface glycoconjugates are important parameters in the detection of malignancy. Thus, the objective of the present study is to evaluate the efficacy of vitamin E on glycoproteins in oral cavity cancer patients treated with radiotherapy. The study includes 26 age and sex matched normal healthy individuals and 26 patients with squamous cell carcinoma of oral cavity. These patients were divided into two groups, one for radiotherapy alone (at a dosage of 6000 cGy in five fractions per week for a period of six weeks) and the other for radiotherapy plus vitamin E supplementation (at a dosage of 400 IU / day of vitamin E) for the entire period of radiotherapy. Levels of hexose, hexosamine, fucose and sialic acid were increased in oral squamous cell carcinoma patients and a significant decrease was observed in radiation treated patients when compared to control. The levels of glycoconjugates were significantly decreased in radiation treated patients supplemented with vitamin E. This measurement may be useful in assessing disease progression and identifying patients resistant to therapy and a possible role of vitamin E on reduction in glycoconjugate levels of radiation treated oral squamous cell carcinoma patients.

### KEY WORDS

Glycoproteins, Oral squamous cell carcinoma, Radiotherapy, Vitamin E.

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### INTRODUCTION

Glycoproteins and glycolipids are major constituents of cell membrane, and hence cell surface glycoconjugates are important in malignancy. Glycoconjugates are released into the circulation through increased turnover, secretion, and / or shedding from malignant cells (1). The increased levels are positively correlated with increasing stages in oral cavity cancer patients (2). The tumor burden and progression of disease is reflected from the higher levels of glycoprotein in oral cavity cancer patients (1) and breast cancer patients (3). Measurement of glycoproteins along with other clinical and biochemical criteria may be valuable in establishing diagnosis, staging of disease, detecting metastases, identifying patients

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at high risk for recurrence and evaluating therapeutic response. Some glycoconjugates like total sialic acid, hexose and fucose which are feasible and simple to analyze have also been reported (4 - 7). Cancer radiation therapy inflicts tremendous damage to healthy cells in the body (8). However, there are specific nutrients, flavonoids and herbs that have been shown to protect the body against cancer radiation therapy. An antioxidant therapy is beneficial to avoid the damage caused by free radicals during radiotherapy in oral submucous fibrosis. Supplementation of antioxidants is needed to reduce the levels of glycoproteins in radiation treated oral malignancy. Vitamin E was chosen as a supplementary agent for the present study due to its free radical scavenging potential (9). Also vitamin E is shown to be protective against cancer of prostate (10) and lungs (11). The objective of the present study is to evaluate the efficacy of vitamin E on glycoproteins in radiation treated oral squamous cell carcinoma patients

### MATERIALS AND METHODS

Oral squamous cell carcinoma patients admitted as in - patients in the department of Oral Oncology, Government Arignar Anna

Memorial Cancer Hospital, Karapettai, Kancheepuram were selected for this clinical trial. Studies were performed in accordance with the ethical standards laid down in an appropriate version. All persons gave informed consent prior to inclusion in the study. Patients with oral squamous cell carcinoma were selected for investigation on confirmation with histopathological examination of the biopsy samples. Stage III and IV patients with oral squamous cell carcinoma which includes cheek, tongue, floor of the mouth, palate, alveolus, retromolar trigone, lip and combined sites were taken for the present study. The present assessment covering a period of six months includes 52 subjects ranging from 35-65 years old of both sexes, out of which 26 were healthy controls (group I). Age and sex matched normal healthy individuals not suffering from any inflammatory disease and with no major illness in the recent past formed the control group. Group II - 26 cases with oral squamous cell carcinoma before radiotherapy. Group II patients were further divided into two groups. 13 cases who had undergone radiotherapy alone (group III). The radiotherapy was given at a dosage of 6000 cGy in five fractions per week for a period of six weeks. Group IV - the other 13 patients had radiotherapy plus simultaneous supplementation of vitamin E at a dosage of 400 IU / day in the form of  $\alpha$  - tocopherol, for the entire period of radiotherapy. Blood samples were collected, serum was separated. Glycoproteins in serum were precipitated hydrolysed (12) and the following parameters such as hexose (13), hexosamine (14), fucose (15) and sialic acid (13) were carried out by standard procedures. Statistical analysis of the data was computed by student's 't'-test. Patients having systemic diseases such as hypertension, diabetes mellitus or any infections were excluded from the study.

## RESULTS

A significant increase ( $p < 0.001$ ) in the levels of serum hexose, hexosamine, fucose and sialic acid were observed in group II patients, and the increase was less significant ( $p < 0.01$ ) in group III patients when compared to group I. The levels of hexose ( $p < 0.01$ ), hexosamine ( $p < 0.05$ ), fucose and sialic acid ( $p < 0.001$ ) were significantly decreased in group IV patients when compared to group III patients (Table 1).

## DISCUSSION

Elevated levels of glycoconjugates due to biochemical changes in cell surface glycoproteins and glycolipids have been observed during malignant transformation (16, 17). The elevated levels of hexose and hexosamine in group II patients of the present study (Table 1) might be a consequence of tissue necrosis caused by rapidly spreading tumor cell, destructing normal surrounding connective tissue. Serum fucose level is a better biochemical tumor marker than sialic acid level in oral squamous cell carcinoma (18). High levels of fucose in group II patients may have resulted from increased activity of serum fucosyl transferase (19). The increase in serum fucose level of the present study can be correlated well with the advancement of the disease.

Sialic acid concentration has been reported to be a reliable marker for the assessment of prognosis and detection of early recurrence. Sialoglycoprotein levels correlated with stage of disease (20), tumor burden (21), degree of metastasis (22) and recurrence of disease (23). Elevated levels of serum sialic acid in precancerous and cancerous condition of the oral cavity have been observed (2). The present study also shows an increase in glycoconjugates in oral squamous cell carcinoma patients when compared to control. Lower levels in group III patients reflect the primary response to the therapy. A significant decrease in the levels of glycoconjugates after radiation treatment, suggests that they may be useful for the follow up of individuals receiving treatment. Supplementation with Vitamin E maintained the levels at near normal indicating a positive prognosis. Vitamin E deficiency increases serum sialic acid levels (24, 25) and also inhibits serum sialidase activity (26). Supplementation of vitamin E prevented total protein-bound carbohydrate complexes in rat serum and tissues (27). Results of the above data were correlated with the previous findings.

From the above data, it was concluded that serum glycoconjugates were higher in oral cancer patients and a significant low levels in radiation treated patients. A decreased level in group IV patients suggests a good prognosis in oral

**Table 1 : Levels of serum hexose, hexosamine, fucose, and sialic acid of the study groups. Values are expressed as mean  $\pm$  SD**

Parameters (mg/dl)	Group I (n=26)	Group II (n=26)	Group III (n=13)	Group IV (n=13)
Hexose	122.4 $\pm$ 16.4	136.2 $\pm$ 14.1***	132.3 $\pm$ 12.2**	124.3 $\pm$ 11.1**
Hexosamine	81.6 $\pm$ 7.6	90.6 $\pm$ 8.7***	87.4 $\pm$ 9.3**	82.9 $\pm$ 8.3*
Fucose	9.2 $\pm$ 2.1	14.3 $\pm$ 2.1***	11.7 $\pm$ 2.8**	9.9 $\pm$ 1.1***
Sialic acid	49.2 $\pm$ 4.9	68.1 $\pm$ 7.1***	63.4 $\pm$ 5.6**	51.1 $\pm$ 6.4***

Statistically significant values of group II and III vs. group I, group IV vs group III are compared and expressed as \* $p < 0.05$ , \*\* $p < 0.01$ , \*\*\* $p < 0.001$

cancer patients treated with radiotherapy. Thus our study suggests that glycoconjugates particularly fucose, sialic acid and hexose can be used as simple and feasible parameters for screening, diagnosis and monitoring of patients. More investigations are required on a large scale to establish the value of these glycoconjugates to be used as a malignancy marker and the efficacy of vitamin E on serum glycoconjugates in oral squamous cell carcinoma patients.

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