

Understanding the significance of serum mucoproteins as biomarkers in pre- and post radiotherapy cases of head and neck malignancies

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Abstract

Mucoproteins being essential and normal constituents of body tissues are widely distributed in the extra cellular matrix as ground substances. They are also present on cell surfaces and in connective tissues. Present study was carried out to authenticate the significance of serum mucoproteins as biomarkers and to know the effect of radiations on the levels of serum mucoproteins, in head and neck malignant cases treated with standard dose of radiotherapy.

96 patients of head and neck malignancies, suffered from early and late stages, referred to Radiotherapy Department of Krishna Hospital, Karad (India) were selected and included in the study.63 volunteers served as healthy controls.

Serum mucoproteins were estimated in malignant patients before initiation of radiotherapy and one month after completion of radiotherapy. Significant increased levels ($P < 0.001$) of serum mucoproteins were observed in malignant patients before radiotherapy, as compared to the levels of healthy controls. After one month of radiotherapy, the serum mucoproteins significantly ($P < 0.001$) decreased in comparison to the pre treated serum mucoprotein values. The fall in serum mucoprotein levels after radiotherapy showed much higher values in early stages than late stages of head and neck malignancies.

The marked increased levels of serum mucoproteins in all the stages of head and neck malignancies before radiotherapy and significant decreased serum mucoproteins after radiotherapy suggested serum mucoproteins as good biomarkers of neoplastic activity. The study concludes that the estimation of serum mucoproteins before and after radiotherapy serves as a significant biomarker in diagnosis and prognosis of head and neck malignancies.

Introduction

Head and neck cancers are group of cancers found in the head and neck region, involving the respiratory tract and the digestive tract, interfering with the functions of eating and breathing. Head and neck cancers include malignant tumors found in the oral cavity, the oropharynx, nasopharynx, and the larynx. In developing country like India the incidence and prevalence of head and neck malignancies has been raised with alarming rates and has become one of the leading death causes of malignancies suffering. In the head and neck malignancies generally there is pre-

disposition with a common male: female ratio of 3:1. 75-80% of oral and laryngeal malignancy occurs among smokers and tobacco chewers.

Mucoproteins are type of conjugated proteins, widely distributed in the body as constituents of cell membranes, connective tissue, basement membrane and ground substance in intracellular spaces. The reference levels of serum mucoproteins are in very low concentrations [1], however various earlier studies have shown increased serum levels of mucoproteins in various cancers [2,3,4]. They have been correlated with the presence and extent of malignant diseases [5,6].

The present study was carried out in the most common type of malignancy, head and neck suffered by Indians. The study was designed to understand the significance of serum mucoproteins as diagnostic and prognostic biomarkers during metastasis and to observe the effect of radiations on its levels in radiotherapy undergone malignant patients. The serum mucoproteins were determined in selected head and neck malignant cases of early [I and II] and late stages [III and IV], before initiating radiotherapy and after one month of completion of radiotherapy.

Materials and Methods

The study was carried out in ninety-six (96), previously untreated clinically and histopathologically proven malignant cases of head and neck that attended the radiotherapy department of Krishna Hospital and Research Center Karad. The study results of malignant cases were compared by collecting venous blood and estimating serum mucoproteins from sixty-three (63) healthy volunteers of Karad city which served as healthy control group.

The patients were advised to take standard dose of radiations (60-65 Gy / 25-30 fractions/ 5-6 weeks) depending upon the stage of malignancy. The patients associated with diseases like Rheumatoid Arthritis, Tuberculosis, Gout, Pneumonia and Myocardial Infarction were excluded from study.

The first venous blood samples were collected from the patients before initiating the radiotherapy and the second venous blood samples were taken a month after completion of radiotherapy. The estimation of Serum Mucoproteins was carried out by simple and cheap laboratory method of Winzler [7].

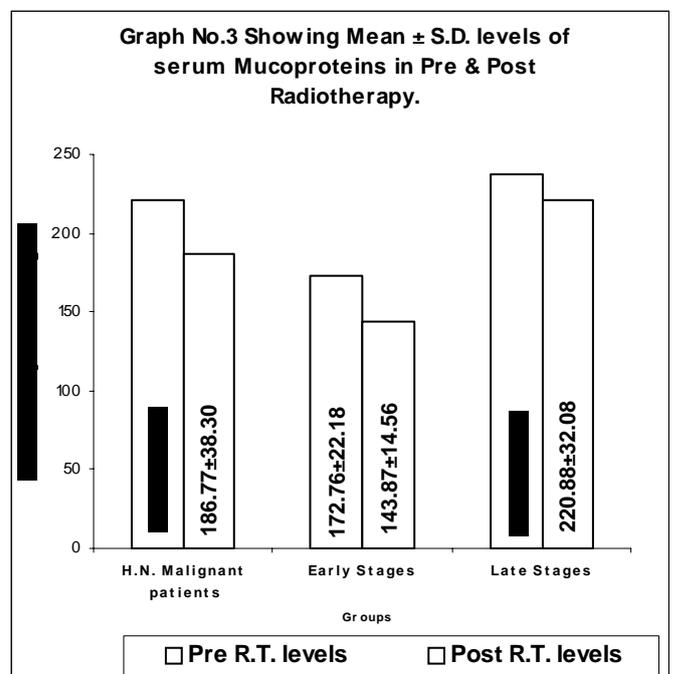
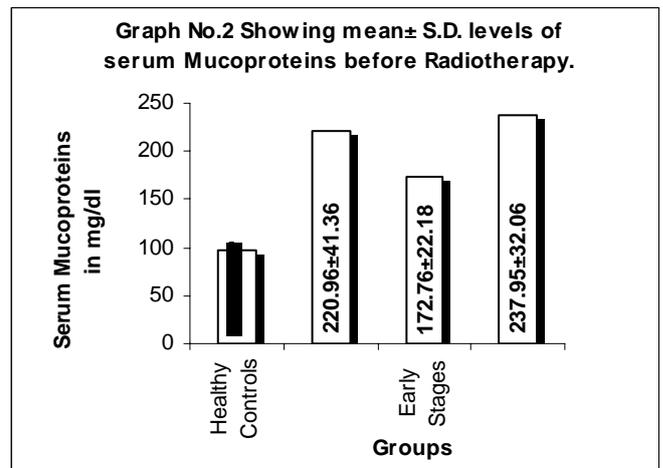
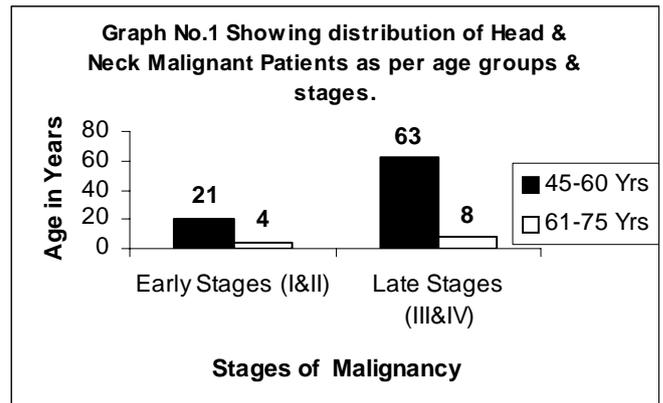
Statistical analysis

The study results were statistically analyzed with the program of SPSS for window version 10.0. The results were expressed in Mean and S.D. The students 't' test was applied for statistical significance.

Results

From ninety-six study cases of head and neck malignancies, eighty-four were from 45-60 years of age group where as twelve malignant patients were from 61-75 years of age group. In the studied head and neck malignant cases it was observed that the percentage of late stage sufferers (73.96%) were higher than the early stage sufferers (26.04%) (As depicted in Table 1 and graph 1).

Table 2 shows the serum mucoprotein levels of healthy controls and pre treated head and neck malignant patients



of early (I and II stage) and late (III and IV stage) stages. The mean serum Mucoproteins (220.96 ± 41.36 mg%) of head and neck malignant patients showed approximate two-fold rise than the mean serum Mucoproteins of heal-

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thy controls (98.14± 11.37mg%). The pretreatment serum mucoprotein values of late stages (III and IV Stages) were higher than the mean serum mucoprotein levels of early stage (I and II Stages) sufferers of head and neck malignancies, which showed statistically significance (p<0.01) on comparison. (Depicted in Table 2).

Effects of radiotherapy on serum Mucoprotein levels are depicted in table no- 3. The post treated serum mucoprotein levels of head and neck malignant cases showed statistical significant (p<0.001) lowered values when compared with the pre treated serum mucoprotein levels of the same. However the post-treated serum mucoproteins of malignant patients were considerably higher than the healthy control values (p<0.001).

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The stage wise effect of radiotherapy in early and late stages of head and neck malignancies, showed that the post therapy mean serum mucoprotein values decreased after treatment. The mean fall of serum mucoprotein values after radiotherapy showed much higher values in early stages than late stages of head and neck malignancies. (Shown in Table 3).

The statistical difference between pre and post radiotherapy values of serum Mucoproteins in head and neck malignant cases of early and late stages showed highly significant difference P< 0.001.

Table 1: Age and stage wise distribution of head and neck malignant cases

Age Groups	Head and Neck Malignant cases (n=96)		Total
	Early Stages (Stages I +II)	Late Stages (Stages III +IV)	
45-60 years	21	63	84
61-75 years	04	08	12
Total and Percentage	25 (26.04%)	71 (73.96%)	96

Table 2: Mean serum mucoprotein levels in healthy controls and pre treated Malignant cases of head and neck malignancies

Groups	Number	Serum Mucoproteins Mean ± S.D in mg %
Healthy Controls	63	98.14 ± 11.37
Head and Neck Malignant Patients	96	220.96 ± 41.36
Early Stages	25	172.76± 22.18
Late Stages	71	237.95 ±32.06

The statistical difference between the serum Mucoprotein levels of the

Table 3: Mean serum mucoprotein levels in pretreated and post treated malignant cases of early and late stages of head and neck malignancies.

Groups	Number	Pre R.T levels Serum Mucoproteins mg%	Post R.T levels Serum Mucoproteins mg%	Mean Fall of Serum Mucoproteins mg%
Head and Neck Malignant patients	96	220.96 ± 41.36	186.77± 38.30	34.19
Early Stages	25	172.76± 22.18	143.87±14.56	28.89
Late Stages	71	237.95 ±32.06	220.88± 32.08	17.07

Mean serum mucoprotein levels in healthy control = 98.14 ± 11.37 mg%

Discussion

The head and neck malignant patients and healthy controls comprised in the present study were in the range of

45-75 years of age. Out of 96 malignant cases of head and neck 90% were males and only 10 % were females. The

predominant number of male sufferers from head and neck malignancies indicates high risk caused due to the habits of smoking, alcoholism, eating tobacco and its products, more in males than females of India. The higher percentage of late stage sufferers may be due to illiteracy, ignorance and poverty which might have not brought the patients to hospitals for their early diagnosis and treatment.

The elevated levels of serum Mucoproteins in malignant patients showed high statistical significance of $P < 0.001$ when compared with healthy control values. The significant rise of serum Mucoprotein levels in head and neck malignancy may be due to the oxidative damage caused to the tissues by free radicals in oxidative stress condition, which in turn may be involved in the process like mutagenesis, carcinogenesis, cellular proliferation, depolymerization of ground substance around tumor, which might have increased the local production and release of serum mucoproteins in serum. The cell membrane lipid-peroxidation, protein oxidation, cellular fragmentation, carbohydrate damage due to subsequent oxidative stress mechanisms may also increase the serum Mucoprotein levels.

The stages of disease had positive correlation with the serum levels of mucoproteins. The fall in mean serum mucoprotein levels following radiotherapy was correlated to clinical response. On treatment there is shrinkage of tumor by killing of tumor cells, which may stop the cell proliferation. This might be the reason of reduction in serum mucoprotein levels after completion of radical radiotherapy in head and neck malignant study cases. The standard radiation dose used during malignancy treatment had significant control on metastasis and signifies effective mode of treatment.

All the study findings makes it clear that the marked elevations of serum Mucoproteins in different stages of head and neck malignancies are related to tumor bulk; as the tumor mass increases, the serum levels of mucoprotein also increase; showing a direct relationship between the severity of the disease and serum mucoprotein as a biomarker. Serial estimations of serum mucoproteins during and after the course of radiotherapy might provide significant hints for the final outcome of the disease; thus proving radiotherapy a beneficial treatment strategy. The study results also showed that the fall in levels of serum

mucoproteins after radiotherapy was significantly correlated to clinical response; hence this biochemical parameter can be used as a biomarker to monitor the progress of disease in combination with other tumor markers during radiotherapy of head and neck malignancies. The present study results are in concordant with the findings of earlier author studies of Joshi et al [8]; H.R Mali [9] and Pahwa .M.B et al [4].

In conclusion the estimations of serum mucoproteins in the laboratory before and after radiotherapy serves as a good diagnostic and prognostic biomarker. The present study has also helped us in understanding an effective and significant role of radiations in treatment of malignancies and levels of serum mucoproteins as a biomarker to show the response of treatment.

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