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ROLE OF CEA MARKER IN DIAGNOSIS OF SQUAMOUS CELL CARCINOMA IN ORAL CAVITY

Biochemistry

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ABSTRACT

Objective: The present study was conducted to find the utility of CEA Marker in diagnosis of Squamous Cell Carcinoma of oral cavity.
Material and method: A total of 360 male and female patients diagnosed with Precancerous conditions and oral Squamous cell carcinoma from stage I to IV were selected. After completing the history and physical examination patients were subjected to routine blood investigations, along with determining CEA Marker levels. The data obtained was then subjected to statistical analysis using SPSS 20.0 version.
Results: The mean values of CEA were found to increase with subsequent stages of OSCC, with maximum value in stage IV (51.8±5.47) and minimum in erythroplakia (6.90±2.35) with statistically significant result. Post-Hoc tukey test was done for intergroup comparisons and it was found to be significant (p-value<0.05), except comparison between OSMF vs Erythroplakia.
Conclusion: The present study determined that there is a positive correlation between CEA biomarker and oral squamous cell carcinoma.

KEYWORDS

Oral squamous cell carcinoma; Precancerous conditions; CEA biomarker.

INTRODUCTION:

Oral cancers (OC) represent the majority of head and neck cancers with more than half million patients being affected each year worldwide.[1] Oral squamous cell carcinoma (OSCC) is the most common oral malignancy, representing up to 80-90% of all malignant neoplasms of the oral cavity.[2] Various etiological factors are responsible for causing squamous cell carcinomas, such as tobacco smoking, heavy alcohol consumption, genetics, Human papillomavirus (HPV) infection, as well as inflammation.[3-4] Oral SCC often develops after the age of 50, with a highest peak in the sixth decade of life.[5] Intraoral and oropharyngeal tumors are more common among men than women, with a male:female ratio of over 2:1.[5] Although there are advancements in surgery, radiation, and chemotherapy, but the five-year survival rate has not been improved significantly and it remains at about 50 to 55 percent.[6]

OSCC can affect any site of the oral mucosa and large lesions can invade several continuous areas. The three most common sites of involvement are tongue, lip and floor of the mouth. Stages are clinically represented as precancerous lesions, such as leukoplakia, erythroplakia or leuko-erythroplakia, and Oral submucus fibrosis (OSMF), with a predictive factor of malignant transformation.[7] Histopathologically, they can be categorized into three degrees of differentiation: Well differentiated with greater than 75% keratinization; Moderately differentiated with 25% to 75% keratinization; and Poorly differentiated with less than 25% keratinization.[8] CEA is one of the most widely used tumor markers worldwide in OSCC.[9]

Therefore, the present study was conducted to find the utility of CEA biomarker as diagnostic and prognostic biochemical parameter in precancerous conditions and Squamous Cell Carcinoma of oral cavity.

MATERIALS AND METHOD:

The study was conducted in SMS Medical College and Attached Hospital Jaipur, Rajasthan. The study was a descriptive observational study conducted from time period from May 2018 to April 2020. The ethical committee clearance was obtained from the Institutional review board with Approval no. IRB/406/MC/EC/2019 and date of approval 22.07.2019.

Sample size was estimated at 5% level of significance with an allowable error of 15% was 338. After adding the non-response error of 10%, an additional 32 subjects were included and rounding it to 360 subjects were selected for this study. A total of 360 male and female patients diagnosed with Precancerous conditions and oral Squamous cell carcinoma from stage I to IV were selected based on inclusion and exclusion criteria. Inclusion criteria includes newly diagnosed patients of Precancerous conditions of oral Squamous cell carcinoma and diagnosed oral Squamous cell carcinoma patients of both the sex based on TNM staging.[10] The exclusion criteria included patients of Oral Squamous cell carcinoma of both sex who have received CT/RT or surgery for their disease; patients with severe Cardiovascular, Cerebrovascular, Hepatic and Renal diseases; and patients having Hypertension, Diabetes, Endocrinal disease, Tuberculosis and PCOS.

Before proceeding with study, an informed consent was taken from all the patients. Patients were then interviewed using a structured questionnaire to ascertain demographic and medical history and undergo a physical examination including name, age, sex, occupation, height, weight, BMI, pulse, BP, respiratory rate, past history, personal history, family history and drug history. After completing the history and physical examination, patients were subjected to blood investigations. All the enrolled subjects underwent laboratory work up as follows. After an overnight fasting 5 mL of venous blood sample was drawn from anticubital vein by using aseptic techniques in plain and 1 mL in EDTA vials. Routine blood investigations were performed -Haemoglobin, renal function tests, liver function tests, Random blood sugar, and lipid profile using commercially available kits. Special investigation performed was evaluating levels of CEA biomarker.

The values of all the laboratory routine and special investigations were recorded. The data obtained was subjected to statistical analysis using the IBM SPSS Statistics 20.0 Data Editor software (Microsoft Corporation Inc., Chicago, IL, USA).

RESULTS:

The mean values of CEA was found to increase with subsequent four stages of OSCC, with maximum value in stage IV (51.8±5.47) and minimum in Stage I (21.8±4.14). This showed the value of CEA biomarker constantly increased with subsequent stages of OSCC (**Table no. 1**).

The mean value of CEA for precancerous conditions showed that OSMF had higher value (10.55±2.99) than erythroplakia (6.90±2.35), (**Table no. 1**). One-way ANOVA statistical analysis was conducted for

intergroup comparison between all stages of OSSC and PCC for CEA. The level of significance was found to be significant (p-value=1.1102e-16; p-value<0.05), (**Table no. 2**). Post-Hoc tukey test comparisons found that all the intergroup comparisons were significant (p-value<0.05), except comparison between OSMF vs Erythroplakia (**Table no. 3**).

DISCUSSION:

The various premalignant lesions that represent a predictive factor of malignant transformation are Oral submucus fibrosis (OSMF), leukoplakia, erythroplakia or leukoerythroplakia.[11] The risk of malignant transformation of erythroplakia is the highest between the others premalignant forms (90%).[12] *Thus in present study we compared the most common premalignant lesions OSMF and Erythorplakia with all four stages of OSCC.*

Clinically, the distinction between a potentially malignant lesion and an early malignancy cannot be ascertained, thus posing a problem in diagnosis. Malignant cells show alterations in the histologic appearance and biochemical behaviour as compared to their normal counterparts. Products which are synthesized by the tumour cells or by the body in such abnormal situation are known as 'tumour markers'. These tumour markers can be used for early screening and detection of cancer.[13] Tumor markers may be produced directly by a tumor or by other tissues in response to a tumor, they can be metabolic products, acute-phase proteins, enzymes, hormones or tumor associated antigens such as Carcino-Embryonic Antigen (CEA). Pathologically elevated levels are arbitrarily defined by the 95% confidence limit of that of a normal population. The correlations made among CEA levels, tumor burden, and time after treatment define the value of CEA as a monitor of tumor burden in the clinical management of these malignancies.

The present study defines the distribution of CEA levels in patients with squamous carcinoma of the head and neck region. The mean values of CEA were found to increase with subsequent stages of OSCC, with maximum value in stage IV and minimum in erythroplakia with statistically significant difference. Similar results were proposed by Silverm NA *et al.*[14] that CEA levels may reflect the presence or absence of the metabolic machinery necessary to produce abnormal CEA levels by the tumor cells. This would explain the high CEA levels found in certain patients with small tumors and the normal values found in certain patients with widely disseminated metastases. The frequency and magnitude of CEA elevations are increased in patients with larger tumors and distant metastases.

A direct correlation between tumor burden and absolute CEA levels has been demonstrated in patients with adenocarcinomas of the colon and breast in a study by LoGerfo *et al.*[15] Similar results were observed by Tormey *et al.*[16] who found a 30% incidence of elevated CEA levels in patients with nodal metastases. Results of our study were in contrast with study conducted by Vincent *et al.*[17] who failed to find a correlation between tumor burden and CEA levels.

The mean values of ESR, CPK-MB, CPK and Blood sugar levels were found to increase from PCC to the stage IV of OSCC. Considering all these above parameters it was found that stage IV of OSCC is worst condition; and on comparing erythroplakia and OSMF, erythroplakia seems to be a better condition than OSMF.

Thus, CEA biomarker proved to be an important investigation parameter for precancerous and oral cancers. So, this special investigation should be considered as an important part of investigation procedure. The present findings were drawn by a smaller sample size but the findings strongly warrant an in-depth study on a larger sample size of oral cancer patients.

CONCLUSION:

The treatment of oral cancer is based on multiple treatment options. That depends on patient's overall condition to tolerate aggressive therapy. A multidisciplinary approach is crucial for management of OSCC. The incorporation of use of new molecularly targeted agents for diagnosis of oral cancers and utilization of current treatment regimens is a priority to decrease the mortality rate of this deadly disease.

Table no. 1: Mean values of CEA for all stages of OSSC and PCC

CEA	Stage I	Stage II	Stage III	Stage IV	OSMF	Erythroplakia
Mean	21.8	29.8	36.75	51.8	10.55	6.90
SD	4.14	4.66	4.68	5.47	2.99	2.35

Table no. 2: One-way ANOVA for intergroup comparison between all stages of OSSC AND PCC for CEA

source	sum of squares SS	degrees of freedom df	mean square MS	F statistic	p-value
treatment	28,327.3667	5	5,665.4733	322.2713	1.1102e- 16*
error	2,004.1000	114	17.5798		
total	30,331.4667	119			

*p-value<0.05 is significant

Table no. 3: Post Hoc tukey test for intergroup comparisons

Treatments Pair	Tukey HSD Q statistic	Tukey HSD p-value	Tukey HSD inferfence
I vs II	8.5329	0.0010053	** p<0.01
I vs III	15.9459	0.0010053	** p<0.01
I vs IV	31.9985	0.0010053	** p<0.01
I vs OSMF	11.9994	0.0010053	** p<0.01
I vs ERY	15.8926	0.0010053	** p<0.01
II vs III	7.4130	0.0010053	** p<0.01
II vs IV	23.4655	0.0010053	** p<0.01
II vs OSMF	20.5323	0.0010053	** p<0.01
II vs ERY	24.4255	0.0010053	** p<0.01
III vs IV	16.0526	0.0010053	** p<0.01
III vs OSMF	27.9453	0.0010053	** p<0.01
III vs ERY	31.8385	0.0010053	** p<0.01
IV vs OSMF	43.9979	0.0010053	** p<0.01
IV vs ERY	47.8910	0.0010053	** p<0.01
OSMF vs ERY	3.8931	0.0731001	insignificant

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