The study of biomarker cytokines (interleukin-6) in oral pre-cancers

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INTRODUCTION

Pre-cancer is a lesion from which a malignant tumor is presumed to develop in a significant number of instances and that may or may not be recognizable clinically or by microscopic changes in the affected tissue.

Oral squamous-cell carcinoma is thought to be preceded by a number of pre-cancer stages which induce morphological changes in cells of the oral mucosa resulting in clinically detectable pre-malignant lesions such as erythroplakia or leukoplakia.(1)

Erythroplakia is bright red velvety plaques which cannot be characterized clinically or pathologically as due to another condition.

Leukoplakia is whitish patch or plaque that cannot be characterized clinically or pathologically as any other disease and which is not associated with any other physical or chemical causative agent except the use of tobacco.(2)

Oral submucous fibrosis (OSF) is a chronic fibrotic disease, characterized by fibroelastic changes and inflammation of the mucosa.

Melanoplakia is the occurrence of pigmented patches in oral mucous membrane.

Candidiasis is a contagious disease caused by a fungus, Candida albicans, characterized by small whitish eruptions on the mouth, throat, and tongue.

Despite the general accessibility of the oral cavity during physical examination, many malignancies are not diagnosed until late stages of disease. In order to prevent malignant transformation of these precursor lesions, multiple screening and detection techniques have been developed to address this problem. The early detection of cancer is of critical importance because survival rates markedly improve when the oral lesion is identified at an early stage.

Interleukin-6 (IL-6)

It is an immune protein in the hematopoietins family. It is a monomer of 184 amino acids produced by T-cells, macrophages, and endothelial cells found on a single gene located at 7p21. IL-6 is released in response to infection, burns, trauma, and neoplasia, and its functions range from key roles in acute-phase protein induction to B- and T- cell growth and differentiation.IL-6 can have direct effects on cells, can mediate the effects of other cytokines, can be co-agonistic or antagonistic in conjunction with other cytokines, and interact with glucocorticoids. The intra-tumoral cytokine stimulates oral cancer cells to enhance secretion of matrix metalloproteinase, which promotes angiogenesis and play important role in tumor cell invasion by degrading ECM.[5]

Previous studies related to OSCC have demonstrated that concentration of Interleukin-6 and other pro-inflammatory and pro-angiogenic cytokines are increased.(3)

OBJECTIVES

This study aims to define the role of Interleukin-6 as salivary biomarkers in early detection of oral squamous cell carcinoma.

1. To study the association between Interleukin-6 and oral precancers.

2. To identify the alteration in Interleukin-6 gene in the saliva of at-risk patients.

3. To assess the Interleukin-6 in salivary samples both quantitatively & qualitatively.

4. To estimate the levels of Interleukin-6 in salivary samples of high risk patients[tobacco abusers in smoked/smokeless form] and compare it with the age matched controls.

METHODOLOGY

A prospective experimental analysis will be conducted by using 5ml whole saliva expectorated by each individual ,who has any of the morphological pre malignant lesion [leukoplakia, erythroplakia,melanoplakia , oral submucous fibrosis,candidiasis} in the oral mucosa, under non stimulatory conditions in the OPD of VMMC & Safdarjung Hospital , New Delhi.

The sample size of 30 such individuals will be taken.

Samples will be obtained by requesting subjects to swallow first, tilt their head forward, and then expectorate all saliva into the centrifuge tube for 10min without swallowing.

Following collection, the saliva will be immediately centrifuged in a cooling centrifuge at 2500rpm for 15min at 4*C to remove squamous cells and cell debris. [4]

The resulting supernatant will be separated into 1ml aliquots and stored at 80*C for further biochemical analysis. [4]

Then, the biomarker Interleukin-6 is analyzed using solid phase sandwiched enzyme linked immuno sorbent assay in laboratory. (4)

The proposed intervention is to use IL-6, if the study becomes favorable, as a biomarker for early detection of oral cancer in high risk patient presenting with precancers.

A written consent form will be signed by each patient after explaining various aspects of the study to the patient.

The patient will be assured and all measures will be taken to maintain the confidentiality of the information given by the patient.

Ethical clearance for this study has been applied for.

IMPLICATIONS

Given the association between Interleukin-6 and adverse outcomes, identification of high-risk oral premalignant lesions and intervention at premalignant stages could constitute one of the keys to reduce the mortality, morbidity and cost of treatment associated with OSCC. In addition as the molecular changes appear well before microscopic and morphological changes, certain patients, known to be at high risk for oral cancer[tobacco abusers smoked/ smokeless] can be diagnosed early. This study will help in the early detection of oral pre-cancers and their transformation into invasive cancers at an early stage by follow up that will last beyond the study.

REFERENCES

1. Qin GZ, Park JY, Chen SY, Lazarus P., Deptt. Of Pathology and Laboratory Medicine, Temple University School of Medicine, Philadelphia.
2. By World Health Organization.
3. Sehgal et al, Ray et al, Janeway et al, Fernandez, Botran, Davidson College
4. Rajkumar, Ramesh,V. Ramyamalini, G. Nandhini, T. Dinesh, B.K Ashwini, S. Nirmala, Deptt. Of Biochemistry, SRM University, Chennai.
5. Acta Otolaryngol. Effects of cytokines on matrix metalloproteinase expression in oral squamous cell carcinoma in vitro., Sundelin Kract goes here... 2005; 125(7): 765-73.