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ANALYSIS OF SALIVARY CYTOKINES AND CHEMOKINES IN EARLY AND ADVANCED STAGES OF ORAL SQUAMOUS CELL CARCINOMA (OSCC)

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Introduction:

OSCC is the sixth most common neoplasia worldwide and it accounts for 80-90% of Head and Neck Cancer (HNC). When diagnosed at advanced stages has a few therapeutic options and a 5-year survival rate ranging between 50-55%. Since inflammation has been linked to the pathology of OSCC, research to date indicates the possibility of using salivary pro and anti-inflammatory proteins for screening of oral disorders. Several studies reveal elevated secretion of immune mediators like IL-1 β , IL-6 and TNF α associated with OSCC. However, so far no reference indicates for differences in the levels of salivary cytokines and chemokines between early and late stages of oral cancer. Therefore, a research to determine novel salivary biomarkers is carried out to deliver new diagnostic & prognostic tools in early and late stages of OSCC.

Objective:

Detection and quantification of target salivary cytokine and chemokine levels in patients at early and advanced stages of OSCC in order to determine if they diverge from healthy controls. The main objective is the identification of a single or multiple biomarkers to provide a non-invasive test facilitating the early diagnosis and therapeutic outcomes of OSCC patients with valuable application in the clinical practice.

Materials and Methods:

A consent form approved by the Ethical Committee review board of the General University Hospital of Valencia was signed by all participants. Thirty-one patients and sixteen healthy subjects agreed to donate saliva for research purpose and were examined for periodontal diseases. Unstimulated whole saliva samples were collected and stored until further use. Immunoassay based on Multi Analyte Profiling technology (Luminex xMAP) for protein analysis was used for targeted quantification of thirteen salivary soluble inflammatory mediators. To validate statistical significance (*P< 0.05) Kruskal-Wallis non-parametric test was performed.

Results:

Patients and controls were age and gender matched. Within the OSCC cohort 15 patients were at early and 16 at advanced stages of disease (mean age 64.4 \pm 3.86 years), of whom 13 were male and 18 female. Figure 1 represents the differences in the expression of inflammatory proteins between the cases. Analysis showed significantly increased concentrations of salivary IL-6, IL-8, IL-10, TNF- α , HCC-1, MIP-4 and PF-4 according to the OSCC progression. Besides, VEGF also demonstrated a tendency for elevated secretion in OSCC samples though validation

in larger cohorts is necessary. The expression levels of IL-1 α , IL-4, EGF, IP-10 and MCP-1 exhibited no significant differences among control and pathological samples.

Conclusion:

Luminex xMAP technology appeared to be a suitable method to validate and measure salivary protein levels. The results suggest that saliva can be used as a promising diagnostic fluid where measurable parameters like cytokines and chemokines at differential levels can discriminate disease process. Further work intends to validate the present results supported by larger patient cohort and correlation with clinical parameters.

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