Serum and Salivary levels of proinflammatory cytokines and polyamines as potential biomarkers in the diagnosis of oral squamous cell carcinoma

A Thesis
Submitted to the council of the College of Dentistry
at University of Baghdad
In partial Fulfillment of the Requirements
For the Degree of Doctor of Philosophy
In Oral Medicine

By
Shanaz Mohammad Gaphor
(B.D.S., M.Sc.)

Supervised by
Prof. Dr. Nazar G. Al-Talabani
Prof. Dr. Abdul-Wahab R. Hamad

2005 AB   **1426 AH**

Abstract

Back ground:

Oral cancer is one of the prevalent cancers of the body and is one of the 10 most common causes of death. Oral cancers are the cause of significant morbidity and mortality throughout the world. Oral squamous cell carcinoma (OSCC) accounts for over 90% of these tumors.

Aim of the study:

This study was designed to detect biochemical markers in serum and saliva of oral squamous cell carcinoma patients and to evaluate their validity in monitoring and diagnosis. The level of certain proinflammatory cytokines and polyamines in the serum and saliva of (30) patients with OSCC and (20) healthy individuals as control group was measured.

Patients and Methods:

Levels of proinflammatory cytokines (IL-1 alpha, IL-6, IL-8 and GM-SF) was detected by enzyme linked immunosorbent assay (ELISA), whereas polyamines (spermidine and spermine) were determined by high performance liquid chromatography (HPLC) in both serum and saliva of patients with OSCC and control group.

Results and Discussion:

Serum IL-6 and IL-8 level were detected at higher concentrations in patients with OSCC than the control group ($P < 0.001$). No significant

differences in serum IL-1 alpha and GM-CSF of patients with OSCC as compared with control group.

The levels of IL-1 alpha, IL-6, IL-8 and GM-CSF in saliva showed significant increase in patients with OSCC when compared with control group.

Salivary IL-1 alpha and GM-CSF were useful in the diagnosis of OSCC patients since the areas under the ROC curve (0.82; 0.67) respectively were significantly different from that of an equivocal test of 0.5. Serum IL-6 was useful in the diagnosis of OSCC patients than salivary IL-6 since the areas under the ROC curve (0.8; 0.73) respectively, were significantly different from that of an equivocal test of 0.5.

The area under the ROC curve for both serum and salivary IL-8 was (0.90), which is significantly different from that of an equivocal test of 0.5, which indicated that serum and salivary IL-8 were very useful in the diagnosis of OSCC patients and separating between OSCC patients and control group.

There were no statistically significant differences in serum and salivary IL-1 alpha, IL-6, IL-8 and GM-CSF in relation to cellular differentiation, lesion status, clinical staging and duration of the disease.

The total serum and salivary polyamines level of OSCC were significantly higher than the control group ($P<0.001$). Both salivary and serum polyamines level were reliably accurate test in separating between OSCC patients and control group since the area under the ROC curve for both serum and salivary polyamines was one which is significantly higher (different) from that of an equivocal test of 0.5. There was significant difference in salivary spermine level among OSCC patients in relation to

lesion status. Spermine levels were reduced in recurrent lesion especially with metastases. There were significant differences in serum polyamines level among OSCC patients in relation to duration of the disease (P<0.05).

Conclusion:

From the results of the presents study, it can be concluded that cytokines are important in proinflammatory and proangiogenic responses and are detectable in serum and saliva of patients with OSCC. These cytokines increase the pathogenicity of OSCC and prove useful as biomarkers for diagnosis. Another finding was that detection of polyamines in serum and saliva are useful and valuable diagnostic markers in diagnosis and early detection of OSCC.