

Interleukin-1 as a Marker of Periodontitis with Oral Carcinoma – A Biochemical Study

Sudhakar U¹, Sivaranjani JA², Dayan MC³

ABSTRACT

AIM: This biochemical study aimed at evaluating the level of interleukin-1beta in patients with oral squamous cell carcinoma as a reflection of amount of bone destruction leading to periodontitis in comparison with the normal healthy individuals.

MATERIAL & METHOD: The subjects were grouped under four major categories like chronic periodontitis, chronic periodontitis with oral squamous cell carcinoma and squamous cell carcinoma alone and the control. Each group consisted of 10 subjects each. Unstimulated whole saliva was collected from each subject. IL-1 in saliva was measured by enzyme linked immunosorbent assay.

RESULTS: In the present study, IL-1 was significantly more in patients with cancer and periodontitis than patients with only cancer. When compared with the normal subjects IL-1 value was significantly more in subjects with carcinoma (0.016).

CONCLUSION: This study presents the first evidence of association between level of salivary biomarker interleukin 1 in subjects with periodontitis and in oral squamous cell carcinoma.

Keywords: Interleukin-1, Chronic periodontitis, Biomarker, Oral squamous cell carcinoma

¹M.D.S

Head of the Department
Department of Periodontics
Thai Moogambigai Dental College, Mugappair,
Chennai, INDIA

²Final Year Post Graduate Student

Department of Periodontics
Thai Moogambigai Dental College, Mugappair,
Chennai, INDIA

³M.B.B.S

Registrar
Department of Medical Oncology
Apollo Cancer Speciality Hospitals, Teynampet,
Chennai, INDIA

INTRODUCTION

Incidence of oral cancer and the survival rate have remained essentially unchanged over the past three decades despite the accessibility of the oral cavity to direct examination, promotion effects against known risk factors of oral cancer, and advances in the treatment and diagnosis arguing forcibly for new approaches (1). New insight regarding the etiology as well as the strategies for prevention are needed. A need for the development of new strategies for prevention become mandatory.

Considerable evidence indicates that chronic infections and persistent inflammation are associated with increased cancer risk (2). Periodontitis is a chronic oral infections thought to be caused by gram negative anaerobic bacteria in the dental biofilm (3). Recent evidence also suggests a significant

role for viruses in the initiation and progression of periodontitis. It leads to irreversible destruction of periodontitis. It leads to irreversible destruction of tissue supporting teeth, clinically detectable as periodontal pockets and alveolar bone loss. Periodontitis results in a continuous release of bacterial and inflammatory markers into the saliva and a lower degree into the blood (4). The mediators travel to distant sites and adversely affect systemic health. Periodontitis, characterized by epithelial proliferation and migration, results in chronic release of inflammatory cytokines, chemokines, prostaglandins, growth factors and enzymes all of which are closely associated with carcinogenesis (5).

Cytokines produced locally have an influence on the development of a particular

Contact Author

Dr.J.Akila Sivaranjani
akilas_87yahoo.com

immune response (6). A number of advances have been made in the field of cytokines regulation of t cell function and so called Type -1 and Type-2 cytokines may play a predominant roles in determining the outcome of the infection (7). IL, is a key mediator of chronic inflammatory disease with the potential to initiate tissue destruction and bone loss in periodontal disease (8). Studies suggests patients with oral cancer have elevated levels of inflammatory cytokines in their saliva. IL-1 is also used as a marker for early diagnosis of oral cancer using salivary diagnostics methods. Studies suggest a synergistic relationship between chronic periodontitis and squamous cell carcinoma independent of smoking status age, race and ethnicity which generate a hypothesis about a possible relationship between periodontal disease and oral neoplasms (9). The present study was done using saliva decided to estimate the

level of IL-1 in patients with periodontitis and oral cancer.

MATERIALS AND METHODS

Patients were briefed about the study and informed consent were obtained. Approval from ethical committee has been obtained. The study population was from the patient pool seen in the department of periodontics Thai Moogambigai Dental College ,Chennai and Department of Oncology Apollo research institute Chennai. The subjects were grouped under four major categories like chronic periodontitis, chronic periodontitis with oral squamous cell carcinoma and squamous cell carcinoma alone and the control. Each group consisted of 10 subjects each.

Unstimulated whole saliva was collected from each subject. Subjects were asked to rinse their mouth with normal water and

then were asked to expectorate whole saliva in the sterile tube.

IL-1 in saliva was measured by enzyme linked immunosorbent assay[Human Dental ELISA kit KOREA]. This IL-1 enzyme linked immunosorbent assay (ELISA) applies a technique called quantitative sandwich immunoassay. The microtiter plate provided in this kit has been pre-coated with a monoclonal antibody specific to IL-1. Standards or samples are then added to the appropriate microtiter plate wells and incubated. After washing to remove unbound IL-1 and other components of the sample, biotin-conjugated polyclonal antibody specific to IL-1 is added and incubated. Laboratory technicians determined the concentrations of salivary biomarkers IL-1. The resulting yellow colour was then read on an ELISA reader and a standard curve was generated to calculate the results.

Statistical Analysis: Chi-square test was used to assess the P-value.

RESULTS

Mean value of IL-1 level for subjects with periodontitis was 4.034 and normal was 3.054 which was statistically significant(P=.006) (Table 1)

The mean value of IL-1 level for subjects with cancer was 3.936 which was statistically significant (P=.016) (Table 2)

The mean value of IL-1 for cancer with periodontitis was 4.036 and subjects without periodontitis was 3.836 which was statistically significant (P= 0.001) (Table 3)

The mean value of IL-1 for cancer with periodontitis was 4.036 and subjects with periodontitis was 4.034 which was statistically not significant (P= 0.977) (Table 4)

DISCUSSION

Periodontitis is a chronic oral infection caused by inflammatory reactions to gram negative anaerobic bacteria (10) which results in continuous release of toxins and inflammatory markers in the blood stream and saliva.

Table 1: Mean value of IL-1 level for subjects with periodontitis and normal subjects

	Disease Condition	N	Mean	Std. Dev	t-Value	P-Value
Interleukin 1 Beta	Normal	5	3.054	0.441	4.779	0.006
	Periodontitis	10	4.034	0.180		

Table 2: Mean value of IL-1 level for subjects with cancer and normal subjects

	Disease Status	N	Mean	Std. Dev	t-Value	P-Value
Interleukin 1 Beta	Normal	5	3.054	0.441	3.963	0.016
	Cancer	5	3.836	0.024		

Table 3: Mean value of IL-1 level for subjects with both cancer and periodontitis and subjects with cancer only

	Disease Status	N	Mean	Std. Dev	t-Value	P-Value
Interleukin 1 Beta	Cancer with Periodontitis	10	4.036	0.120	5.088	<0.001
	Cancer	5	3.836	0.024		

Table 4: Mean value of IL-1 level for subjects with both cancer and periodontitis and subjects with periodontitis only

	Disease Status	N	Mean	Std. Dev	t-Value	P-Value
Interleukin 1 Beta	Cancer with Periodontitis	10	4.036	0.120	0.029	0.977
	Periodontitis	10	4.034	0.180		

IL-1 beta is the major occurring in the gingival associated periodontitis. It is formed and released in response to several immune stimulatory agents like lipopolysaccharides and activate endothelial cells to upregulate ICAM -1 which may increase diapedesis of leucocytes (11). All these IL-1 effects increase the inflammatory response and can subsequently cause degradation of the periodontal ligament and alveolar bone (12).

In the present study, IL-1 was significantly more in patients with cancer and periodontitis than patients with only cancer. When compared with the normal subjects IL-1 value was significantly more in subjects with carcinoma (0.016). This is to our knowledge is one of the first study to estimate the level of IL-1 in both oral cancer and chronic periodontitis. Recent evidence suggests a significant role for viruses in the initiation and progression of periodontitis. More interestingly, studies suggests that periodontal pockets acts as a reservoir for Human papilloma Virus (HPV) (8) cytomegalovirus and Epstein bar virus which are the suspected agents associated with oral cancer. The question of how infection and inflammation can influence carcinogenesis has interested scientists for the past one and half centuries but only now are come up with the certain principles and complexity of this association are emerging. Chronic periodontitis can play a direct or indirect role in carcinogenesis (13).

- Direct effect of micro organism : Micro organisms and their products such as endotoxins, metabolic by products and enzymes [collagenase proteases etc] are toxic to surrounding cells and may directly induce mutations in tumor suppressor genes or alter the signaling pathways that affect the cell proliferation.

- Indirect effect through inflammation-chronic infection may stimulate the formation of epithelialized tumors through an indirect mechanisms involving activation of surrounding inflammatory cells . Micro organisms activate,
 - ◆ The host cells like macrophages, monocytes, lymphocytes to generate reactive O₂ species (H₂O₂ + OXY RADICALS) and matrix metallo proteases which can induce DNA damage damage in epithelial cells
 - ◆ Produce cytokines, chemokines, growth factors and other signals that provide an environment for cell survival proliferation, migration , angiogenesis and inhibition of apoptosis. This environment may help epithelial cells to accumulate mutations and drive these mutant epithelial cells to proliferate migrate and give them a growth advantage.

CONCLUSION

In the present study there was a significant increase in the level of IL-1 in patients with carcinoma and chronic periodontitis. This study present us to our knowledge the first evidence of association between level of salivary biomarker interleukin 1 in subjects with periodontitis and in oral squamous cell carcinoma. The present study had a smaller sample size, the association needs to be compared by larger studies with a more comprehensive assessment. A specific association between chronic periodontitis and oral cancer is plausible and needs to be explored .This will have a potential impact on understanding the etiology of oral cancer as well as on its prevention and control.

REFERENCES

1. Canto MT, Devesa SS. Oral cavity and

pharynx cancer incidence rates in united states 1975-1998. *Oral oncology* 2002;**38**:610-17.

2. Karin M, Lawrence T, Nizet V. Innate immunity gone away: linking microbial infection to chronic inflammation and cancer. *Cell* 2006;**124**:823-35.

3. Mine Tezal, Mayreen A, Sullivan, Andrew Hyland *et al.* Chronic periodontitis and the head and neck squamous cell carcinoma. *Cancer Epidemiology Biomarkers Prevention* 2009;**18**(9): 2406-12.

4. Champagne CME, Buchanan W, Reddy MS, Pressier JS, Beck JD, Offenbaxher S. Potential for gingival crevice fluid measures as predictors of risk of periodontal disease. *Periodontal* 2000, **2003**;**31**:167-80.

5. Loesche WJ, Grossman NS. Periodontal diseases as a specific, albeit chronic infection :diagnosis and treatment. *Clinical Microbiology Rev* 2001;**14**:727-52.

6. E Gemmell, GJ Seymour. Cytokine profiles of extracted from humans with periodontal diseases. *J Dental Research* 1998;**77**(1):16-26.

7. E Gemmell, GJ Seymour. Cytokine profiles of cells extracted from humans with periodontal diseases. *J Dent Res* 1998;**77**(1):16-26.

8. Horimia M, Willberg J, Ruokonen H, Syrjanen S. Marginal periodontium as a potential reservoir of human papilloma virus in oral mucosa. *J Periodontal* 2005;**76**(3):358-63.

9. Saygunl, Kubar A, Ozdemir A, *et al.* Periodontitis lesions are source of cytomegalovirus and Epstein Barr Virus. *J Periodontal Res* 2005;**40**:187-91.

10. Tezal M, Grossi SG, Genco RJ. Is Periodontitis associated with oral neoplasms? *J Periodontology* 2005; **76**:406-10.

11. Carlos TM, Harlan JM. Leukocyte-endothelial adhesion molecules. *Blood* 1994;**84**(7):2068–01.

12. Aksentijevich I, Masters SL, Ferguson PJ, *et al.* An autoinflammatory disease with deficiency of the interleukin-1-receptor antagonist. *The New England Journal of Medicine* 2009;**360**:2426–37.

13. Mine Tezal, Maureen A. Sullaiavan Mary E *et al.* Chronic periodontitis and risk of tongue cancer. *Arch Otolaryngol Head Neck Surg* 2007;**133**:450-54.