



Assessment of c-reactive proteins and homocysteine levels in chronic periodontitis patients

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Abstract

Background: To assess the c-reactive proteins and homocysteine levels in chronic periodontitis.

Materials & methods: A total of 30 systemically healthy subjects were divided into two groups: Group I, non-periodontitis subjects and group II, chronic generalized periodontitis subjects. Gingival index was calculated. The p – value less than 0.05 was considered significant.

Results: The two groups showed plaque index with score in group I as 0.65 and in group II was 2.21. The mean CRP (mg/L) levels for both groups were 0.84 and 2.36, respectively. CRP values of the two groups were significantly different from each other, with CRP levels in the group II greater than those in the group I subjects.

Conclusion: Elevated levels of serum homocysteine and serum CRP levels were seen in subjects with chronic periodontitis.

Keywords: Homocysteine, Periodontitis, CRP.

Introduction

Periodontitis is defined as the inflammatory disease of supporting tissues of the teeth caused by specific microorganisms or groups of specific microorganisms, resulting in progressive destruction of the periodontal ligament and alveolar bone with pocket formation, recession or both. ¹ The pathogenic role of the subgingival microbiota in the initiation and progression of periodontitis is widely accepted. Periodontal pathogens affect local and systemic immune and inflammatory responses. The local inflammatory response to these bacteria or bacterial products is characterized by infiltration of the periodontal tissues by inflammatory cells including polymorphonuclear neutrophils (PMNs), macrophages, lymphocytes and plasma cells. ² Activated macrophages release cytokines and some individuals respond to microbial challenge with an abnormally high delivery of such inflammatory mediators as PGE₂, IL-1 and TNF. These cytokines are involved in the destruction of both the periodontal connective tissue and alveolar bone. ^{3,4}

Systemic acute phase response is characterized by features, such as fever, neutrophilia, changes in lipid metabolism, and induction of various acute phase proteins, such as C-reactive protein (CRP), fibrinogen, and serum amyloid. ⁵ CRP is a type I acute phase protein that is produced by the liver in response to diverse inflammatory stimuli. ⁶ These stimuli include heat, trauma, infection, and hypoxia. In healthy individuals CRP levels are found in trace amounts, that is, <0.3 mg/L serum of CRP could exceed 100 mg/L in the presence of overwhelming systemic infection, which provides a useful marker for tracking the course of infection. ⁷ Hcy, a sulfur-containing amino acid, which in the recent past has

become a biomolecule of great importance for biochemists and clinicians alike. Hcy is exported into plasma where it circulates, mostly in its oxidized form, bound to plasma proteins as a protein-Hcy mixed disulfide with albumin (protein-SS-Hcy).⁸ Under normal circumstances, most but not all of the Hcy formed in transmethylation reactions is remethylated back to methionine or is converted into cysteine in transsulfuration reactions. The B-complex vitamins play an essential role in the transformation and the excretion of the Hcy metabolism pathway, the elevated levels of Hcy that is, hyper-Hcy (HHcy) has been associated with pathologic alteration in the vasculature, which is recognized as an independent cardiovascular disease risk factor.⁹⁻¹¹ The literature evidence also shows that a rise in plasma-Hcy concentration beyond 15 μmol (5–15 μmol) is a risk factor for cardiovascular disease.¹² Hence, this study was conducted to assess the c-reactive proteins and homocysteine levels in chronic periodontitis.

Materials & methods

A total of 30 systemically healthy subjects were divided into two groups: Group I, non-periodontitis subjects and group II, chronic generalized periodontitis subjects. Gingival index was calculated. Samples were centrifuged in the centrifuge machine at 3000 rpm for 10 min to separate the serum from blood. All participants were subjected to quantitative CRP analysis using enzyme-linked immunosorbent assay. Laboratory investigations were done. All the data was collected and results were analyzed using SPSS software. The p – value less than 0.05 was considered significant.

Results

A total of 30 subjects were included. The two groups showed plaque index with score in group I as 0.65 and in group II was 2.21. The mean CRP (mg/L) levels for both groups were 0.84 and 2.36, respectively. CRP values of the two groups were significantly different from each other, with CRP levels in the group II greater than those in the group I subjects.

Table 1: clinical parameters and serum CRP levels

Groups	PI	GI	CAL (mm)	CRP (mg/dL)
Group I	0.65	0.55	0.70	0.84
Group II	2.21	2.02	4.08	2.36

GI : Gingival index, PI: plaque index, CAL: clinical attachment loss

The mean plasma Hcy was found to be 23.45 and 11.05 mmol/L, respectively, for cases and controls. The difference was statistically significant (P = 0.001).

Table 2: plasma homocysteine

Parameters	Cases Mean	Controls Mean	p- value
Plasma homocysteine (micro mol/L)	23.45	11.05	0.001*

* : significant

Discussion

Periodontitis is a chronic inflammatory disease initiated by a dysbiotic dental biofilm and followed by a progressive destruction of periodontal tissues.¹³ Bacteria and their products progressively affect the periodontium integrity, which can trigger a local inflammatory response but also a systemic response.¹⁴ Raised levels of pro-inflammatory mediators have been reported in patients with periodontitis who also exhibit distinct hematological changes including raised levels of C-reactive protein (CRP).¹⁵ Hence, this study was conducted to assess the c-reactive proteins and homocysteine levels in chronic periodontitis.

In the present study, a total of 30 subjects were included. The two groups showed plaque index with score in group I as 0.65 and in group II was 2.21. The mean CRP (mg/L) levels for both groups were

0.84 and 2.36, respectively. CRP values of the two groups were significantly different from each other, with CRP levels in the group II greater than those in the group I subjects. A study by Kanaparthi A et al, the mean CRP levels were high in subjects with generalized aggressive and chronic periodontitis compared with controls. This was found to be statistically significant. A statistically significant difference ($P = 0.012$) was found in the CRP level between groups I and II and between groups II and III, and between groups I and III. An increase in serum CRP levels in subjects with generalized aggressive periodontitis and chronic periodontitis as compared with the controls.¹⁶

In the present study, the mean plasma Hcy was found to be 23.45 and 11.05 mmol/L, respectively, for cases and controls. The difference was statistically significant ($P = 0.001$). Another study by Penmetsa GS et al, showed that the Hcy was detectable in all the samples. At baseline, the mean levels of plasma Hcy were found to be low in the control group, whereas in the test group, it is found to be higher. These plasma-Hcy levels and all periodontal parameters were reduced significantly after nonsurgical periodontal therapy. Plasma-Hcy levels are reduced after nonsurgical periodontal therapy but not to the levels comparable with those found in healthy individuals. Therefore, nonsurgical periodontal therapy may be used as an adjunctive Hcy-lowering therapy, contributing toward primary prevention against cardiovascular diseases.¹⁷ Joseph R et al, a case-control study involved 85 age- and sex-matched subjects with chronic periodontitis and 91 healthy controls. Patients were grouped into moderate and severe periodontitis. Case and control groups had similar levels of fasting blood sugar, lipid profile, and body mass index. The mean plasma Hcy was found to be 19.22 ± 8.27 and 10.27 ± 2.50 $\mu\text{mol/L}$ for cases and controls, respectively. A significant elevation in plasma Hcy levels was observed in cases ($P < 0.05$). No significant differences were observed in plasma Hcy levels between moderate and severe chronic periodontitis ($P = 0.722$).¹⁸ Serum CRP concentration rises rapidly in the acute-phase response and can exceed 300 mg/l by 48 h after a severe stimulus, such as myocardial infarction, acute systemic bacterial infection, major trauma, or surgery. Until recently, CRP values < 10 mg/L were considered normal, while acute bacterial infections have been reported in 80% to 85% of patients with CRP values > 100 mg/L. However CRP values previously considered as high normal have been reported to be predictive of atherosclerotic complications.¹⁹ A positive association between CRP and destructive periodontal disease was found in an analysis of third National Health and Nutrition Examination survey (NHANES III), providing a potential mechanism to link destructive periodontal disease with an increased risk of atherosclerotic complications.²⁰

Conclusion

Elevated levels of serum homocysteine and serum CRP levels were seen in subjects with chronic periodontitis.

References

1. Newman MG, Takei HH, Klokevold PR, Carranza FA. Clinical Periodontology. 10th ed. Philadelphia: Saunders; 2006. Classification of Diseases and Conditions Affecting the Periodontium; pp. 103–4.
2. Noack B, Genco RJ, Trevisan M, Grossi S, Zambon JJ, Nardin ED. Periodontal infections contribute to elevated systemic C-Reactive protein level. J Periodontol. 2001;72:1221–7.
3. Shapira L, Soskolone WA, Sela MN, Offenbacher S, Barak V. The secretion of PGE₂, IL-1b, IL-6 and TNF- α by adherent mononuclear cells from early onset periodontitis patients. J Periodontol. 1994;65:139–46.
4. Page RC. The role of systemic inflammatory mediators in the pathogenesis of periodontal disease. J Periodontol Res. 1991;26:230–42.
5. Williams RC, Offenbacher S. periodontal Medicine. Periodontol. 2000;2000(23):9–156.

6. Saito T, Murakami M, Shimazaki Y, Oobayashi K, Matsumoto S, Toshihiko K. Association between alveolar bone loss and elevated serum C-reactive protein in Japanese men. *J Periodontol.* 2003;74:1741–6.
7. Salzberg TN, Overstreet BT, Roger JD, Califano JV, Best AM, Schenkein HA. C-reactive protein level in patients with Aggressive periodontitis. *J Periodontol.* 2006;77:933–9.
8. Andersson A, Isaksson A, Hultberg B. Homocysteine export from erythrocytes and its implication for plasma sampling. *Clin Chem.* 1992;38:1311–5.
9. Debreceni B, Debreceni L. The role of homocysteine-lowering B-vitamins in the primary prevention of cardiovascular disease. *Cardiovasc Ther.* 2014;32:130–8.
10. Refsum H, Ueland PM, Nygård O, Vollset SE. Homocysteine and cardiovascular disease. *Annu Rev Med.* 1998;49:31–62.
11. Bautista LE, Arenas IA, Peñuela A, Martínez LX. Total plasma homocysteine level and risk of cardiovascular disease: A meta-analysis of prospective cohort studies. *J Clin Epidemiol.* 2002;55:882–7.
12. Den Heijer M, Lewington S, Clarke R. Homocysteine, MTHFR and risk of venous thrombosis: A meta-analysis of published epidemiological studies. *J Thromb Haemost.* 2005;3:292–9.
13. Roberts FA, Darveau RP. Microbial Protection and Virulence in Periodontal Tissue as a Function of Polymicrobial Communities: Symbiosis and Dysbiosis. *Periodontol 2000* (2015) 69:18–27.
14. Hajishengallis G. Periodontitis: From Microbial Immune Subversion to Systemic Inflammation. *Nat Rev Immunol* (2015) 15:30–44.
15. Paraskevas S, Huizinga JD, Loos BG. A Systematic Review and Meta-Analyses on C-Reactive Protein in Relation to Periodontitis. *J Clin Periodontol* (2008) 35:277–90.
16. Kanaparthi A, Kanaparthi R, Niranjan N. Evaluation of serum C-reactive protein levels in subjects with aggressive and chronic periodontitis and comparison with healthy controls. *Dent Res J (Isfahan).* 2012 May;9(3):261-5.
17. Penmetsa GS, Bhaskar RU, Mopidevi A. Analysis of Plasma Homocysteine Levels in Patients with Chronic Periodontitis Before and After Nonsurgical Periodontal Therapy Using High-Performance Liquid Chromatography. *Contemp Clin Dent.* 2020 Jul-Sep;11(3):266-273.
18. Joseph R, Nath SG, Joseraj MG. Elevated plasma homocysteine levels in chronic periodontitis: a hospital-based case-control study. *J Periodontol.* 2011 Mar;82(3):439-44.
19. Slade GD, Offenbacher S, Beck JD, Heiss G, Pankow JS. Acute phase inflammatory response to periodontal disease in the U.S. population. *J Dent Res.* 2000;79:49–57.
20. Pearson TA, Menash GA, Alexander RW, Anderson JL, Cannon RO, Criqui M, et al. Markers of inflammation and cardiovascular disease. Application to clinical health and public health practice: A statement for health care professionals from the Centers for Disease Control and Prevention and the American Heart Association. *Circulation.* 2003;107:499–511.