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Short Communication

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Association of Periodontal Diseases With C Reactive Protein

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The aim of this study was to evaluate the relationship between periodontal diseases and C reactive protein level. Fifteen patients (7 male, 8 female, mean age 34±11.6) with chronic periodontitis and 15 ages and sex matched (7 male, 8 female and mean age 29±10.4) periodontally healthy subjects recruited from the patients referred to the department of periodontics, Mashhad Faculty of Dentistry. In all the patients and controls Body Mass Index (BMI) was under 30 kg m⁻². Periodontal probing depth of Ramfjord teeth were recorded for both groups. Peripheral blood samples were collected and sent to the laboratory to determine the amount of CRP using a semi-quantitative method. The amount of CRP in the test group was 4.1 mg L⁻¹. In the control group it was 0.18 mg L⁻¹. CRP in the test group was significantly higher than the control group (p = 0.008). There was no significant correlation between the mean pocket depth and the CRP levels. Sex and age did not affect the amount of plasma CRP. Periodontal diseases can increase the amount of plasma CRP. This might be due to the infective nature of periodontal diseases.

Key words: C-reactive protein, periodontitis, acute phase protein, inflammation

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INTRODUCTION

In recent years, the concepts of the pathogenesis of atherosclerosis and cardiovascular events have broadened from a lipid-centric view of etiology to the appreciation of the importance of the inflammatory processes. Although obesity, oxidized lipids, and other factors are known to contribute to cardiovascular inflammation, the role of infection is believed to serve as a critical inflammatory stimulus that contributes to both atherogenesis and acute events via plaque destabilization. This inflammatory process can involve the vasculature directly by interaction of the organisms or bacterial by-products with the vessel wall or indirectly via modulation of hemostasis or hepatic activation of the acute phase response that leads to increased circulating levels of acute-phase reactants such as C-Reactive Protein (CRP), IL-6 and TNF- α (Offenbacher and Beck, 2005; Ide *et al.*, 2004).

C-Reactive Protein (CRP) is an acute-phase reactant produced by the liver in response to diverse inflammatory stimuli, including heat, trauma, infection and hypoxia (Mustapha *et al.*, 2007).

In patients with overwhelming systemic infection, serum levels of CRP can exceed 100 mg L^{-1} , providing a useful marker for tracking the course of the infection (Slade *et al.*, 2000). However, the clinical relevance of much smaller increases in CRP has been highlighted recently in epidemiological studies demonstrating that individuals with high-normal values of CRP have increased risks for chronic diseases that have an inflammatory basis, including cardiovascular disease (Ridker *et al.*, 1997; Loos *et al.*, 2000; Rahmati *et al.*, 2002). Serum C-Reactive Protein (CRP) has been shown to be a risk predictor for cardiovascular disease (Rahman *et al.*, 2005; Persson *et al.*, 2005; Mattila *et al.*, 2002; Noack *et al.*, 2001). Established risk factors for high-normal values of CRP with in the general population include older age, cigarette smoking, chronic bacterial infections and chronic bronchial inflammation (Mendall *et al.*, 1996). Periodontitis is a chronic inflammatory infection of the tissue surrounding and supporting the teeth which is associated with gram-negative bacteria in patients (Beck *et al.*, 1996). Recent epidemiological studies have shown that individuals with periodontitis have a significantly increased risk of developing coronary heart disease (Beck *et al.*, 1999). In addition to conventional risk factors, chronic infection and subsequent production of systemic inflammatory markers may be associated with this increased risk (Yamazaki *et al.*, 2005). Periodontitis induces a peripheral inflammatory and immune response, reflected in elevated

concentrations of C-Reactive Protein (CRP) and IgA-class antibodies to periodontal pathogens. The prevalence of CVD seems to be highest in those individuals in whom periodontitis coexists with elevated CRP levels (Mattila *et al.*, 2005).

Several studies have shown that sera from patients with periodontal infections contain significantly elevated levels of CRP compared to periodontally health individuals (Rahman *et al.*, 2005; Persson *et al.*, 2005; Salzberg *et al.*, 2006; Moutsopoulos and Madianos, 2006; Havemose-Poulsen *et al.*, 2006; Loos, 2005; Buhlin *et al.*, 2003; Loos *et al.*, 2000; Ebersole *et al.*, 1997; Briggs *et al.*, 2006) and periodontal therapy leads to a decrease in serum CRP levels (Yamazaki *et al.*, 2005; Taylor *et al.*, 2006; Elter *et al.*, 2006; D'Aiuto *et al.*, 2004a, b, 2005, 2006). Saito *et al.* (2003) showed that alveolar bone loss around posterior teeth was associated with elevated CRP in Japanese men. Ide *et al.* (2003) could not show the association between periodontal disease and changes in levels of any of the systemic markers. If a relationship exists between periodontal disease and systemic CRP within the population at large, it has the potential for substantial clinical relevance in helping to explain circumstances in which an intra-oral source of infection can create a systemic inflammatory response, therefore placing apparently healthy patients at increased risk of cardiovascular disease (Beck *et al.*, 1996).

The aim of this study was to evaluate the association between plasma level of C reactive protein and periodontal disease in Iranian patients.

MATERIALS AND METHODS

This was a case control study which was performed during the year 2004. Thirty volunteers entered the study (14 male and 16 females mean age 30.9 ± 11.3). Patients in the case group (7 male, 8 female, mean age 34 ± 11.6) were selected among those referred to the department of periodontology, in the Mashhad Faculty of Dentistry, Iran for treatment of periodontitis. All the patients were examined by a periodontist and were selected after having written informed consent. Inclusion criteria were: (1) Having chronic periodontitis, (2) No history of any infections or any infective systemic diseases, (3) Body mass index (BMI) $< 30 \text{ kg m}^{-2}$ and (4) No history of smoking. Age and sex matched controls (7 male, 8 female, and mean age 29 ± 10.4) were selected among healthy persons without periodontitis or any other systemic diseases. Both groups were controlled for confounding factors for periodontitis and CRP concentration such as smoking. A questionnaire was filled for each person in both groups. The first section in the questionnaire was

demographic specifications. In the second part CRP value and probing depth of Ramfjord teeth were recorded. Patients seat on the unit and were examined using Williams periodontal probe (Hufriedy, USA) and Dental mirror. All the persons in case and control groups were referred to a special laboratory in Mashhad University of Medical Sciences. Peripheral blood samples were collected and CRP was measured by a semi-quantitative method (using Edison Kit, N.J). According this kit the normal value for CRP in adults was 0.47 mg L⁻¹.

Statistical analysis: The findings were analyzed with Chi square, Man Whitney and student T tests using SPSS software package ver.11.5.

RESULTS AND DISCUSSION

Findings showed that the mean value for CRP in case group was significantly greater than controls (4.1±6.9 VS. 0.18±0.32, p = 0.008).

With increase in pocket depth the CRP value elevated but there was not significant association between packet depth and CRP value. Sex and age did not have any effect on CRP levels in both groups (Table 1). Patients in the case group had significant greater WBC compared to controls.

Besides classic risk factors such as hyperglycemia, dislipidemia, hyperinsulinemia, hypertension, and cigarette smoking for vascular atherogenic changes, much attention has been paid to chronic subclinical inflammations, which promote thrombosis.

Periodontal diseases are infections characterized by inflammation and destruction of supporting tissues of the affected teeth (Rahman *et al.*, 2005; Briggs *et al.*, 2006). Epidemiological studies from the United states reported that, after adjustment for known cardiovascular risk factors, the risk of Coronary Heart Disease (CHD) was increased between 50 and 70% in men with periodontitis (Briggs *et al.*, 2006; Elter *et al.*, 2006; Franek *et al.*, 2006).

Gram-negative anaerobes are present in large numbers in subgingival dental plaque in periodontal pockets. Endotoxin, derived from gram negative microorganisms, induces high levels of acute-phase proteins after its interaction with receptors expressed on the surface of neutrophils and monocytes (Yamazaki *et al.*, 2005; Briggs *et al.*, 2006), which are present in large numbers in periodontal inflammation. Recent epidemiological studies have shown that levels of acute-phase proteins, including C-Reactive Protein (CRP), are increased in otherwise healthy adults with poor periodontal status (Rahman *et al.*, 2005; Persson *et al.*, 2005; Salzberg *et al.*, 2006; Moutsopoulos and Madianos,

Table 1: CRP (Mean±SD) in males and females and age groups

Characteristics	Case	Control	p-value
Sex			
Male	6.15±9.04	0.11±0.17	0.027
Female	2.30±4.20	0.25±0.41	0.027
Age			
25,<25	0.27±0.31	0.30±0.40	0.880
36-40	6.10±8.30	0.50±0.00	0.010
>40	1.50±2.90	0.50±0.00	0.380

2006; Havemose Poulsen *et al.*, 2006; Loos, 2005; Buhlin *et al.*, 2003; Loos *et al.*, 2000; Ebersole *et al.*, 1997; Slade *et al.*, 2003).

Since C-reactive protein and other systemic markers of inflammation have been identified as risk factors for cardiovascular diseases, this study was done to investigate whether an association could be demonstrated between CRP levels and chronic periodontitis in an Iranian population. Present findings were similar to those reported by other investigators (Slade *et al.*, 2000; Rahman *et al.*, 2005; Persson *et al.*, 2005; Mendall *et al.*, 1996; Salzberg *et al.*, 2006; Moutsopoulos and Madianos 2006; Havemose Poulsen *et al.*, 2006; Loos, 2005; Buhlin *et al.*, 2003; Loos *et al.*, 2000; Ebersole *et al.*, 1997; Slade *et al.*, 2003; Wu *et al.*, 2000) and showed that patients with periodontitis had greater CRP levels. Increased levels of CRP have been postulated as being a strong predictor for the development of cardiovascular disease. One of the typical chronic subclinical conditions which have been postulated to predict the future development of CHD and elevation of CRP is obesity. In fact, obese subjects have been reported to exhibit higher CRP values than lean subjects (Iwamoto *et al.*, 2003). In our study, one of the inclusion criteria was BMI <30 kg m⁻²; thus our samples were not apparently obese.

CRP is a systemic marker of inflammation, and it is possible that the raised CRP level in periodontitis could be relevant to any relationship with CHD. In this study, there was not any association between periodontitis and CRP level related to age and sex. The data relating to CRP should be interpreted with caution because of the limited size of this study. Single measurements may also be misleading because intercurrent infections and other factors can affect the values of this marker.

The periodontal- CRP association observed in this study was not possibly causal but rather that increase in both periodontal disease and CRP were a consequence of the trait. Periodontal disease occurs as a joint response to local pathogens and to an underlying hyper inflammatory trait, which also causes elevation of systemic inflammatory mediators. However, an additional synergistic mechanism is proposed in which local periodontal infection creates an elevated systemic inflammatory response. Large amounts of CRP are

produced by hepatocytes in response to circulating cytokines such as TNF- α and IL1 produced at the site of tissue destruction. This CRP production by hepatocytes occurs at the expense of albumin and other constitutive proteins, a process labeled reprioritization of hepatic protein synthesis. However, competing demands for protein synthesis in cases of acute, overwhelming inflammation can lead to anomalous short term changes in acute-phase reactants (Ebersole *et al.*, 1997).

CONCLUSION

In conclusion, the results of this study showed that patients with periodontitis have elevated levels of CRP and WBC. Periodontal disease needs to be viewed more broadly in terms of systemic inflammation, either as a consequence of an underlying hyperinflammatory trait or as a factor contributing to systemic inflammation.

Inflammatory factors may increase inflammatory activity in atherosclerotic lesions, potentially increasing the risk for cardiac or cerebrovascular events. Further researches with larger samples are recommended.

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