Comparison of C - reactive protein Levels in Chronic Periodontitis Patients with Normal *S*ubjects

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Received 4 September 2017 and Accepted 24 September 2017

Abstract

Background: Chronic periodontitis causes systemic inflammation and increases C-reactive protein (CRP). CRP has been implicated as a possible mediator of associating periodontitis and several systemic diseases. The aim of the present study was to investigate systemic levels of CRP in patients with chronic periodontitis in comparison to periodontally healthy individuals. **Materials and methods:** A total of 80 individuals were included in this study. 40 patients with severe chronic periodontitis aged 40, and 40 sex matched periodontally healthy subjects were recruited from the patients attending Dpartment of Periodontics, Faculty of Dentistry, Zahedan. Body Mass Index (BMI) was under 25 kg/m2 in all the patients and controls. Peripheral blood samples were taken and CRP levels were estimated in serum samples using the C - reactive protein – hs (CRP-hs) LATEX – High sensitivity (Biosystem S.A). **Result:** CRP levels in women in the test group (3.64 +- 2.77 mg/l) was significantly higher than the women in the control group ($p < 0.001$); however, the difference between males in the two study groups was not significant (p=0.13). **Conclusion:** Periodontitis results in higher systemic levels of CRP. Elevated inflammatory factor may increase inflammatory activity in atherosclerotic lesions and potentially increase the risk for cardiovascular events.

Keyword: LATEX – high sensitivity, C – reactive protein, systemic inflammation, chronic periodontitis, healthy subjects.

Ansari Moghadam S, ZadFattah S, Risbaf Fakour S, Ansari Moghaddam A, Naebi M. Comparison of C - reactive protein Levels in Chronic Periodontitis Patients with Normal *S*ubjects. J Dent Mater Tech 2017; 6(4): 181-85.

Introduction

C- reactive protein (CRP) reflects activation of inflammatory system and in combination with other risk factors plays a role in prediction of first coronary events (1).

There is increasing evidence that chronic infections along with inflammatory mechanisms play a major role in thermogenesis and cardiovascular diseases (2). C – Reactive protein production is part of the non-specific acute phase response to most forms of inflammation (3).

Cardiovascular diseases are increasingly recognized as having a major systemic inflammatory component, as such, detection of systemic inflammatory markers, plays an increasingly important role in risk assessment for vascular events such as MI and cerebral infarction.

Elevation of acute phase proteins such as C-reactive protein (CRP) in serum is a well-accepted risk factor for cardiovascular diseases. The question often asked is "what is the source of inflammation that triggers elevated acute-phase protein production when clinically evident infection is absent?" Recent efforts have focused on periodontitis as a potential trigger for systemic inflammation (4).

Periodontal diseases are infections characterized by inflammation and destruction of supporting tissues of affected teeth (5). Although periodontitis is chronic in nature, acute-phase elements are also part of the innate immunity in periodontitis and confirm that in periodontitis, a systemic inflammation is present (1, 6).

Epidemiological studies have shown that levels of acute phase proteins including CRP increase in healthy adults with poor periodontal status (7, 8).

If a relationship exists between periodontal disease and systemic CRP, it has the potential for 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 (9, 10).

Some references have stated that moderately elevated serum CRP (> 2mg/l) concentration is a systemic marker of inflammation and a documental risk factor for CVD in otherwise healthy persons(1, 11) . In another study, it was stated that CRP levels of <1 mg/l, 1-3 mg/l and >3 mg/l were associated with lower, moderate and higher cardiovascular risks, respectively (12).

Recent investigations suggest that even a moderate increase in CRP levels, such as those found in periodontitis patients, may predict a risk for atherosclerosis and CVD (13, 16). CRP may activate the complement system and be involved in foam cell formation in atheroma's (13).

A study performed by Gupta S et al. showed significant association between periodontitis and CRP levels ,however, this association was not found for BMI and smoking with CRP levels (17).

Bolla V et al. compared CRP levels in subjects with chronic and aggressive periodontitis. Results showed that the mean CRP levels were greater in CP compared to GAP subjects, but the difference was not statistically significant (18).

Chandy S et al. showed serum as a diagnostic marker in inflammatory conditions and indicated that levels of CRP and fibrinogen may serve as important biomarkers for evaluating the association between periodontitis and cardiovascular diseases (19).

In most of the previous studies, the effect of severity of periodontal disease (clinical attachment loss) on CRP levels has not been evaluated, however, in this study, CRP levels in periodontitis patients have been compared with CAL≥5 and a CAL of <5.

We hypothesized that periodontitis may result in an enhanced systemic inflammatory response with higher CRP levels. Because of the potential association between periodontitis and CVD, the main purpose of the present study was to evaluate levels of CRP in patients with periodontitis, as well as to examine whether the CRP plasma level is related to the severity of periodontitis.

Materials and Methods

Of 80 people included in this study, 40 suffered from severe chronic periodontitis (20 females and 20 males, mean age 30.35 +- 6.57) and 40 subjects who were age and gender matched were periodontally healthy (20 females and 20 males, mean age 30.32 +- 6.18). All subjects were in normal range of Body Mass Index (BMI) (BMI< 25 kg/m2).

The patients with periodontitis attending Department of Periodontology at the Dental Clinic of Zahedan were selected for this study. Periodontal examination was performed and clinical parameters of periodontal disease including probing depth (PD) and clinical attachment loss (CAL) were evaluated. The patients were examined and grouped according to their periodontal status and those with severe chronic periodontitis were selected for the present study. After the purpose of the study was explained, informed consent was obtained from all subjects.

This study was approved by the Ethics Committee of Zahedan University of Medical Sciences. In addition to observing ethical issues, all subjects underwent periodontal treatment. The diagnostic criteria for severe chronic periodontitis included inflammation, bleeding during probing, deep periodontal pockets and attachment loss ≥5 mm.

Exclusion criteria were: (1) known systemic disease (2) regular use of medications (3) presence of other infections or fever (4) periodontal therapy in the past 6 months (5) use of antibiotics, NSAIDS or mouth rinses in the past 3 months (6) history of trauma or tooth extraction during the past few months (7) pregnancy or lactating females (8) Patients with active oral lesions (active caries), mucomembranous lesions and smokers (7).

Serum was collected from participants by standard procedures at the time of clinical examination and under standard cold chain was sent to Mehran Clinical Laboratory. Serum was analysed with C - reactive protein –hs (CRP – hs) LATEX high sensitivity (Biosystem S.A) with quality system certified according to EN ISO 13485 and ISO 9001 standard.

One technician who was blinded to the periodontal status of participants performed all assays.

After determination of CRP level of all subjects quantitatively, CRP levels were used to divide patients into low CRP concentration (<=5mg/l) and high level categories (CRP concentration > 6 mg/l) according to quality control and detection limit of 0.06 mg/l and interval limit of 0.06 – 15 mg/l and repeatability (with in run) cv 1.5 % as reported by Mehran Laboratory, Zahedan. Data were analysed using appropriate statistical tests including independent t-test, chi –square and correlation coefficient.

Results

In the present study, adjustment was made for factors that are known to be associated with elevated levels of CRP such as age, Body Mass Index (BMI) and smoking. Also all subjects were in normal range of BMI (<25 kg/m2).

Mean values for CRP in subjects with severe chronic periodontitis (3.64 +- 2.66) increased compared to control subjects (1.76 +-0.91) and was statistically significant (p<0.001) (Table .1) Table 1 has been evaluated by the Independent T-test.

The percentage of subjects with elevated CRP levels of more than 5mg/l was higher in periodontitis patients (22.5 %) compared to control subjects (2.5 %) and the difference was statistically significant (p=0.01)(Table .2) Table 2 was evaluated by Chi-square test.

While evaluating the percentage of tooth sites with clinical attachment loss (>= 5 mm), we found that the mean percentage of tooth sites with clinical attachment loss >=5 mm was higher in test group with mean value of CRP levels >6 mg/l (56.35 +- 18.43) than the test group with mean value of CRP levels <5 mg/l (40.39 +- 19.04) (p=0.03). This finding suggests a positive correlation between severity of periodontal disease and CRP levels (Table .3) Table 3 has been evaluated by the Independent T-test.

We also found that the CRP level was higher in women in the test group compared to controls (p<0.001) while the difference between males in the two study groups was not significant (p=0.14) (Table .4). Table 4 has been evaluated by the Independent T-test.

Table1. Comparison of CRP levels between control and test groups (Mean ± SD)

Periodontal status	Serum CRP levels	
Periodontitis patients	3.64±2.66	p<0.001
Healthy subjects	1.76±0.91	

Table 2. Comparison of CRP levels > 6 mg/l between control and test groups

Periodontal status	CRP>6mg/l	CRP<5mg/l	
Periodontitis patients	22.5%	77.5%	p=0.01
Healthy subjects	2.5%	97.5%	

Table 3. Percent of tooth site s with CAL>=5 mm (severity of periodontal disease) in patients with CRP>6mg/l in comparison to patients with CRP levels<5mg/l (Mean±SD)

CRP levels of test groups	Percent of tooth sites with CAL>=5mm	
CRP>6 mg/l	56.35±18.43	p=0.03
CRP<=5mg/l	40.39±19.04	

Table 4. Comparison of CRP levels in test and control groups according to sex (Mean ±SD)

	CRP levels	
Test group males	3.09±2.66	p=0.14
Control group males	2.1±1.06	
Test group females	4.19±2.62	p<0.001
Control group females	1.41±0.57	

Discussion

Epidemiological studies have implicated periodontitis as a risk factor for development of cardiovascular diseases (CVD). Persistent infections such as periodontitis induce inflammatory and immune response which may contribute to coronary atherogenesis and may lead to coronary heart disease (CHD) in conjunction with other risk factors (2).

CRP, as a systemic marker of inflammation, is also a predictive marker in periodontitis and may be part of the explanation for why periodontitis is associated with CVDs.

It is hypothesized that daily episodes of bacteremia originating from periodontal lesions are possible causes for changes in systemic markers in periodontitis (1).

The analyses of data from a sample in the present study support the existence of a significant relationship between periodontal health status and CRP. The result of this study is in accordance with the findings of previous studies (1, 2, 5, 10, 13, and 20). Also, in the present study, it was observed that the extent of CRP levels increase in periodontitis patients and relates to the severity of the disease after adjusting for age, smoking and Body Mass Index; these results confirmed the findings of the previous studies (13, 20).

Serum CRPzconcentration is reported to be positively correlated with age, smoking and BMI (13, 15). Thus, we adjusted these potential counfounding parameters between the two groups. Also, increase in CRP levels is non-specific; CRP is an indicator of a wide range of disease processes including trauma, infection and inflammation (20).

To minimize these variations, only apparently healthy individuals were included in this study and the participants with a history of infection, fever, trauma or recent consumption of medication were excluded.

Our study faced certain limitations: Firstly, the study design was cross-sectional so it was impossible to determine the causality of the association; also we do not know whether the positive association between CRP and periodontitis is going to be consistent over time in this population. Another limitation of our study was the limited size of our study population so the data relating to CRP should be interpreted with caution.

Thirdly, single measurement of CRP may also be misleading because intercurrent infections can affect the values of this marker. It is also mentioned that age, gender, use of tobacco and high blood pressure are the classical risk factors associated with atherosclerotic cardiovascular disease (22, 23).

We observed gender differences in the present study that showed women had higher CRP values than men, which is in accordance with findings of Mccawly (23) and Sander (24), but is in contrast to Yakob' findings (22) that showed women had lower CRP values. This controversy may be the result of different sample sizes, different CRP Kite analyses and also the different types of studies, cross-sectional or other. However, even in yakob's study irrespective of a low CRP level, it was shown that periodontitis might be a notable risk marker for future cardiovascular diseases particularly in women; in other words, periodontitis might still present a risk for atherosclerotic disease in women that is not dependent on CRP.

Obviously, further researches focusing on larger sample sizes are needed to establish these findings.

Conclusion

The ability to predict cardiovascular risk in periodontally diseased individuals would be of value in prevention and treatment of such diseases.

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