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ORIGINAL RESEARCH

Effect of Periodontal Therapy on Serum C-Reactive Protein Levels in Patients with Gingivitis and Chronic Periodontitis: A Clinicobiochemical Study

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ABSTRACT

Aim: The aim of the present study was to evaluate the effect of periodontal therapy on serum C-reactive protein (CRP) levels in patients with gingivitis and chronic periodontitis.

Materials and methods: A total of 60 subjects (30 males and 30 females) were included in the study with 20 subjects in each of the groups classified based on community periodontal index (CPI) scores: I: Healthy, II: Gingivitis, III: Mild periodontitis. Periodontal therapy was performed on groups II and III patients. Venous blood was collected from each subject at baseline and 3 months after periodontal therapy. The collected sample was subjected to biochemical analysis to detect CRP levels by using immunoturbidimetric method.

Results: The present study demonstrated that the periodontitis group had a higher mean CRP levels (2.49 ± 0.47 ng/ml) as compared to the gingivitis group (1.40 ± 0.32 ng/ml) and healthy group (0.56 ± 0.20 ng/ml). The mean CRP values after periodontal therapy were found to be reduced to 0.44 ± 0.23 ng/ml in group II and 1.30 ± 0.36 ng/ml in group III patients.

Conclusion: Within the limitations of this study, it can be concluded that CRP level progressively increases from periodontal health to disease. A decrease in CRP levels with periodontal treatment was also observed.

Clinical significance: Due to its opsonizing abilities CRP plays an important role in the innate host defence. It can be hypothesized that CRP is a potential biomarker of periodontal disease. A number of studies have reported elevated serum CRP levels in periodontitis subjects. Long standing periodontal disease and raised CRP levels enhance the risk of cardiovascular disease, cerebrovascular accidents and preterm low birth weight infants. There is also evidence that effective periodontal therapy can lower serum CRP levels. However, the data of interventional studies on CRP in gingivitis and periodontitis is scarce.

Keywords: C-reactive protein, Gingivitis, Chronic periodontitis, Periodontal therapy.

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INTRODUCTION

C-reactive protein (CRP) is an acute-phase reactant plasma protein produced in response to diverse inflammatory stimuli.[1] Due to its opsonizing abilities and its capability to activate human complement; CRP plays an important role in the innate host defence against different microorganisms, such as bacteria and fungi. The same opsonophagocytosing properties can lead to clearance of host cell material, including nuclear constituents.[2] Among all the acute-phase reactants, CRP in particular has been the focus of attention as a key marker of atherosclerosis.[3] Since, the levels of CRP rise earlier than those of other reactants, CRP has been used as an early marker of tissue damage.[4,5] CRP is predominantly synthesized by liver hepatocytes and was recognized because of its ability to precipitate with the C-polysaccharide extract of *Streptococcus pneumoniae*. CRP is normally present in milligram per liter quantities but may increase dramatically to hundreds of grams per milliliter within 72 hours following tissue injury. The amount decreases with the subsidence of the disease process and the recovery of the patient.[6] Several reports have implicated, long standing periodontal disease and raised CRP levels enhance the risk of cardiovascular disease, cerebrovascular accidents and preterm low birth weight infants. Studies have also documented the correlation of CRP levels and periodontitis but there is modest evidence on the effect of periodontal therapy in lowering the levels of CRP.[7] However, the data of interventional studies on CRP in gingivitis and periodontitis is scarce. Hence, the aim of this study was to evaluate the effect of periodontal treatment on serum CRP levels in patients with gingivitis and chronic periodontitis.

MATERIALS AND METHODS

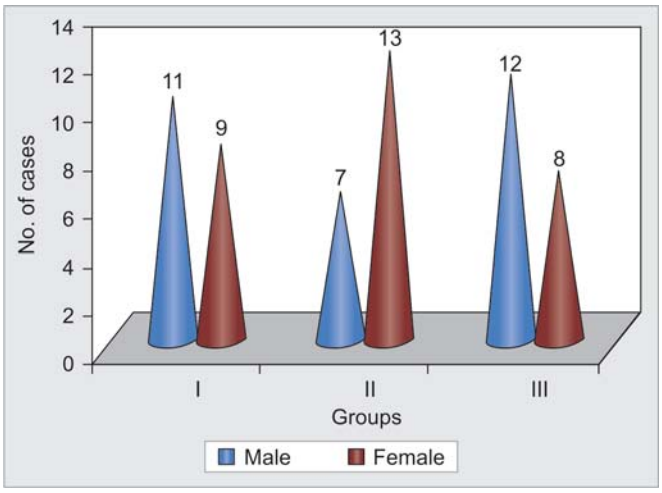
The study was designed as a single-center, longitudinal and interventional study. The study duration was 3 months, in which venous blood was collected at baseline and 3 months after periodontal therapy. Subjects were selected from Dr Patil's Clinic, Gulbarga, Karnataka, India. Study was approved by the local ethical committee. All the selected subjects were informed about the nature of the study and signed an informed consent was obtained.

Group sample sizes were decided by power analysis with 85% power. A total of 60 dentate and systemically healthy subjects (30 males and 30 females) were recruited for the study (Graph 1).

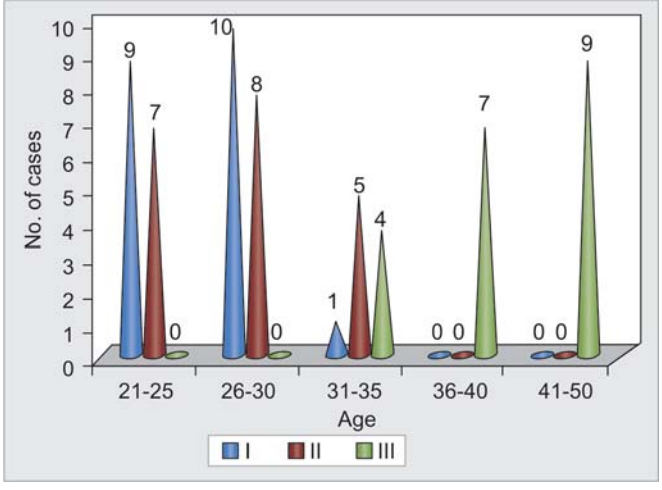
Subjects participating in the study were 21 to 45 years of age (Graph 2).

INCLUSION-EXCLUSION CRITERIA

Age- and gender-matched subjects without a history of periodontal therapy or previous use of antibiotics or anti-inflammatory medication within the preceding 6 months were included in the study. For group II, subjects diagnosed with gingivitis, showing clinical signs of inflammation without loss of attachment and with bleeding on probing were selected. For group III, subjects diagnosed with mild chronic periodontitis, with periodontal pocket of 4 to 5 mm and clinical attachment losses of 1 to 3 mm were selected. Periodontitis was not graded based on severity. Subjects with smoking habit, coronary artery disease, hypertension, metabolic disorders like diabetes mellitus and with severe infections and other inflammatory conditions like rheumatoid arthritis were excluded.



Graph 1: Sex distribution



Graph 2: Age distribution

Due to the epidemiological and interventional nature of the study community periodontal index (CPI) index was used. The subjects were assigned to one of the three groups (20 subjects in each group) based on CPI scores: Group-I (control): Subjects with clinically healthy periodontium (CPI score of 0), group-II (gingivitis group): Subjects with gingivitis (CPI score of 1 or 2) and group-III (periodontitis group): Subjects with periodontitis (CPI score of 3). Venous blood was collected from all the selected subjects at baseline. Group-II subjects underwent periodontal therapy in the form of scaling and group-III subjects underwent periodontal therapy in the form of scaling and root planing. Oral hygiene instructions were given for home care. Three months after periodontal therapy, venous blood samples were collected from all the subjects. Patients were then called for regular supportive periodontal therapy without any surgical intervention for treatment.

COLLECTION OF BLOOD AND CRP ESTIMATION

Venous blood was collected by venepuncture from the antecubital vein of the left forearm under aseptic precautions. Blood samples were sent for biochemical analysis. CRP examination was done manually by immunoturbidimetric method using Agappe kit (Agappe Diagnostics Ltd, Kerala, India) in ERBA Chem 7 semiautoanalyzer (ERBA Diagnostics Mannheim GmbH, Mannheim, Germany). The absorbance of the antigen-antibody complex was measured at 340 nm.

RESULTS

The study was carried out on a total of 60 systemically healthy subjects with normal gingiva (group-I), gingivitis (group-II) and periodontitis (group-III). All the subjects finished the study; there were no dropouts. CRP was assessed in all the subjects before and after periodontal therapy. The subjects included in the study had a mean age of 38.05 ± 10.65 years. The selected subjects were divided into above-mentioned three groups based on the CPI score. The mean CPI score was found to be 0 in group-I, 1.45 ±

Table 1: CPI score before periodontal therapy

CRP	Group I		Group II		Group III	
	No.	%	No.	%	No.	%
0	0	0	0	0	0	0
1	0	0	11	55.0	0	0.0
2	0	0	9	45.0	0	0.0
3	0	0	0	0.0	20	100.0
Total	0	0	20	100.0	20	100.0
Mean ± SD	0		1.45 ± 0.51		3.00 ± 0.00	

Table 2: Mean serum CRP values before therapy

CRP	Group I		Group II		Group III	
	No.	%	No.	%	No.	%
<1.0	20	100.0	0	0.0	0	0.0
1.0-2.0	0	0.0	20	100.0	5	25.0
2.0-3.0	0	0.0	0	0.0	15	75.0
Total	20	100.0	20	100.0	20	100.0
Mean ± SD	0.56 ± 0.20		1.40 ± 0.32		2.49 ± 0.47	

0.51 in group II and 3.00 ± 0.00 in group III before periodontal therapy (Table 1).

The mean CRP values at baseline were found to be 0.56 ± 0.20 ng/ml in group I; 1.40 ± 0.32 ng/ml in group II and 2.49 ± 0.47 ng/ml in group III patients (Table 2).

Intergroup comparison of baseline CRP values among the three groups using ANOVA test revealed a statistical significant difference ($p < 0.001$). CRP levels were significantly increased in groups II and III as compared to control group (Table 2).

Fisher exact test revealed a significant difference ($p < 0.001$) in CRP values among the three groups: 0.84 between groups I and II; 1.93 between groups I and III and 1.09 between groups II and III (Table 3).

Comparison of pretreatment and post-treatment CRP levels was carried out using a Student's t-test. It was observed that there was a significant decrease ($p < 0.001$) in CRP values post-therapy in both groups II (1.40 ± 0.32 to 0.44 ± 0.23) and III (2.49 ± 0.47 to 1.30 ± 0.36). An additional observation made was that the post-therapy values reached normal levels in group II, but remained marginally higher than group II in group III (Table 4).

Table 3: Fisher exact test for comparison of serum CRP values before treatment

	CRP	
	Min-max	Mean ± SD
Group I	0.06-0.78	0.56 ± 0.20
Group II	1.02-1.98	1.40 ± 0.32
Group III	1.98-3.50	2.49 ± 0.47
Significance	F = 153.437; p < 0.001*	
Difference		
Groups I *vs* II	0.84	
Groups I *vs* III	1.93	
Groups II *vs* III	1.09	
p-value		
Groups I *vs* II	<0.001*	
Groups I *vs* III	<0.001*	
Groups II *vs* III	<0.001*	

*Significant ($p < 0.005$)

DISCUSSION

While most studies of periodontitis have emphasized the local nature of periodontitis, it appears that systemic manifestations of this disease are also detected through the production of CRP and other acute-phase proteins and procoagulant mediators.[8,9] The reason for the interest in plasma/serum levels of CRP in periodontitis is due to the epidemiological research indicating association of periodontitis with CVD and that it is an exceptionally stable analyte in plasma and immunoassays for it are robust, well standardized, reproducible and readily available.[10]

The periodontal literature has documented different time intervals for revaluation after periodontal therapy. These time intervals range from 2 weeks to 6 months.[11] Based on the rate of healing, Badersten[12] has cited that 3 months post-treatment is a suitable interval for the primary evaluation of initial nonsurgical therapy, even in areas with preliminary deep lesions. Beyond this time interval, the subgingival microbial repopulation occurs in the absence of improved plaque control.

The elevated CRP levels in periodontitis group is well documented in numerous large scale cross-sectional studies which have shown a positive association between chronic periodontal infections and elevated CRP levels.[13-15]

Table 4: Evaluation of serum CRP values pre- and post-therapy

CRP	*Before treatment*	*After treatment*	*Delta*	*p-value*
Group II	1.40 ± 0.32	0.44 ± 0.23	0.965 ± 0.12	<0.001**
Group III	2.49 ± 0.47	1.30 ± 0.36	1.205 ± 0.32	<0.001**
p-value	<0.001**	<0.001**	0.004**	-

**Significant (p < 0.005)

Recent studies have investigated the potential role of periodontal therapy on systemic inflammation, but the results are somewhat conflicting.[16] Patients treated by nonsurgical mechanical periodontal therapy showed a significant increase in plasma CRP, tumor necrosis factor (TNF)-α, and interleukin (IL)-6 levels immediately after the intervention, indicating a systemic acute-phase response, apparently due to a massive bacterial inoculation in conjunction with instrumentation.[17] Our study reported lowered CRP levels after periodontal therapy, which are not consistent with a meta-analysis of three randomized controlled studies and seven single cohorts.[18] Small tendency for a reduction in CRP levels with treatment was observed which was not statistically significant. These results were attributed to less number of powered RCTs included in the analysis and also to the incomplete resolution of oral infection following periodontal therapy reported in many studies.

Since, CRP is a nonspecific protein and its level increases in response to any trauma or infection, the interventional nature of our study gives a better understanding of its role in periodontitis since its values have been shown to reduce after periodontal therapy. Gingival crevicular fluid (GCF) also has been used for CRP estimation. Studies have concluded that serum CRP levels have been more accurate than GCF.[19] Hence, further long-term longitudinal studies are needed so that the correlation between CRP and periodontitis can be fully understood.

CONCLUSION

Collectively, these data suggest that serum in the active phase of periodontal disease possesses a greater amount of CRP when compared to periodontally healthy and gingivitis sites. As the severity of inflammation increases, there is a significant increase in the CRP levels as indicated by higher CRP levels in periodontitis compared to gingivitis suggesting that there is a direct relationship between CRP levels and periodontal destruction. With the subsidence of disease process after periodontal therapy, the levels of CRP are reduced. The values almost reach the normal levels in gingivitis cases suggesting that CRP might play a role in the inflammatory process. Since, the levels of CRP have been shown to reduce after periodontal therapy, it may be used as a potential biochemical marker for assessment of periodontal disease activity in gingivitis and periodontitis.

CLINICAL SIGNIFICANCE

CRP is a type I acute-phase protein. Due to its opsonizing abilities and its capability to activate human complement, CRP plays an important role in the innate host defence against different microorganisms, such as bacteria and fungi. It can be hypothesized that CRP is a potential biomarker of periodontal disease. A number of studies have reported elevated serum CRP levels in periodontitis subjects. Long standing periodontal disease and raised CRP levels enhance the risk of cardiovascular disease, cerebrovascular accidents and preterm low birth weight infants. There is also evidence that effective periodontal therapy can lower serum CRP levels. However, the data of interventional studies on CRP in gingivitis and periodontitis is scarce.

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