THE EFFECT OF PERIODONTAL THERAPY ON SERUM C-REACTIVE PROTEIN & HBA1C LEVELS IN CHRONIC PERIODONTITIS PATIENTS WITH OR WITHOUT TYPE 2 DIABETES MELLITUS : A CLINICO BIOCHEMICAL STUDY

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Abstract

Objectives: The purpose of this study was to analyze The Effect of Periodontal Therapy on Serum C-Reactive Protein & HbA1c Levels in Chronic Periodontitis Patients with or without type 2 diabetes mellitus : A Clinico Biochemical Study

Study Design: A cohort of thirty subjects, 15 with diabetes and moderate to severe periodontitis & 15 without diabetes and moderate to severe periodontitis were recruited. Periodontal parameters were measured, and blood samples were obtained to evaluate C-reactive protein . Group 1 & 2 were treated with periodontal therapy.

Results: Levels of Serum C-Reactive Protein were highest in chronic Periodontitis and T2DM group. Periodontal clinical parameters PI, GI, PPD, CAL were recorded higher in chronic periodontitis and T2DM group when compared to when healthy participants who have chronic periodontitis. A statistically significant correlation between parameters such as HbA1c, PI, GI, PPD, CAL and CRP was seen.

Conclusions: The results showed an decrease in the levels of C-Reactive & HbA1c after periodontal therapy

Key words: Periodontitis, CRP, Diabetes Mellitus

Introduction

Periodontitis is a term used to describe an inflammatory process, initiated by the plaque biofilm, that lead to loss of periodontal attachment to the root surface and adjacent alveolar bone, and which ultimately results in tooth loss.1

Periodontitis has been referred to as the sixth complication of diabetes.2Epidemiological data confirm that diabetes is a major risk factor for periodontitis; susceptibility to periodontitis is increased by approximately threefold in people with diabetes.3 There has, recently, been much emphasis on the 'two-way' relationship between diabetes and periodontitis. That is, not only is diabetes a risk factor for periodontitis, but periodontitis could also have a negative effect on glycaemic control.4

Patients suffering from severe periodontitis have increased local production of inflammatory cytokines (IL-7, TNF and IL-6) and moderate systemic inflammatory response (defined by raised concentration of CRP, fibrinogen and moderate leucocytosis).5 Infection or inflammation activates leukocytes, which further induce the synthesis and secretion of C-reactive protein (CRP). CRP is an acute-phase reactant protein which is synthesized by the liver in response to the inflammatory cytokines interleukin-6 (IL-6), IL-1, and tumor necrosis factor-alpha. An elevated serum concentration of CRP is an evidence of active tissue–damaging process and CRP is an indicator of current disease activity.6

Thus, persistent inflammation in the body and at their acute stage induces the elevation of CRP level in blood serum and saliva.7,8

 It has also been reported that serum CRP levels are elevated in patients with impaired glucose tolerance (IGT)9or diabetes.10 A few prospective studies have shown that increased CRP levels are an independent risk factor for future diabetes.11,12

Numerous studies have been conducted comparing the CRP levels in assessing the disease activity of various systemic inflammatory disorders and in diagnosing and

management of systemic infections.13,14,15 Therefore CRP is useful as a proinflammatory marker in patients of chronic periodontitis with or without diabetes mellitus.

Material and Methods
Study Design
This randomized controlled clinical study was conducted at Desh Bhagat Dental College & Hospital, Mandi Gobindgarh. Study protocol was approved by Desh Bhagat Dental College & Hospital Research Committee, and participants signed an approved consent form to participate in the study. Thirty subjects with moderate to severe periodontitis with or without diabetes ranging in age from 20 to 50 were recruited from the periodontology department for this study and divided into two groups:

Group 1: Chronic Periodontitis with Type 2 Diabetes Mellitus

Group 2: Chronic Periodontitis without Type 2 Diabetes Mellitus

Inclusion & Exclusion Criteria
Patients with diabetes were diagnosed according to the criteria published by the American Diabetes Association in 1997, Participants had diabetes for more than 1 year, and none of them had other major illnesses or severe diabetic complications. Patients had not taken antibiotics for at least 3 months prior to baseline and did not have any active infection. Eligible subjects had 14 or more natural teeth, of which at least five had a site with probing pocket depth (PPD) $\geq$ 5 mm and clinical attachment level (CAL) $\geq$ 3 mm. From this point, subjects with moderate to severe periodontal disease were included. They had not had periodontal treatment or professional cleaning of the teeth for at least 1 year prior to the study. Pregnant and breastfeeding women were excluded.

Procedure
Fasting venous blood was collected in vacuum tubes early in the morning, and C-reactive protein (hs-CRP) was measured. CRP levels were assessed using aErba Mannheim Diagnostic kit with specific methodology in a spectrophotometer according to the manufacturer's instructions. The test samples were treated with a specific antibody to human CRP in a suitable buffer. The turbidity induced by the formation of immune complexes was measured at 546 nm, and the values were automatically calculated from a known standard. The lower detection limit for the assay was 0.1 mg/l. A commercial control serum was used to verify the assay performance. Patients also received an oral soft tissue examination including periodontal measurements of plaque index (PI), bleeding on probing (BOP), PPD, and CAL for all teeth present. O'Leary PI was measured in four areas per tooth (mesiobuccal, midbuccal, distobuccal, and midlingual) (20), and the other periodontal parameters were registered on six sites by tooth (mesiobuccal, midbuccal, distobuccal, mesiolingual, midlingual, and distolingual).

All patients with or without diabetes from Desh Bhagat Dental College & Hospital were screened (One hundred thirty-six), and 30 were found to match the selection criteria for study. They were told not to change their diet, exercise, or medication dose unless absolutely necessary and to inform investigators if any change occurred. Baseline examination was performed prior to the beginning of the periodontal treatment. Intra-examiner reproducibility was calculated and showed that periodontal clinical attachment measurements were in agreement within 2 mm more than 9 0% of the time. Group 1 had baseline Hs-CRP measured just before the beginning of the periodontal treatment. Subjects were instructed on the modified Bass brushing technique and interproximal cleaning. After that, scaling and root planning (SRP) under local anesthesia was performed using ultrasonic devices and manual Gracey curets (Hu-Friedy®, Chicago USA).

Periodontal Therapy was scheduled in one or two sessions 1 week apart according to the periodontal disease severity and the number of teeth present. No less than 30 min were assigned to each quadrant. Chlorhexidine rinses 0,2% were prescribed after SRP (20 ml during 30 s, twice daily) and maintained for 12 weeks to the end of the clinical protocol. No other rinses or toothpaste was used during the study. Twelve weeks after treatment, blood samples were taken again, and CRP levels were analyzed. At the same time, periodontal parameters were measured again. Periodontal surgical treatment was recommended to patients with probing pocket depths $\geq$6mm.

Results

Among 30 subjects (Males18, Females-12) included in the study . CRP & HbA1c levels were detected in all the samples. The mean and standard deviation of Plaque Index (PI) in Group 1, Group 2 was $2.65 + 0.51$ and $2.15 + 0.59$ at baseline and $2.10 + 0.51$ and $1.80 + 0.49$ after three months of periodontal therapy respectively. The mean and standard deviation of Gingival Index (GI) in Group 1, Group 2 was $2.10 + 0.52$, 1.90 ± 0.52 at baseline and $1.90 + 0.53$, 1.50 ± 0.51 after three months of periodontal therapy respectively. The mean and standard deviation for Probing pocket depth (PPD) in Group 1, Group 2 was $5.55 + 0.71$, $3.32 + 0.69$ at baseline and $5.15 + 079$, $3.10 + 0.61$ respectively. The mean and standard deviation for Clinical attachment level (CAL) in Group 1, Group 2was $5.20 + 0.49$, $4.50 + 0.65$ at baseline and , $4.80 + 0.48$, 4.20 ± 0.53 after three months of periodontal therapy respectively.

This infers that the clinical parameters which included PI, GI, PPD and CAL were highest in group 1 . The group 1 & 2 showed considerably reduced scores of clinical parameters after periodontal therapy. This shows that diabetes along with chronic periodontitis has a higher destructive effect on the periodontal health.

The mean and standard deviation of HbA1c levels in Group 1, Group 2 was $6.80 + 0.25$, $4.90 + 0.23$ at baseline and $6.70 + 0.21$, $4.80 + 0.23$ after three months of periodontal therapy respectively.

Hence, it can be inferred that the levels of HbA1c in chronic periodontitis and T2DM groups is significantly reduced after periofontal therapy because chronic periodontitis can interfere with the glycemic control in T2DM patients.

The mean and standard deviation for Clinical CRP in Group 1, Group 2 was $12.5 + 1.10$, $9.0 + 0.95$ at baseline and $11.3 + 1.10$, 8.9 ± 0.89 after three months of periodontal therapy respectively.

Hence, it can be inferred that the levels of CRP in chronic periodontitis and T2DM groups is significantly reduced after periofontaltherapy .

The mean and standard deviation for PI, GI, PPD, CAL HbA1c, CRP , IL-17 Group 1, Group 2 at baseline

Parameter	Group	N	MEAN	SD	P VALUE
PI	Group 1 Group 2	15 15	2.65 2.15	0.51 0.59	<0.001
GI	Group 1 Group 2	15 15	2.10 1.90	0.52 0.52	<0.001
PPD	Group 1 Group 2	15 15	5.55 3.32	0.71 0.69	<0.001
CAL	Group 1 Group 2	15 15	5.20 4.50	0.49 0.65	<0.001
HbA1c	Group 1 Group 2	15 15	6.80 4.90	0.25 0.23	<0.001
CRP	Group 1 Group 2	15 15	12.5 9.0	1.10 0.95	<0.001

* - Statistically Significant; SD – Standard deviation; N – Group sample size; GI – Gingival Index; PI – Plaque Index; PPD – Probing Pocket Depth; CAL- Clinical attachment loss; HbA1c – glycated haemoglobin; CRP – C Reactive Protein

The mean and standard deviation for PI, GI, PPD, CAL HbA1c, CRP , IL-17 Group 1, Group 2 after 3 months of periodontal therapy

Parameter	Group	N	MEAN	SD	P VALUE
PI	Group 1 Group 2	15 15	2.10 1.80	0.51 0.49	<0.001
GI	Group 1 Group 2	15 15	1.90 1.50	0.53 0.51	<0.001
PPD	Group 1 Group 2	15 15	5.15 3.10	0.79 0.61	<0.001
CAL	Group 1 Group 2	15 15	4.80 4.20	0.48 0.53	<0.001
HbA1c	Group 1 Group 2	15 15	6.7 4.8	0.21 0.23	<0.001
CRP	Group 1 Group 2	15 15	11.3 8.9	1.10 0.89	<0.001

* - Statistically Significant; SD – Standard deviation; N – Group sample size; GI – Gingival Index; PI – Plaque Index; PPD – Probing Pocket Depth; CAL- Clinical attachment loss; HbA1c – glycated haemoglobin; CRP – C Reactive Protein .

Discussion

The present study was conducted to evaluate the effect of Periodontal Therapy on Serum C-Reactive Protein & HbA1c levels in Chronic Periodontitis Patients with or without type 2 diabetes mellitusThe present study was conducted in the Department of Periodontics and Implantology at Desh Bhagat Dental College & Hospital, Mandi Gobindgarh

C-reactive protein (CRP) is a very strong acute phase protein. In healthy, young subjects and resting situations the serum concentration is < 1.5 mg/l. In acute phase situations, however, the concentration can increase up to a thousand-fold.7 CRP is synthesized mainly in hepatocytes, but mRNA and CRP have been shown to be present in monocyte-derived macrophages in atherosclerotic plaques, lymphocytes and alveolar macrophages. 8 Its synthesis is regulated mainly by inteleukin (IL)-6, IL-1 and tumor necrosis factor. Peak values of CRP usually disappear within a few days of the inflammatory stimulus. The CRP concentration is associated with cardiovascular disease and with other inflammatory diseases, such as rheumatoid arthritis. Also, several components of the insulin-resistance syndrome, such as obesity and increased blood pressure, are associated with altered CRP values and which has been confirmed by several other groups.9 Also, patients with insulin-dependent diabetes mellitus have increased CRP levels.

The present study determines whether the presence of periodontitis and periodontal treatment could influence the serum levels of C-reactive protein, HbA1c levels. The results of the present study highlight 3 points. Firstly, an increase in serum CRP, & HbA1c levels concomitantly with the severity of the disease. Secondly, a properly performed periodontal therapy results in the improvement of the periodontal parameters irrespective of the state of the disease. Thirdly, a reduction in systemic inflammation as evidenced by the reduction in CRP, HbA1c levels with periodontal therapy. Fredriksson et al. in a study, estimated a median

CRP of 2 mg/l for periodontitis patients, 0 mg/l among controls. In another study, Loos et al.11 observed the highest CRP values in patients with a generalized form of periodontitis (median 1.45 mg/l); for patients with a more localized form of periodontal disease, the median CRP value was 1.30 mg/l, while healthy controls presented with a median of 0.90 mg/l.

In the present study, the CRP, HbA1c levels in periodontitis patients reduced significantly after periodontal therapy. This is in agreement with other studies that reported a significant reduction in CRP, HbA1c level after treatment.

Another aspect of the present study was the correlation between individual parameters and CRP, HbA1c level. Parameters such as plaque index, gingival index, probing pocket depth and clinical attachment level gain showed a positive correlation with changes in CRP, HbA1c after three month following treatment. Since these parameters showed a positive correlation, they can be used as predictors for changes in CRP, HbA1c level.

Conclusion

As the number of patients in this study was relatively small, these results have to be interpreted with caution. The present study envisaged to determine the relationship between periodontitis and periodontal treatment upon the serum levels of C-reactive protein HbA1c. In the present study, the patients without DM lower mean CRP levels as compared to the patients with chronic periodontitis with DM . In periodontitis patients, mean levels of CRP & HbA1c decreased after the periodontal therapy. It is concluded that periodontal therapy could be one of the important aspects in the prevention of adverse cardiovascular events and glycemic control.

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