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Evaluation Of Salivary PGE2 In Chronic Periodontitis Before And After Phase I Therapy A Clinical-Biochemical Study

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Abstract:
To evaluate the levels of prostaglandin E2 (PGE2) in chronic periodontitis and assess the relationship between the PGE2 and chronic periodontitis before and after phase I therapy.
The study consisted of 15 patients with generalized chronic periodontitis. They were assessed based on the clinical parameters; Gingival index (GI), Plaque index (PI), Bleeding on probing (BOP), pocket depth (PD), Clinical attachment level (CAL) along with the evaluation of salivary PGE2 levels at baseline and completion of Phase I therapy. They were further assessed after 6 weeks for the clinical parameters and PGE2 levels were determined by enzyme-linked immunosorbent assay (ELISA). The clinical parameters (GI,PI,BOP,PD,CAL) showed a significant ($p<0.0001$) decrease after phase I therapy assessed after 6 weeks. PGE2 levels were also decreased significantly with a greater mean difference (207.1) after phase I therapy. There was also a positive correlation between the changes in the PGE_2 levels after Phase I therapy and the clinical parameters recorded. The study suggests that PGE2 can be used as a diagnostic biomarker and a potential chair-side diagnostic kit along with the use of saliva for sample collection as a reliable and non-invasive approach for the detection of biomarkers.

Keywords: periodontitis , prostaglandin, saliva

INTRODUCTION

Periodontal disease is an inflammatory process involving innate and adaptive immune responses characterized by the irreversible loss of connective tissue attachment and supporting alveolar bone. These changes often lead to an aesthetically and functionally

compromised dentition.[1]Today, it is well known that the synthesis of high levels of pro-inflammatory mediators from gingival tissues in response to period on top athogens results in the destruction of soft and hard periodontal tissues and clinical expression of periodontal disease.[2]

Prostaglandin E_2 (PGE_2) is one of the key mediators in periodontal inflammation by stimulating the suppression of lymphocyte production, decreasing the collagen synthesis by fibroblasts and influencing osteoclastic bone resorption.[6] Theoretically, most of the inflammation and periodontal destructive changes that occur in periodontal disease such as gingival redness, edema, collagen degradation and bone loss, could be caused solely by the presence and direct actions of PGE_2.[7] PGE_2 not only mediates inflammatory responses, such as increase in vascular permeability and dilatation, but also can act as a potent stimulator of bone resorption and formation. This dynamic mechanism can be affected according to the concentration of PGE_2.[8]

There is great number of evidence that PGE_2assist regulation of IL-1β production and is involved in the inflammatory reaction and tissue destruction. It is accepted that $PGE_2$is a key cytokine of inflammation and clinical attachment loss and bone loss. The rates of proinflammatory cytokine PGE_2in crevicular fluid, saliva and gingival tissue, in patients with chronic periodontitis are increasing proportionally to the severity of periodontal disease.[9]The examination of these cytokines may enhance the understanding of pathogenesis of periodontitis and their assessment in the treatment process may result in better control of the patient's disease.

In the light of the above facts, PGE_2 has the potential to elicit or serve as an indicator of periodontal inflammation or destruction. To evaluate this potential, an attempt has been made in this study to evaluate the salivary PGE_2 levels in chronic periodontitis patients before & after Phase I therapy.

MATERIAL AND METHODS

A total number of 75 patients were selected for this study. The patients included were having Generalised Chronic Periodontitis exhibiting clinical attachment loss ≥ 4mm and probing depth ≥ 5mm in atleast 6 sites. The patients for this study were selected from the Out-Patient Department of Periodontics. The study protocol was approved by the Ethical Committee of the institution. The patients had signed a consent form to participate prior to the commencement of the study. The patients were evaluated at baseline for the levels of PGE_2 and the clinical parameters. This was followed by Phase I therapy, which included scaling and root planning performed in two appointments within a week's duration. The patients were kept on plaque control regimen involving oral hygiene instructions along with the interdental aids. The patients were then evaluated again after a period of 6 weeks for the PGE_2 levels and clinical parameters, whereby no treatment was provided.

Saliva sample collection:
Two ml of unstimulated whole saliva was collected from all patients by expectorations into a sterile container. Collected samples were placed immediately in ice storage and transported to the laboratory. The samples were then analysed using ELISA assay based on the competitive binding technique.

Statistical analysis
The data was analysed using statistical software SPSS 20 (Statistical package for social sciences, version 20). The Paired t test was used to test the difference of mean between paired observations (PI, GI, CAL, PD, PGE_2), whereas the Pearson's Chi Square test was used to test the difference of the BOP scores. Correlation of PGE_2 level with PI, GI, CAL, PD, BOP before and after Phase 1 therapy along with the effective change due to therapy was done using Correlation coefficient (Pearson). Significance value of 0.05 level was considered to decide the relationship.

RESULTS
The results were analyzed based on the findings before and after phase I therapy (6 weeks). The parameters assessed were the salivary PGE_2 levels and the clinical parameters (PI, GI,BOP,PD,CAL) at baseline and 6weeks after Phase I therapy. The correlation of PGE_2level with PI,GI,CAL,PD and BOP before and after Phase I therapy along with the effective change due to therapy was carried out to determine the association between them.

The mean PI score before Phase I therapy was 2.3$\pm$0.3 and after Phase I therapy was 1.1$\pm$0.1. After Phase I therapy, the mean reduction in the PI score was 1.2, which was statistically significant (<0.001). (Table 1)The mean GI score before Phase I therapy was 2.2$\pm$0.3 and after Phase I therapy was 1.1$\pm$0.1. After Phase I therapy, the mean reduction in the GI score was 1.09, which was statistically significant (<0.001).(Table 2)The mean PD score before Phase I therapy was 4.5$\pm$1.05 and after Phase I therapy was 2.8$\pm$0.8.After Phase I therapy, the mean reduction in the PD score was 1.7, which was statistically significant (<0.001). (Table 3)The mean CAL score before Phase I therapy was 5.1$\pm$1 and after Phase I therapy was 3.3$\pm$0.8. After Phase I therapy, the mean reduction in the CAL score was 1.8, which was statistically significant (<0.001). (Table 4)

The mean reduction in BOP score was 89.2%, wherein after phase I therapy, the treatment had caused no or just 1 surface bleeding in 95.9%,while 3.6% and 0.5% were with 2 and 3 bleeding surfaces respectively. This difference of reduction in the percentage of BOP scores was statistically significant($p<0.05$).(Table 5).The mean PGE_2 score before Phase I therapy was 329.1 $\pm$12.5 pg/ml and after Phase I therapy was 121.9 $\pm$12.7 pg/ml. After Phase I therapy, the mean reduction in the PGE_2 score was 207.1 $\pm$ 9 pg/ml, which was statistically significant (<0.001). (Table 6)

There was a statistically very highly significant ($p<0.001$) positive correlation of CAL, GI, PD, PI, BOP and PGE_2 levels in chronic periodontitis patients.PGE_2 had statistically very highly significant ($p<0.001$) positive correlation with CAL ($r=0.727$), GI ($r=0.91$), PD ($r=0.69$), PI ($r=0.94$) and BOP ($r=0.98$). Thereby, suggesting the changes in the PGE_2 levels after Phase I therapy correlated with the clinical parameters (PI, GI, PD, CAL, BOP) recorded. These parameters showed a significant reduction, compared before and after Phase I therapy. (Table 7)

DISCUSSION

Periodontal disease is a chronic microbial and inflammatory process characterized by the presence of sulcular pathogenic bacteria, impaired host immune response, destruction of the connective tissue involved in tooth attachment, and resorption of alveolar bone. Bacterial pathogens are required to initiate the disease process. The inflammatory mediators have been detected at elevated levels in gingival crevicular fluid and whole saliva of patients who have periodontal disease, making them putative biomarkers of the disease.

Today it is well known that the synthesis of high levels of pro-inflammatory mediators from gingival tissues in response to periodontopathogens results in destruction of soft and hard periodontal tissues and clinical expression of periodontal disease. There is enough evidence that PGE_2 is an important mediator in the initiation and progression of periodontal disease. Detection of numerous cytokines in high levels in gingival tissues and crevicular fluid may be an indicator ofthe activity of periodontitis.

The reduction of PGE_2 levels after periodontal therapy may be a potential criterion for successful periodontal therapy. The occurrence of increased PGE_2 levels in GCF or gingival tissue is able to indicate risk from the progression of destruction in a specific periodontal site. The current conception of the pathogenesis of periodontitis suggests that an additional host modulation approach may inhibit the production of pro-inflammatory mediators in periodontal tissues and may enhance the treatment result.[2]

Based on this consensus, various studies have been carried out to indicate the presence of PGE_2 to be an inflammatory biomarker suggesting the progression and severity of chronic periodontitis. Offenbacher et al 1993[12] supported the concept that host-produced PGE_2 mediates much of the tissue destruction that occurs in periodontal disease and thereby, considers it as the principal determinant of disease expression. Nakashima K et al 1994[62] found significantly higher concentrations of GCF PGE_2 in chronic periodontitis subjects suggesting, the use of PGE_2 as a marker for periodontal inflammation. Preshaw PM et a 2002[66] found a gradual and significant increase in the GCF PGE_2 concentrations along with the progression of chronic periodontitis. Similarly, Chu-Hang Liao et al 2014[70] found increased release and expression of PGE_2 in chronic periodontitis with the progress of periodontal tissue damage.

In view of current knowledge, the present study was aimed to evaluate the association of PGE_2 and generalized chronic periodontitis. In the present study, a total number of 15 patients, fulfilling the inclusion and exclusion criteria were selected.

In this study, the improvement in the clinical parameters along with a reduction in PGE_2 levels after Phase 1 therapy has been in accordance with previous studies, where Alexander DC et al[71] found significant improvements in all the clinical variables (PI,GI,PD,BOP) along with significant reductions in the concentrations of PGE_2. Also, Tsai CC et al[72] showed a positive correlation between the marked reduction in the PGE_2 levels and the clinical parameters after Phase I therapy of the periodontal treatment.

The mean PGE_2 levels before and after Phase I therapy were 329.1 and 121.9 pg/ml respectively with a mean reduction of 207.1pg/ml, which was statistically significant. This study showed a significant reduction in PGE_2 levels after Phase I therapy, correlating with the improvement in the clinical parameters in the chronic periodontitis subjects examined in the study.

Recent studies were done on the association of PGE_2 concentrations with chronic periodontitis after periodontal therapy is in accordance with the results of this study. Sanchez et al 2013[73] found increased salivary PGE_2 concentrations in the periodontitis patients, which significantly decreased after periodontal treatment thereby suggesting, the use of PGE_2 as biomarkers for assessing the progression and severity of chronic periodontitis. Kumar AK et al 2013[39] showed a statistically significant difference in the PGE_2 concentrations before and after periodontal therapy in the chronic periodontitis patients with significant improvement in all the clinical parameters and thereby considering the use of PGE_2 as a biomarker in the progression of periodontal disease. Reina S et al 2013[49] found elevated levels of PGE_2 in the saliva of untreated severe chronic periodontitis patients, with a significant reduction in the inflammatory biomarker (PGE_2) after periodontal Phase I therapy.

As seen in the study, the clinical parameters differed significantly at baseline and 6 weeks, due to the improvement in them, which was contributed by the Phase I therapy. This non-surgical therapy resulted in the elimination of the etiological factors associated with chronic periodontitis. Therefore, there was the resolution of inflammation along with reduced severity and progression of periodontitis. This was also evident by the reduced levels of the inflammatory mediator PGE_2 seen after 6weeks, indicating the improvement to periodontal health.

CONCLUSION

Though this study has given significant results with respect to the parameters, it very much requires a broader perspective with respect to the number of subjects considered. Therefore, further research on a wider basis would help quantify the role of PGE_2 in day-to-day practice. Also, it is required to examine the behavior of PGE_2 along with the other associated inflammatory biomarkers together, which will help to provide a more accurate assessment of the association between the pathogenesis and the progression

of chronic periodontitis. Based on this, there would be a better evaluation of the diagnostic and prognostic aspects of periodontal disease.

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TABLES:

Table No 1: Comparison of Plaque Index (PI) before and after Phase I therapy in chronic periodontitis.

	PI Before	PI After
Minimum	1.8	0.9
Maximum	2.8	1.3
Mean	2.355	1.122
Std. Deviation	0.333	0.109
Mean difference (S.D)	1.2(0.3)	
t	18.01	
P value	<0.001	

Table No 2: Comparison of Gingival Index (GI) before and after Phase I therapy in chronic periodontitis.

	GI Before	GI After
Minimum	1.4	0.9
Maximum	2.7	1.2
Mean	2.178	1.092
Std. Deviation	0.364	0.106
Mean difference (S.D)	1.09(0.28)	
t	14.94	
P value	<0.001	

Table No 3: Comparison of Pocket Depth (PD) before and after Phase I therapy in chronic periodontitis.

	PD Before	PD After
Minimum	3.4	2.1
Maximum	7.1	5.1
Mean	4.5	2.8
Std. Deviation	1.056	0.822
Mean difference (S.D)	1.7(0.3)	
t	20.86	
P value	<0.001	

Table No 4: Comparison of Clinical Attachment Level (CAL) before and after Phase I therapy in chronic periodontitis.

	CAL Before	CAL After
Minimum	4.0	2.4
Maximum	7.4	5.4
Mean	5.098	3.300
Std. Deviation	1.000	0.830

Mean difference (S.D)	1.8(0.21)
t	33.7
P value	<0.001

Table No 5: Comparison of change of Bleeding on Probing (BOP) surfaces before and after Phase I therapy in chronic periodontitis.

BOP Surface		After			Total
		0 to1	2	3	
Before	less 4	83(89.2%)	10(10.8%)		93(100%)
	4	350(95.9%)	13 (3.6%)	2 (0.5%)	365 (100%)
Total		433(94.5%)	23(5.1%)	2(0.4%)	458(100%)

Pearson Chi-Square Test	Value	df	P value
	8.487	2	0.0143