Original Article

Effect of Periodontal Therapy on Serum Lipid Levels

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Abstract

Background & objectives: Periodontitis is a destructive inflammatory disease of the supporting tissues of the teeth that occurs in response to a predominantly Gram-negative bacterial infection originating from dental plaque. Periodontitis presents with increased systemic inflammation and is known to contribute to rise in serum lipid levels. The aim of present study was to determine influence of periodontal therapy on serum lipid levels.

Methods: A total of 105 consecutive subjects were studied. Group I (n=35) included subjects with chronic generalised periodontitis who were not given periodontal therapy during study period and served as control group. Group II (n=70) comprised of subjects with chronic generalized periodontitis who were rendered needful periodontal therapy. Serum levels of triglycerides, total cholesterol, HDL & LDL cholesterol were measured at day 0 (baseline) and reassessed on day 60.

Results: In the treatment group, serum triglycerides (Pre=127.81±59.32 & Post = 121.20 ± 58.94 mg/dL, p < 0.001)), total cholesterol (Pre=176.33±38.31 & Post=171.39±31.19 mg/dL, p=0.045) and mean LDL-cholesterol levels (Pre=91.91±28.54 & Post=83.94±26.00 mg/dL, p < 0.001) showed a significant decline from the pre-treatment values. HDL-cholesterol levels did not change significantly in both groups. Other lipid levels were not significantly altered in the control group.

Conclusions: Patients of chronic generalised periodontitis who were offered periodontal therapy showed improvement in the various lipid parameters except HDL-cholesterol, which was not significantly altered. Chronic periodontitis in otherwise healthy individuals may therefore, be contributing to the systemic inflammatory burden in these patients and adversely altering the lipid profile.

Key words: Cardiovascular disease, Inflammation, Periodontitis, Risk factor

Introduction

Periodontitis represents a chronic oral infection that leads to gingival inflammation, destruction of tooth-supporting tissues, namely periodontal ligament and alveolar bone and eventual exfoliation of teeth. The etiological agents for periodontitis are the Gram-negative, anaerobic micro-organisms present within the dental plaque. These micro-organisms produce endotoxins in the form of lipopolysaccharides (LPS) that are instrumental in generating a host-mediated immune response. LPS gain access to the gingival tissue and stimulate an inflammatory response characterised by infiltration of neutrophils, lymphocytes, macrophages and mast cells [1]. The net effect of this stimulation is the production of Interleukin-I α and β (IL-I α and β), Tumour Necrosis Factor α (TNF- α), IL-6 (all of which can stimulate bone resorption) and matrix metalloproteinases (a group of calcium & zinc dependent enzymes) which digest collagen. Therefore it is this host-mediated immune response that eventually leads to periodontal tissue destruction.

Recently there has been great interest in the systemic effects of pro-inflammatory cytokine levels in serum, potentially elevated by periodontitis. Evidence suggests that low level, chronic exposure to gram negative microorganisms and/or their LPS can manifest a state of altered lipid metabolism; the main features of which are hypertriglyceridemia and lipid oxidation. The

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underlying mechanism for these alterations is the release of TNF-α and Il-1 ß in response to Gram-negative LPS exposure. These two cytokines exert effects on lipid metabolism by influencing the production of other cytokines [2,3], altering hemodynamics/ amino acid utilization of various tissues involved in lipid metabolism [4,5] or modifying the hypothalamic–pituitary–adrenal axis, increasing plasma concentrations of adrenocorticotropic hormone (ACTH), cortisol, adrenaline, nor-adrenaline and glucagon [6,7]. The above modifications in turn, lead to enhanced hepatic lipogenesis [8], increased synthesis or reduced clearance of triglycerides [9,10] and reduced clearance of LDL due to reduced lipoprotein lipase activity [11,12].

Studies have suggested that in advanced periodontitis, levels of IL- 1ß and TNF-α are sufficiently elevated in gingival crevicular fluid (GCF) to be "dumped" systemically, falling within the detectable range of biological serum assays [13-15]. This increase in plasma concentrations of cytokines leads to a state of altered lipid metabolism. This observation in the plasma levels of IL- 1ß and TNF-α has the potential to trigger the mechanisms that lead to hyperlipidemia. Consequently, resolution of inflammation caused by periodontitis by imparting therapy; is expected to reduce the serum lipid levels. The present study was carried out in the above background, with the aim of evaluating the effect of periodontal therapy on serum lipid levels.

Materials and Methods

Patient selection & study design: Consecutive 105 subjects in the age range of 35-55 years (mean age 42.89±5.66 yrs), sufferring from periodontitis were selected from outdoor patient department of Periodontics at Maulana Azad Institute of Dental Sciences, New Delhi, irrespective of sex, religion and socioeconomic status. The other inclusion criteria was the presence of a minimum of 24 teeth and a probing depth of 5 mm or more with a clinical attachment loss (CAL) of $\geq$3mm in at least 30% sites. There were 67 (63.8%) males and 38 (36.2%) females in study. Subjects with known systemic ailments, or having any other oral lesion, or with a positive history of any periodontal therapy within past 6 months or history of antibiotic use within past three months were excluded from the study. Pregnant women or those planning pregnancy and smokers too were excluded from the study. The design, duration and purpose of the study was discussed with the subjects and written informed consent was obtained from them. The smaller sample size in the control group is because fewer patients consented to be off-therapy as compared to a larger number who consented to have therapy. Ethical approval was obtained from the institutional review board.

At baseline, for each subject, the periodontal disease status was evaluated at 4 sites per tooth (mesiobuccal, buccal, distobuccal and lingual) by a single trained periodontist using UNC-15 probe (Hu-Friedy's, USA). The Gingival Index - GI (Loe and Silness, 1963), Probing Pocket Depth (PD) and Clinical Attachment Level (CAL) was recorded. Thereafter, for the baseline assessment of serum lipids, blood samples were taken.

All subjects were called early morning after 12 hours of fasting. 4 ml of blood was drawn by venous puncture from each of the subjects following the standard protocol for the same. All the samples were collected in the serum separation vacutainers. Samples were centrifuged in the centrifuge machine at 2500-3000 rpm for 8- 10 minutes to separate the serum from the blood. Separated serum was collected in appendox and stored in deep freeze at -50 degree centigrade. These specimens were stored so that the evaluation of samples which would be taken on the completion of the study could be done simultaneously to minimize inter-kit error. The subjects were divided in to two groups-

Group I: Subjects in this group (n=35) did not receive any treatment during the study period and served as control population. Their blood samples were taken and periodontal status was recorded at baseline. They were not given any kind of medication; neither were they taught about the brushing method nor about other oral hygiene measures. These subjects were recalled 2 months after their initial blood samples were taken, for obtaining second blood sample in accordance with protocol followed at the baseline.

Group II: The patients in this group (n=70) were imparted therapy for periodontal disease. The periodontal therapy rendered comprised of full mouth disinfection that included mechanical plaque control, together with full mouth scaling and root planning under local anaesthesia. The patients were placed on strict oral hygiene maintenance

programme. The effect of phase I therapy was evaluated after 1 month and in case the residual periodontal pockets were present, surgical procedure was performed in the required sites. The number of sites receiving surgical procedures varied from patient to patient. Regular recall was made after 2-3 weeks to check oral hygiene maintenance. Their second blood sample was collected after two months of initiating active periodontal therapy.

Statistical analysis: The data collected was subjected to statistical analysis to evaluate the effect of periodontal intervention on the lipid profiles of the subjects in the two groups. Data obtained was analysed by SPSS version 13.0 statistical software and p-value less than 5% was taken as significant. Association between gender and study groups was tested by Chi-square test.

Unpaired Student's t-test was used to compare all the baseline parameters (age, sex, triglycerides, total, HDL & LDL-cholesterol) between the two groups i.e. control and treatment group. The change in the values of lipid profile parameters (pre-post) were also compared by the unpaired Student's t-test. Paired students t-test was performed to compare the pre and post values of triglycerides, total, HDL & LDL-cholesterol separately for each group.

Results

Table 1 outlines the summary of baseline parameters in the two groups, which were similar.
Table 2 details the comparison between pre and post treatment measurements of serum lipid parameters in the two groups. In the treatment group, average serum triglycerides, total cholesterol and LDL-cholesterol values showed significant reduction from the pre-treatment levels. Mean HDL was increased by 1.86 mg/dL from pre-treatment value but this increase was not significant at 0.05 level of significance (p=0.070). However in the control group average values of various lipid parameters did not show any significant change.

Table 3 shows the mean and standard deviation (SD) of change (pre - post) of values in triglycerides, total cholesterol, HDL and LDL-cholesterol values. A statistically significant decrease in the mean triglycerides and LDL-cholesterol values was observed in the treatment group vis-à-vis the control group. The change in total cholesterol did not reach statistical significance between the two groups. Although the HDL values increased in both the groups, but there was no statistically significant difference between the changes in the two groups.

Discussion

Over the last 50 years, the prevailing view among dentists and physicians was that periodontal infections were localized only to the marginal periodontium and rarely had systemic implications in healthy individuals. More recent evidence, however, has shown that patients with periodontitis present with increased systemic inflammation, as indicated by raised serum levels of various inflammatory markers when compared with those in unaffected control populations [16-19]. It is also well known that there is a causal relationship between serum lipid levels and systemic health, particularly cardiovascular disease, diabetes, tissue repair capacity, immune cell function, and serum levels of proinflammatory cytokines. A significant association between periodontitis and cholesterol has been reported [20].

The present study evaluated the effect of periodontal disease on the serum lipid levels and found that periodontal therapy resulted in significant decrease in the levels of serum total cholesterol, trigycerides and LDL-cholesterol. The subjects included in this study had no major differences in possible confounders when the two groups were compared.

Periodontal disease is now recognised to produce numerous changes in systemic health, changing the blood chemistry with a rise in inflammatory mediators, proteins and lipids in the serum. These factors explain, at least in part, the probable association between periodontitis and the susceptibility for certain systemic diseases, such as the increased risk of cardiovascular disease that is highly prevalent in the world.

Acute systemic or local chronic infections seem to induce changes in the plasma concentration of cytokines and hormones, which determine changes in the lipid metabolism. The study by Feingold et al [8] showed that the administration of low doses of endotoxins in rats resulted in hypertriglyceridemia, suggesting the presence of a similar response in local infections such as periodontal disease, in which there is a chronic systemic exposure to

Table 1- Baseline characteristics of the two groups

Characteristics	Group I (Untreated, n=35)	Group II (Treatment, n=70)	P value (Unpaired t-test)
Age (years)	43.31±6.67	42.37±5.66	0.45
Sex-male	23 (65.71%)	43 (61.42%)	0.668
Triglycerides (mg/dL)	120.97±60.61	127.81±81	0.581
Cholesterol (mg/dL)	172.03±35.17	176.33±38.31	0.579
HDL-cholesterol (mg/dL)	60.17±10.72	61.14±11.83	0.683
LDL-cholesterol (mg/dL)	87.13±28.28	91.91± 28.54	0.419

Table 2- Lipid parameters at baseline and at 60 days in the two groups

Lipid parameters	Group I (Untreated, n=35)			Group II (Treatment, n=70)		
parameters	Baseline Mean ± SD	At 60 days Mean ± SD	P value (Paired t-test)	Baseline Mean ± SD	At 60 days Mean ± SD	P value (Paired t-test)
Triglycerides	120.97±60.61	121.71±60.07	0.335	127.81±59.32	121.20±58.94	0.00
Cholesterol	172.03±35.17	173.57±36.65	0.615	176.33±38.31	171.39±31.19	0.045
HDL-cholesterol	60.17±10.72	60.97±11.45	0.315	61.14±11.83	63.00±11.94	0.07
LDL-cholesterol	87.13±28.38	87.56±27.10	0.814	91.91±28.54	83.94±26.00	0.00 (p<0.001)

Table 3- The mean and SD of change (pre - post) in serum lipid values

Lipid parameters	Group I (Untreated, n=35)	Group II (Treatment, n=70)	P value (Unpaired t-test)
Triglycerides (mg/dL)	-0.74±4.49	6.61±8.34	0.000
Cholesterol (mg/dL)	-1.54±17.96	4.94±20.27	0.111
HDL-cholesterol (mg/dL)	-0.80±5.23	- 1.86±6.74	0.418
LDL-cholesterol (mg/dL)	-0.43±12.73	7.97±17.68	0.014

microorganisms and lipopolysaccharides. The study of Memon et al [21] proved that the induction of periodontitis by *Porphyromonas gingivalis* in rats resulted in an increased level of triglycerides. And more recently, using similar methodology, the same result was observed in another work [22].

The results of the present study are in concurrence with the study by Katz et al [20] on the association between hypercholesterolemia, cardiovascular disease and severe periodontal disease and Moeintaghavi et al [23] on hyperlipidemia in patients with periodontitis. According to the results of these studies, patients with periodontitis had significantly higher levels of triglycerides and cholesterol.

The studies which evaluated the effect of periodontal therapy on serum lipids and lipoprotein associated inflammatory mediators also suggested that the treatment of periodontal disease has beneficial effects on lipid metabolism. In one study conducted in systemically healthy subjects with periodontitis, Pussinen et al [24] stated that periodontitis is associated with macrophage activation via increased serum LPS concentration. Additionally, there was a significant increase in the ratio of HDL/LDL after periodontal treatment in this study. In another study, Pussinen et al [25] reported that there were statistically significant decreases in CRP and serum amyloid A levels after periodontal treatment in systemically healthy subjects with periodontitis. That study also suggested that periodontitis diminishes the anti-atherogenic potency of HDL and increases the risk for coronary heart disease.

Lösche et al [26] and Cutler et al [27] analysed the total and LDL-cholesterol levels and triglycerides of individuals with periodontal disease and reported that their plasma levels were significantly higher than healthy individuals.

Lösche et al [26] evaluated 32 patients with moderate to severe periodontitis before and 3 months after local periodontal treatment and reported significant reduction in the serum activity of lipoprotein-associated phospholipase A_2 (an independent cardiovascular risk factor) with treatment. In a similar study [28], 65 subjects presenting with severe generalized periodontitis were assessed. Subjects were divided into 3 groups, consisting of untreated control; standard periodontal therapy; and an intensive periodontal treatment including standard periodontal treatment with adjunctive local delivery of minocycline. In that study both standard periodontal therapy and intensive periodontal therapy resulted in significant reductions in serum C-Reactive Protein (CRP) compared with the untreated contro;l and the intensive periodontal therapy group also showed a decrease in total and LDL cholesterol after 2 months following the periodontal treatment.

Higher serum levels of total cholesterol, LDL and triglycerides have been found in subjects with periodontal disease, and hyperlipidemic patients have a significantly higher percentage of sites with probing depth greater than 3.5 mm than subjects with normal metabolic status [29]. The interrelationship between periodontitis and hyperlipidemia provides an example for systemic disease predisposing to oral infection, and once the oral infection is established, it exacerbates systemic disease.

The underlying mechanism may be the inflammatory local production of cytokines (IL-1, TNF-α) and its effect on other systemic mediators (IL-6) might induce alterations of lipid metabolism, such as increased LDL and triglycerides, due to increased hepatic lipogenesis, lipolysis from adipose tissue, or reduced blood clearance [30]. Bacterial toxins (LPS) can also induce changes in cholesterol concentrations [31]; leading to reduction in HDL and increase in LDL-cholesterol [32].

The finding that periodontal therapy brought about significant changes in the lipid profiles of study subjects reinforces the hypothesis that there exists a relationship between periodontitis and cardiovascular disease. This indicates that severe, generalized periodontitis in the otherwise healthy individuals contributes to the systemic inflammatory burden predisposing them to cardiovascular disease. Proposed mechanistic explanations include: (i) the local, infection-driven production of inflammatory mediators (IL-1, IL-6) 'dumped' into the systemic circulation [32] (ii) the ability of periodontal pathogens and/or their toxins to disseminate and thus induce a distant inflammatory response and (iii) a combination of the above.

Limitations have been the undesired companion of

every study and by that very virtue they open the gateways for further research. The present study inevitably had a great number of subject variables involved such as physical activity, food habits, socio-economic conditions, obesity, age, stress and lifestyle which differ in accordance with the environment in which the individual lives. These variables are difficult to control and may have influenced the results.

The present study reveals that subjects suffering from periodontitis, who were rendered periodontal therapy showed improvement in their serum lipid parameters; which in effect goes one step ahead of the proven correlation that exists between periodontitis and serum lipid levels.

Key Points

1. A relationship exists between periodontal disease and serum lipid levels within the population at large.
2. Subjects with chronic generalised periodontitis who were rendered periodontal therapy showed significant decrease in mean cholesterol, triglycerides and LDL values.
3. This has a 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.

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