

Full Length Research Paper

Assessment of periodontal treatment on lipid control in patients with cardiovascular disease

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Several studies have sought to explain the possible causal relationship between periodontal disease and cardiovascular disease. The aim of this study was to find evidence that periodontal treatment is associated with changes in lipid levels in patients with cardiovascular disease after a 12-month follow-up period. Eighty patients were selected and divided into 4 groups of 20 patients each, as follows: 2 groups of patients with cardiovascular disease and conventional periodontal treatment or full-mouth scaling and root planing; and 2 groups of patients without systemic involvement and conventional periodontal treatment or full-mouth scaling and root planing. The patients were evaluated by laboratory examinations and clinically evaluated for 12 months. Improvement in the clinical and lipid parameters in patients with cardiovascular disease was observed. The best results were obtained by mechanical control and full-mouth scaling and root planing. It may be concluded that periodontal treatment contributes to control the lipid levels, particularly in patients with cardiovascular disease.

Key words: Periodontal disease, cardiovascular disease, total cholesterol, triglycerides.

INTRODUCTION

There is emerging evidence that inflammation plays a key role in the development of cardiovascular disease from atheroma formation to its rupture and development of clinical events. Several epidemiological studies have investigated and support an association between high levels of inflammatory markers and increased risk and progression of Doença cardiovascular (Packard and Libby 2008; D'Aiuto et al., 2013). Some studies have shown direct evidence for the common relationship between systemic health and oral health, that is, the potential effects of periodontal disease in the much broader range of organic systems (Oz et al., 2007; Moura Foz et al., 2010). The field of periodontal medicine emphasizes important issues between the association of periodontal disease and cardiovascular diseases (D'Aiuto

et al., 2013). These authors in systematic search found 31 clinical trials investigating the impact of periodontal therapy on serum lipid levels of which 11 randomized controlled trials included seven trials of individuals with periodontitis alone and four trials involving individuals with periodontitis and other co-morbidities (that is, diabetes, metabolic syndrome, and hypercholesterolemia). Arterial hypertension, dyslipidemia, genetic predisposition, smoking, obesity, sedentary lifestyle, and diabetes mellitus are well-known classic risk factors for atherosclerosis and they can cause acute myocardial infarction or ischemic cerebral vascular accident (Suzuki et al., 2010). However, these risk factors do not justify the variation in the incidence of cardio-vascular diseases and cerebrovascular diseases. Within this context, periodontal

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disease has been studied as a risk factor for cardiovascular alterations (Bharti and Khurana, 2009).

The biological plausibility of the association between periodontal diseases and cardiovascular diseases is well studied and it includes some of the following possible mechanisms: high concentrations of cholesterol and the action of oral bacteria in the process of atherosclerosis or the participation of acute-phase proteins that may increase in chronic periodontitis (Izumi et al., 2009).

Recent studies showed that patients diagnosed with hyperlipidemia have significantly higher values of periodontal parameters than the control subjects with normal metabolic status (Fentoglu et al., 2009, 2010). The inter-relationship between periodontitis and hyperlipidemia provides an example of a systemic disease predisposing to oral infection, and once the oral infection establishes, it exacerbates the systemic disease (Fentoglu et al., 2010).

Possible mechanisms for the relationship among local infections, inflammation and systemic alterations, which might be related to chronic inflammation such as periodontitis, are capable of starting and maintaining the high systemic levels of several cytokines in the acute-phase response associated with inflammation (D'Aiuto et al., 2013). Periodontitis is associated with the increase in the level of C-reactive protein and fibrinogen, irrespective of coronary diseases (Balan, 2010). Furthermore, there is evidence that suggests that the increase in the levels of systemic markers of inflammation, such as the C-reactive protein and interleukin-6 (IL-6), is associated with cardiovascular diseases (Balan, 2010).

Conventional periodontal treatment (scaling and root planing procedures) can lead to a known clinical success and this is usually an effective therapeutic approach for the treatment of chronic periodontitis due to the reduction of periodontal pathogens followed by an increase in beneficial bacteria (Kalsi et al., 2011). With the purpose of preventing the transmission of pathogens from non-treated periodontal pockets to the recently debrided ones, the one-stage full-mouth disinfection protocol was proposed by a group of researchers coordinated by MQuirynen et al. (1995), which was later modified without the use of an antiseptic by Lang et al. (2008).

In view of this possible causal relationship between periodontal diseases and cardiovascular diseases, confirming the hypothesis that the periodontal diseases would be a risk factor for cardiovascular diseases, the aim of this study was to find evidence that periodontal treatment is associated with changes in lipid levels in patients with cardiovascular disease after a 12-month follow-up period through clinical parameters of periodontal disease and laboratory parameters.

MATERIALS AND METHODS

One hundred and twenty-four patients attended the Dental Clinic of Unioeste (Cascavel, Parana, Brazil), Department of Periodontics, of which forty patients (ages between 30 and 54 years) who had cardiovascular diseases or did not show any type of systemic

compromise were selected. The other 40 patients selected could not present any type of systemic compromise. The inclusion criteria for all the groups were as follows: patients with chronic periodontitis with at least four sites with probing depth above 5 mm, clinical attachment level greater or equal to 4 mm, bleeding on probing, and clinical evaluation of gingival inflammation. The teeth had to be in normal position, with a minimum number of 20 teeth in dental arches and the clinical examination was performed on the buccal, lingual, palatal, mesial and distal tooth surfaces.

For the exclusion criteria, the non-cardiopathic patients could present any other systemic compromise. However, all patients must present a negative history of antibiotic therapy within the last six months; must not have used steroidal or non-steroidal anti-inflammatory drugs within three months prior to the study; must present a negative history of pregnancy, negative history of contraceptive use or any other type of hormone therapy; negative history of smoking or definite cessation at least five years prior to the study; negative history of periodontal treatment within the last 12 months. This study was approved by the Human Research Ethics Committee of Unioeste, report No 203/2010 – CEP, and all the patients signed and received a copy of the free and informed consent. With regard to the diet and medication of these patients, no observations were made because all the criteria and guidance of the doctor responsible for monitoring the cardiovascular disease had to be strictly followed. As for the groups of patients without any cardiovascular compromise, no changes were made in the diet or food habits.

Clinical examination

Clinical examinations were performed using a Williams-type periodontal probe No. 23 by a single, previously calibrated examiner to determine: (1) Silness and Løe plaque index (Silness and Loe, 1964); (2) LÖE and SILNESS gingival index (Loe and Silness, 1963); (3) Probing depth: distance from the bottom of the sulcus up to gingival margin at six points: mesio-buccal, buccal, disto-buccal, disto-lingual/palatal, lingual/palatal and mesio-lingual/palatal of each tooth assessed; (4) Clinical attachment level: also determined at the same points of probing depth.

Laboratory examination

Each patient participating in the study was required to take a blood test, at any time determined by the patient, but always at the same laboratory, following these parameters: (1) total cholesterol, (2) cholesterol fraction, and (3) triglycerides.

After the initial clinical and initial laboratory examinations, the patients were randomly divided into 4 groups of 20 patients each as shown in Table 1. All patients received periodontal therapy (conventional periodontal therapy or full-mouth scaling and root planing), oral hygiene instructions, and supra- and subgingival scaling, which were performed using Gracey curettes (Hu-Friedy, Chicago, IL, USA). Conventional periodontal therapy is to provide education/information, to motivate oral hygiene, and to perform scaling and root planing. Traditional scaling and root planing procedures were performed in quadrants or sextants at regular intervals of one or two weeks. All groups received instruction on how to perform correct control of dental plaque through mechanical removal and supportive periodontal therapy. The patients were assessed for 12 months and clinical examinations were performed throughout the months of the study. At all time intervals, the patients were instructed again in the study. With regard to the laboratory examinations, all patients were required to perform examinations (0 to 12 months) at the same time intervals.

After the data had been rigorously analyzed and was within the normality curve, the data of the groups were assessed

Table 1. Distribution of 80 patients according to the treatments proposed.

Group	Group 1: Patient with cardiovascular disease	Group 2: Patient with cardiovascular disease	Group 3: Patients with no systemic compromise	Group 4: Patients with no systemic compromise
Initial	-Clinical and laboratory exams. -Mechanical control (modified Bass technique + dental floss) -Conventional periodontal therapy	-Clinical and laboratory exams. -Mechanical control (modified Bass technique + dental floss) -Full-mouth scaling and root planning therapy	-Clinical and laboratory exams. -Mechanical control (modified Bass technique + dental floss) -Conventional periodontal therapy	- Clinical and laboratory exams. - Mechanical control (modified Bass technique + dental floss) - Full-mouth scaling and root planning therapy
12 months	-Clinical and laboratory exams. -Mechanical control (modified Bass technique + dental floss) -Supporting Periodontal Therapy	-Clinical and laboratory exams. -Mechanical control (modified Bass technique + dental floss) -Supporting Periodontal Therapy	-Clinical and laboratory exams. -Mechanical control (modified Bass technique + dental floss) -Supporting Periodontal Therapy	- Clinical and laboratory exams. - Supporting Periodontal Therapy - Mechanical control (modified Bass technique + dental floss)

using the analysis of variance (ANOVA) and Tukey's test ($P < 0.05$).

RESULTS

Table 2 shows the mean clinical periodontal parameters achieved in all groups treated and the time intervals according to Table 1. All groups showed a significant reduction in the plaque index at the end of treatment, confirming the effectiveness of periodontal treatment. The results for the gingival index indicate that all groups showed a statistically significant reduction, particularly groups 2 and 4 that showed a significant reduction after full-mouth scaling and root planing was used during treatment. A significant improvement was found in the probing depth after full-mouth scaling and root planing, although small differences in the reduction of probing depth were found, particularly in group 2 with a significant reduction of 1 mm, and this therapy was quite effective in this group of patients. As for the clinical attachment level, an improvement was observed in all the groups, particularly groups 1 and 2 that showed a significant improvement, and both therapies were

efficient in all groups.

Table 3 shows the mean values (mg/dl) of the lipid levels for all groups treated at the time intervals assessed, as shown in Table 1. Observing the levels of total cholesterol, a significant improvement in level of cholesterol was observed in groups 1, 3 and 4, especially after 12 months, despite an increase during the period, but a significant increase was only found in group 2, although this parameter was already high at the beginning of treatment. As for the high density lipoprotein (HDL) levels, a significant increase was found in all groups, which shows the effectiveness of periodontal treatment in this parameter, and it is important to demonstrate the relationship between the periodontal treatment and the lipid level. The results in the low density lipoprotein (LDL) levels showed a significant reduction in all groups within the 12-month period, particularly in groups 2 and 4, which shows the action of full-mouth scaling and root planing on the lipid parameter. A reduction in the triglyceride levels in all groups was observed, showing the effectiveness of periodontal treatment, again in groups 2 and 4, which showed a great reduction after full-mouth scaling and root planing.

DISCUSSION

Cardiovascular diseases are the main causes of death in contemporary society, despite the declining tendency of incidence and mortality, thus encouraging the development of a large number of studies and research with the purpose of improving prevention, diagnostic and treatment methods (Moura Foz et al., 2010). Periodontal disease has also been the object of several studies and research in the last decades as it represents one of the major public health problems due to its relatively high prevalence, even in developed countries, being considered the most prevalent chronic disease that affects human dentition. In this connection, this study was conducted with the purpose of finding evidence that suggest the association between periodontal and cardiovascular diseases through the behavior of lipid parameters that may influence the development of cardiovascular disease.

Most recently, a comprehensive review was performed by an American Heart Association (AHA) working group (Lockhart et al., 2012), which concluded that "periodontal disease is associated with atherosclerotic vascular disease

Table 2. Measurements (means \pm standard deviations) of the clinical periodontal parameters achieved in all groups treated and the periods respective.

Group	Period	Plaque index (%)	Gingival index (%)	Probing depth (mm)	Clinical attachment level (mm)	P value
Group 1	Initial	60.75 \pm 1.61 ^A	26.53 \pm 1.61 ^A	1.66 \pm 0.11 ^A	2.63 \pm 0.15 ^A	P<0.05
	12 months	35.84 \pm 1.50 ^B	4.91 \pm 1.30 ^B	1.65 \pm 0.32 ^A	2.18 \pm 0.16 ^B	
Group 2	Initial	77.20 \pm 0.87 ^C	28.34 \pm 1.87 ^C	2.49 \pm 0.42 ^B	2.73 \pm 0.12 ^C	P<0.05
	12 months	36.30 \pm 1.42 ^D	5.00 \pm 1.65 ^B	1.41 \pm 0.36 ^C	2.56 \pm 0.11 ^D	
Group 3	Initial	33.75 \pm 0.95 ^E	0.445 \pm 0.01 ^D	1.40 \pm 0.31 ^D	2.65 \pm 0.10 ^A	P<0.05
	12 months	27.67 \pm 0.68 ^F	0.90 \pm 0.08 ^E	1.52 \pm 0.42 ^E	2.58 \pm 0.11 ^D	
Group 4	Initial	44.47 \pm 0.62 ^G	2.23 \pm 0.62 ^F	1.32 \pm 0.25 ^F	2.71 \pm 0.12 ^C	P<0.05
	12 months	32.12 \pm 0.94 ^H	0.00 \pm 0.00 ^G	1.06 \pm 0.32 ^G	2.54 \pm 0.10 ^D	

*Different letters represent statistically significant difference among means in the same parameters and periods respective.

Table 3. Measurements (means \pm standard deviations) of the lipid serum level achieved in all groups treated and the periods respective.

Group	Period	Total cholesterol (mg/dl)	HDL cholesterol (mg/dl)	LDL cholesterol (mg/dl)	Triglyceride (mg/dl)	P value
Group 1	Initial	202.28 \pm 4.51 ^A	46.28 \pm 1.51 ^A	112.70 \pm 4.07 ^A	149.76 \pm 6.45 ^A	P<0.05
	12 months	153.45 \pm 5.14 ^B	79.57 \pm 1.41 ^B	105.50 \pm 3.33 ^B	124.10 \pm 5.14 ^B	
Group 2	Initial	194.00 \pm 4.00 ^C	44.00 \pm 2.00 ^C	139.00 \pm 5.26 ^C	118.60 \pm 5.96 ^C	P<0.05
	12 months	199.22 \pm 8.12 ^D	78.44 \pm 2.22 ^D	126.80 \pm 4.56 ^D	82.00 \pm 2.68 ^D	
Group 3	Initial	147.85 \pm 5.21 ^E	56.56 \pm 1.65 ^E	75.60 \pm 3.54 ^E	83.27 \pm 5.32 ^E	P<0.05
	12 months	109.90 \pm 7.12 ^F	60.70 \pm 2.12 ^F	61.50 \pm 2.22 ^F	38.10 \pm 6.36 ^F	
Group 4	Initial	163.00 \pm 6.32 ^G	45.46 \pm 3.31 ^A	99.46 \pm 3.89 ^G	112.42 \pm 4.32 ^G	P<0.05
	12 months	130.43 \pm 5.13 ^H	58.90 \pm 1.31 ^G	59.30 \pm 1.31 ^F	74.50 \pm 4.51 ^H	

**Different letters represent statistically significant difference among means in the same parameters and periods respective to total cholesterol, HDL, LDL and triglyceride.

independent of known confounders". AHA further concluded that there was no evidence for a causal link and that, therefore, "statements that imply a causative association between periodontal disease and specific atherosclerotic vascular disease events [...] are unwarranted" (Dietrich et al., 2013).

One of the hypotheses of this mechanism linking between periodontitis and atherosclerosis would be predicted based on inflammatory mechanisms initiated by bacteria associated with periodontal lesions, locally or systemically, that then influence the initiation or propagation of the atherosclerotic lesion. Such lesions may be initiated by inflammatory stimuli including systemic and locally produced inflammatory cytokines and chemotactic agents that cause changes in the endothelium such

as up-regulation of adhesion molecules. These changes promote interactions with leucocytes, such as monocytes, that promote leucocyte migration into the intimal layer of the artery. Lipid streaks, comprised of modified LDL within macrophages and dendritic cells in the intimal layer, can initiate and propagate this inflammatory response. Up-regulation of the endothelium additionally leads to release of chemotactic cytokines such as monocyte chemoattractant protein-1 that further attract monocytes or other cells that can transport migration by degradation of the extracellular matrix (Schenkein and Loos, 2013).

Although a number of the studies have investigated the effect of periodontal treatment on the lipid profile (Oz et al., 2007; Taylor et al., 2010), there are no studies in the literature that have moderate evidence that does not

support a positive effect of non-surgical periodontal therapy on lipid parameters and the impact of periodontal treatment on systemically compromised patients regarding the lipid parameters, since these patients may have a different response when compared with healthy patients, because of their disease or even the medication they use (D'Aiuto et al., 2013).

The results of the present study show that there was an improvement in the clinical periodontal levels in individuals who do not present alterations in these levels and in patients with cardiovascular diseases in which periodontal treatment showed a significant improvement on these results, as shown in Table 2. Periodontal treatment was effective in all groups, particularly for the groups that received full-mouth scaling and root planing, showing that the control of periodontal disease can be performed, irrespective of the systemic condition of the patient, but with greater success when the patient cooperates during treatment.

D'Aiuto et al. (2005) analyzed the short-term effects of intensive periodontal therapy in the inflammatory markers and cholesterol and found alterations in inflammation irrespective of age, gender, body mass, and ethnicity, but a significant interaction among smokers and therapeutic regimes was found. This study showed a decrease in total cholesterol and LDL after two months of periodontal therapy concluding that periodontitis causes moderate systemic inflammation in systemically healthy individuals and that periodontal treatment may be an adjuvant therapy to control the cholesterol levels in individuals, corroborating our results (Table 3), particularly of patients in groups 1 and 2 who already presented lipid disorders.

Although the role of periodontitis associated with diet and behavior may not be excluded, periodontal treatment alone has only shown to be effective in improving the lipid profile. One possible explanation for this finding could be that the cytokines IL-1 β and TNF- α present during periodontal disease also have an effect on the lipid metabolism by influencing the production of other cytokines, altering hemodynamic, using amino acids from several tissues involved in lipid metabolism, or by modifying the hypothalamic-pituitary-adrenal axis and increasing the concentrations of adrenocorticotropic hormones, cortisol, adrenaline, noradrenaline and glucagon in the plasma. It is believed that the elevation of serum lipids result from the increase in hepatic lipogenesis, lipolysis in adipose tissues, blood circulation and increased synthesis or reduced elimination of triglycerides and LDL due to the reduction in the activity of the lipoprotein lipase (Moeintaghavi et al., 2005).

With regard to the results in Table 3, the improvement in the HDL levels showed the positive action of periodontal therapy, corroborating the study of Oz et al. (2007) and Taylor et al. (2010), who showed the beneficial effect of periodontal treatment on lipid metabolism, since the levels of LDL and cholesterol reduced after periodontal treatment, particularly in groups 1 and 2. On the other

hand, the study of Sridhar et al. (2009) showed that periodontitis did not influence the alteration of the serum lipid levels and that there would be no correlation between these levels and periodontal attachment loss, corroborating a systematic review of D'Aiuto et al. (2013) which demonstrated there is however limited evidence that these acute and chronic changes will either increase or reduce cardiovascular disease burden of individuals suffering from periodontitis in the long term.

Conclusion

Within the limitations of this study, it may be concluded that periodontal treatment contributes to control the lipid levels, particularly in patients with cardiovascular disease. In addition, the control of the development of periodontal disease may also be achieved in patients with cardiovascular diseases.

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