Original

Lipid profile and high-sensitivity C-reactive protein levels in obese and non-obese subjects undergoing non-surgical periodontal therapy

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Abstract: Periodontal treatment may improve the metabolic control of dyslipidemia. The aim of this study was to evaluate the lipid profile and high-sensitivity C-reactive protein (hs-CRP) levels in obese and non-obese patients undergoing periodontal therapy. Patients with generalized chronic periodontitis were divided into obese ($n = 28$) and non-obese groups ($n = 26$). The periodontal parameters (visible plaque index, gingival bleeding index, probing depth, clinical attachment level, and bleeding on probing), anthropometric measurements (body mass index, waist circumference, and body fat), and serum analyses (triglycerides, total cholesterol, high-density lipoprotein, low-density lipoprotein, fasting glucose, glycated hemoglobin, and hs-CRP) were measured at baseline and 90 days after periodontal treatment. The results showed that the obese subjects presented alterations in triglycerides, total cholesterol, low-density lipoprotein, and hs-CRP at baseline when compared with non-obese patients ($P < 0.05$). Periodontal treatment could improve the periodontal parameters in both groups similarly ($P > 0.05$). Obese subjects showed a significant decrease in the levels of triglycerides, total cholesterol, low-density lipoprotein, and hs-CRP post-therapy ($P < 0.05$), while non-obese patients

showed improvement only in hs-CRP ($P < 0.05$). In conclusion, periodontal treatment could improve the periodontal parameters and circulating hs-CRP in obese and non-obese subjects. Lipid profile was modified only in obese patients post-therapy. (J Oral Sci 58, 423-430, 2016)

Keywords: obesity; lipids; dyslipidemia; chronic periodontitis; periodontal diseases.

Introduction

Recently, studies examining the relationship between periodontal disease and hyperlipidemia have shown that a greater systemic involvement may occur in patients exhibiting periodontal involvement (1-4). Chronic exposure to bacterial lipopolysaccharides (LPS) can promote recruitment of defense cells which secrete alpha tumor necrosis factor (TNF- α) and interleukin-1 beta (IL-1 β), thus increasing lipogenesis and lipolysis. Increased lipid levels may promote alterations in phagocytosis and polymorphonuclear neutrophil and macrophage chemotaxis, and also damage tissue healing (1).

An association between the presence of periodontal pathogenic bacteria (*Tanarella forsythia*) and high levels of total cholesterol (TC) and low-density lipoprotein (LDL) was observed in patients with periodontitis, suggesting a potential relationship between periodontitis and atherosclerosis (5). High levels of LDL and triglycerides (TGR) were found to be associated with high alveolar bone loss using X-rays in the periodontitis group (6). Similarly, other authors found significant

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relations between the levels of TC, LDL, and TGR, and clinical periodontal disease (3,5). Despite this evidence, there is no consensus in the literature regarding this topic, as other studies reported no significant relation between periodontal status and lipid level alterations (7). In the case of an association between periodontitis and hyperlipidemia, periodontal therapy can effectively contribute to improving local and systemic inflammatory processes and enhancing endothelial function (8), and evidence suggests that it was able to improve hyperlipidemia metabolic control (9-12) and systemic markers such as CRP (12).

Hyperlipidemia is also often related to obesity, and may be one of the biological inflammatory mechanisms involved in the relation between obesity and periodontitis (13,14). This hypothesis was put forward by Saxlin et al. (15) who reported no association between the levels of circulating lipids and periodontal infections in non-obese individuals. However, a significant association was observed between high TGR and low level LDL and periodontal infections in obese individuals.

Some findings show that periodontal therapy does not alter metabolic parameters in obese or non-obese patients (16,17), with the exception of TGR (17). The available evidence regarding the relationship between lipid profile and obesity and chronic periodontitis are still controversial and scarce, and well-designed clinical studies assessing the response to periodontal therapy in such patients are necessary in order to better clarify this relationship.

Obesity, dyslipidemia, and periodontitis are conditions that may increase the risk for cardiovascular diseases and inflammation, and may be measured systemically using the acute phase C-reactive protein (CRP) (18,19). CRP is an inflammatory marker that can promote the phagocytosis of injured cells and tissue remnants in combination with other proteins, thus increasing inflammation and tissue damage (20). It is hypothesized that periodontitis may alter the lipid profile and CRP levels in obese and normal weight individuals, but controlled clinical studies are still required to clarify these relationships. Hence, the aim of this study was to evaluate the lipid profile and high-sensitivity CRP in obese and non-obese patients undergoing periodontal therapy.

Materials and Methods

This study was approved by the UNIFEB Research Ethics Committee (protocol no. 01/08), and included 54 patients seeking treatment at the dental clinics at UNIFEB. All subjects participated voluntarily and signed an informed consent form.

Sample size calculation

The sample size for inter-group comparison was calculated by means of independent *t* tests for means of clinical attachment levels in obese (3.8 ± 0.35) and non-obese (4.1 ± 0.34) patients (data from a pilot study). Therefore, considering a power of 85% and $\alpha = 0.05$ (BioEstat 5.0, Belém, PA, Brazil), the sample size was estimated to be 24 patients in each group.

Calibration and reproducibility

A single researcher was trained and calibrated to assess the periodontal clinical parameters. Thereafter, full mouth periodontal examinations were performed in six patients, considering clinical attachment level (CAL) as reference in six sites per tooth. The examinations were performed in the same patients at two separate time points with an interval of 1 week. The agreement between the data from both examinations was verified using intra-class correlation test, and found to exhibit excellent replicability (0.9271 ; $P < 0.0001$).

Sample selection

Obese and non-obese patients were selected from the dental clinics at UNIFEB according to some general inclusion and exclusion criteria. The inclusion criteria were: both sexes, age between 35 to 55 years, presence of at least 20 teeth, general chronic periodontal disease (more than 30% of sites) (21), at least six teeth with probing depth ≥ 5 mm and clinical attachment loss ≥ 3 mm, and bleeding on probing. Exclusion criteria: smokers or former smokers who had stopped less than 5 years prior to the study, history of antibiotics or anti-inflammatory drug use in the three months prior to study, patients with diabetes or other systemic diseases, those who did not show up for the follow-up appointments, pregnant or lactating women, continuous use of any kind of hormones, mental or physical limitations that could make oral hygiene difficult, and history of periodontal therapy in the previous 12 months.

The selected patients were divided in two groups (obese and non-obese) according to the number suggested by the sample size calculation and in keeping with specific inclusion criteria.

Obese group (test): Body Mass Index (BMI) ≥ 30 kg/m²; obesity was confirmed by waist-hip ratio (WHR) (≥ 0.85 for women and ≥ 0.9 for men) (22), waist circumference (WC) (> 88 cm for women and > 102 cm for men), and bio impedance or bioelectrical impedance, which measures the percentage of body fat (BF) ($\geq 35\%$ for women and $\geq 25\%$ for men) (23).

Non-obese group (control): BMI between 18.5 and 24.9

kg/m², and WHR, WC, and BF measures smaller than those of the obese group. Laboratory exams, periodontal clinical parameters, and anthropometric measures were performed in both groups at baseline and 3 months after the completion of non-surgical periodontal therapy.

Anthropometric parameters

The formula adopted by the World Health Organization (24), wherein weight is divided by the square of height (weight/height²), was used to calculate the BMI. The weight was measured in kilograms using a portable scale evaluated by the INMETRO (National Institute of metrology, standardization and Industrial quality, Brazil). Height was measured by means of a metal ruler with a 0.5 cm variation attached to a steel support. The patients were barefoot when their weight and height were measured, and were considered obese when their BMI was ≥ 30 kg/m² and non-obese when BMI was between 18.5 and 24.9 kg/m². WC measurement was carried out using a measurement tape with a 1 cm variation at the umbilical scar, and measures of WC ≥ 102 cm for men and ≥ 88 cm for women suggested obesity (25). Hip circumference measures were also taken using the same measurement tape, and these measures were used to calculate the WHR (26). Patients were considered obese if WHR was ≥ 0.85 for women and ≥ 0.9 for men (22). In order to have a complementary and accurate assessment of both fat and lean mass, electrical impedance (or bioimpedance) was performed using a specific device (Omron Healthcare Co, Ltd, Tokyo, Japan) (27) in accordance with the manufacturer's instructions. Patient data was fed into the device prior to its use. Thereafter, patients were asked to stand with their legs apart and arms in a 90 degree-position, the device was set, and a low-intensity electrical charge was passed through the body. BF values were considered normal if they were $<25\%$ for men and $<35\%$ for women (23). Associating methods such as BMI, WHR, and bioimpedance is crucial in order to obtain an accurate diagnosis of obesity, since BMI has little diagnostic accuracy on its own as it does not differentiate fat from muscle fibers (27). All measurements were made by a trained and qualified professional.

Periodontal clinical parameters

Clinical measurements were carried out by a single trained and calibrated examiner (EMB) using Williams periodontal probes (Hu-Friedy, Chicago, IL, USA) and sterilized flat mouth mirrors. The following periodontal parameters were measured: visible plaque index (VPI): present (+) or absent (-); gingival bleeding index (GBI, inflammation in the gingival margin): present (+) or

absent (-); probing depth (PD, distance from the gingival margin to the bottom of the gingival sulcus measured in millimeters), bleeding on probing (BOP, inflammation in the bottom of the periodontal pocket): present (+) or absent (-); and clinical attachment level (CAL, distance from the cemento-enamel junction to the bottom of the pocket measured in millimeters). VPI, GBI (28), PD, BOP, and CAL (21) were measured in six sites per tooth (mesiobuccal, mid-buccal, distobuccal, mesiolingual, mid-lingual, and distolingual).

Periodontal treatment

Periodontal therapy was performed in a single session by another qualified professional (ALVC), and included supra and subgingival scaling and root planning using Gracey and McCall curettes (Hu Friedy) and delivery of dental hygiene instructions and motivation.

Blood parameters

Patients were referred to have their blood work done at an outsourced laboratory (Santa Casa de Saúde de Barretos, Barretos, SP, Brazil). The following exams were requested: triglycerides (TGR, mg/dL), total cholesterol (TC, mg/dL) and fractions of high density lipoproteins (HDL, mg/dL) and low density lipoproteins (LDL, mg/dL), high-sensitivity C-reactive protein (hs-CRP, mg/dL), fasting plasma glucose (mg/dL), and glycosylated hemoglobin (%).

Statistical analysis

Data analysis was performed using the software BioEstat 5.0, Belém. All data were assessed 1 week before and 3 months after the completion of non-surgical periodontal therapy. Comparison between obese and non-obese groups was carried out using the Mann-Whitney *U* test (non parametric data), while the Wilcoxon test (non parametric data) was used to compare baseline data to that from 3 months after therapy. Differences were considered significant when $P < 0.05$, and all data were reported as mean and standard deviation. For VPI, BGI, BOP, PD, and CAL (≤ 3 mm, 4-6 mm and ≥ 7 mm) data, percentages were calculated within each category.

Results

Fifty-four patients participated in the present study, and the obese and non-obese groups exhibited similar sociodemographic characteristics. Twenty-eight participants were obese and 26 were non-obese, with mean ages (standard deviation) of 45.7 years (8.4 years) and 42.7 years (7.5 years), respectively. The mean (standard deviation) number of teeth was 22.7 (2.0) and 24.1 (1.7)

Table 1 Anthropometric parameters for obese and non-obese groups

Anthropometric parameters	Group	Baseline	90 days post-therapy	<i>P</i> value
BMI (kg/m ²)	Obese	35.3 (4.8) ^{aa}	35.7 (5.5) ^{aa}	0.07
	Non-obese	23.0 (2.2) ^{bb}	21.2 (2.1) ^{bb}	0.9
WC (cm)	Obese	107.4 (10.7) ^{c†}	106.6 (11.1) ^{c†}	0.06
	Non-obese	82.1 (7.7) ^{da}	81.8 (8.2) ^{da}	0.5
WHR	Obese	0.92 (0.07) ^{eb}	0.90 (0.06) ^{eb}	0.06
	Non-obese	0.85 (0.06) ^{ff}	0.84 (0.08) ^{ff}	0.4
Body fat (%)	Obese	40.7 (4.7) ^{ga}	40.8 (5.6) ^{ga}	0.9
	Non-obese	24.7 (4.5) ^{hb}	25.4 (5.0) ^{hb}	0.7

Mean (Standard Deviation); BMI: Body mass index, WC: Waist circumference, WHR: Waist:Hip ratio. Different superscript letters in the columns indicate statistically significant differences between obese and non-obese group (Mann-Whitney; $P < 0.0001$). α , β , $\dagger$: Similar symbols in the rows indicate no statistically significant intragroup differences before and after treatment (Wilcoxon; $P > 0.05$).

Table 2 Blood parameter measurements for obese and non-obese group

Blood parameters	Group	Baseline	90 days post-therapy	<i>P</i> value
TC	Obese	250.0 (14.1) ^a	210.6 (16.3) ^c	0.0022*
	Non-obese	172.7 (15.9) ^b	155.2 (22.5) ^d	0.24
HDL	Obese	51.1 (3.5) ^e	50.4 (4.3) ^b	0.83
	Non-obese	47.5 (7.1) ^e	51.0 (3.0) ^b	0.68
LDL	Obese	170.8 (11.3) ^d	152.7 (14.0) ^f	0.01*
	Non-obese	120.8 (24.0) ^e	117.1 (13.4) ^g	0.46
TGR	Obese	172.1 (14.2) ^f	154.3 (15.9) ^a	0.02*
	Non-obese	72.85 (13.2) ^g	63.4 (9.5) ^b	0.07
hs-CRP	Obese	3.75 (0.5) ⁱ	2.62 (0.2) ^v	<0.05*
	Non-obese	1.45 (0.1) ^f	1.01 (0.08) ^u	<0.05*
Plasma glucose (mg/dL)	Obese	99.8 (13.4) ^h	102.0 (15.9) ^j	>0.05
	Non-obese	89.6 (15.9) ^h	94.4 (4.4) ^j	>0.05
Glycated hemoglobin (%)	Obese	5.4 (1.0) ⁱ	4.4 (0.8) ^k	>0.05
	Non-obese	4.7 (0.95) ⁱ	5.0 (1.1) ^k	>0.05

Mean (Standard Deviation); Different superscript letters in the columns indicate statistically significant intergroup differences between obese and non-obese subjects (Mann-Whitney, $P < 0.05$). *Statistically significant intragroup differences before and after treatment (Wilcoxon, $P < 0.05$). Reference values: Total cholesterol (TC, mg/dL): up to 200 (desirable), 200 to 239 (limit), >239 (high); high-density lipoprotein (HDL, mg/dL): 40 to 85 (desirable); low-density lipoprotein (LDL, mg/dL): <130 (desirable), 159 (limit), and >159 (high risk); triglycerides (TGR, mg/dL): <150 (optimal), 150 to 199 (moderate), 200 to 499 (high), and >500 (very high); fasting plasma glucose (mg/dL): >126; and glycated hemoglobin (%): >7 (diabetes condition). hs-CRP: high-sensitivity C-reactive protein.

for the obese and non-obese groups, respectively, while the male:female ratio was 6/22 in the obese and 8/18 in the non-obese groups.

Anthropometric parameters

Table 1 shows the mean (standard deviation) of the anthropometric parameters (BMI, WC, WHR, and bioimpedance) of both groups. It is noteworthy that all the anthropometric parameters in the obese group were higher than those in the non-obese group ($P < 0.05$), and were characteristic of obesity. These parameters remained within the obesity and normalcy levels until the end of the study (Table 1).

Serological parameters

Obese patients with periodontitis presented with higher

levels of TC, LDL, and TGR compared to the non-obese group at baseline ($P < 0.05$), demonstrating that obesity can influence the lipid profile. On the other hand, the non-obese group with periodontitis presented reference values within desired standards, suggesting that periodontitis itself did not influence hyperlipidemia (Table 2). It could also be seen that obese patients who received basic periodontal therapy exhibited significant reduction in the serological levels of TC, LDL, and TGR ($P < 0.05$), while the non-obese group was more likely to exhibit improvement in these levels, although this difference was not statistically significant ($P > 0.05$). Hs-CRP significantly reduced after periodontal therapy in the non-obese and obese subjects ($P < 0.05$; Table 2).

Table 3 Percentage of periodontal clinical parameters

Periodontal Parameters	Group	Baseline	90 days post-therapy	<i>P</i> value
VPI (%)	Obese	76.2 (4.1) ^a	18.1 (2.1) ^b	NS
	Non-obese	72.9 (3.8) ^c	16.9 (3.9) ^d	
GBI (%)	Obese	51.1 (7.3) ^e	9.3 (0.9) ^f	NS
	Non-obese	46.7 (6.7) ^g	7.9 (1.7) ^h	
BOP (%)	Obese	48.5 (2.6) ⁱ	7.1 (1.9) ^j	NS
	Non-obese	45.6 (3.1) ^k	7.9 (2.1) ^l	
PD ≤3 mm (%)	Obese	54.8 (5.1) ^m	89.2 (7.5) ⁿ	NS
	Non-obese	58.7 (5.6) ^o	90.6 (5.4) ^p	
PD 4-6 mm (%)	Obese	39.9 (6.2) ^q	8.7 (3.3) ^r	NS
	Non-obese	37.5 (4.1) ^s	7.7 (1.8) ^t	
PD ≥7 mm (%)	Obese	5.3 (4.1) ^u	2.1 (1.9) ^v	NS
	Non-obese	6.6 (3.9) ^w	1.7 (0.6) ^y	
CAL ≤3 mm (%)	Obese	52.2 (4.9) ^x	73.2 (3.4) ^z	NS
	Non-obese	47.8 (4.3) ^a	75.6 (4.6) ^b	
CAL 4-6 mm (%)	Obese	39.5 (5.4) ^c	23.8 (4.40) ^d	NS
	Non-obese	44.3 (4.4) ^e	21.8 (3.9) ^f	
CAL ≥7 mm (%)	Obese	8.3 (2.9) ^g	3.0 (2.6) ^h	NS
	Non-obese	9.7 (3.6) ⁱ	2.6 (2.1) ^j	

Mean (Standard Deviation); VPI: visible plaque index; GBI: gingival bleeding index; BOP: bleeding on probing; PD: probing depth; CAL: clinical attachment level. Different superscript letters in the rows indicate statistically significant intragroup differences between baseline and 3 months after treatment (Wilcoxon, $P < 0.05$). NS: non-significant differences between obese and non-obese groups ($P > 0.05$, Mann-Whitney).

Periodontal clinical parameters

Table 3 shows that both groups responded well to the periodontal therapy, with apparent improvement in all periodontal clinical parameters post-treatment ($P < 0.05$) and no significant differences between them ($P > 0.05$), suggesting that obesity did not negatively affect improvement of periodontal condition post-therapy.

Discussion

The results of the present study showed that the non-obese group presented normal reference values in the lipidogram, which improved after periodontal therapy but did not differ significantly ($P > 0.05$). These results do not agree with those of Oz et al. (29), who assessed the influence of periodontal therapy on hypercholesterolemia metabolic control in patients with periodontitis and reported a significant reduction in TC and LDL compared with initial values.

Similarly, the results also do not agree with those of other studies that suggested that periodontal therapy improved hyperlipidemia metabolic control (10,11). It is important to highlight that it is still unknown whether lipid level alterations may be considered as a cause or consequence of periodontitis (30). Perhaps, no significant alteration was observed due to the fact that the lipid patterns were already normal, which could be different if only patients with dyslipidemia were assessed. However, this study was important to assess periodontal therapy

response in obese and non-obese patients.

According to some authors, lipid profile alterations may occur in patients with periodontitis (1-4). A hypothesis for the increase of systemic involvement is chronic exposure to bacterial LPS, which can promote the recruitment of defense cells (specifically macrophages) that secrete TNF- α and IL-1 β and cause a hyperlipidemic state that promotes alterations in phagocytosis, polymorphonuclear neutrophil and macrophage chemotaxis, and impairs tissue healing (1,2).

Evidence shows that when there is a combination of obesity and periodontitis, the lipid profile presents a significant increase, especially with regard to TC, LDL, and TGR. It is possible that obese individuals with high TGR levels and/or low HDL levels may be at a higher risk of developing periodontal infections (15). On the other hand, Saxlin et al. evaluated the role of serum lipids as mediators between body weight and periodontal infections, and suggested that the effect of body weight on periodontal conditions was most likely mediated by mechanisms other than lipids (15).

Since available evidence on this topic is still controversial and scarce, further controlled clinical studies are required in order to better elucidate the clinical response and mechanisms involved in the relation between hyperlipidemia, obesity, and periodontal disease. In spite of elevated lipid levels in obese patients with periodontitis, our results show that periodontal therapy

was beneficial and helped reduce TC, LDL, and TGR, even if obesity itself was not addressed. The patients in this study remained obese until the end of the experiment, suggesting that the reduction of these parameters is likely related to periodontal therapy. Considering that periodontitis can also alter lipid profile (11,30,31), its treatment may reduce some markers such as TC and LDL (29).

In addition to treating periodontitis, the dentist should advise the patient about additional risk factors that may interfere with the disease or treatment results including diet, body weight, lifestyle, and environmental stress (32), and also emphasize that help from a physician and nutritionist will be very beneficial to the treatment, thus targeting obesity as well as periodontitis simultaneously (33). This is very important as abdominal fat tissue is metabolically active and promotes excess release of free fatty acids which, in turn, lead to an increase in lipid metabolism. Weight loss may increase HDL levels and decrease TGR levels (34).

Moreover, the results of the present study showed a good response to periodontal therapy, with improvement of all clinical parameters (PI, GBI, BOP, PD, and CAL) in both groups. These findings are in agreement with those of Zuza et al. who suggested that obesity does not interfere with periodontal therapy response, even though it is a proinflammatory and metabolically active condition (35).

Periodontitis may influence the levels of hs-CRP, and their serum elevation is associated with increased risk of cardiovascular diseases (36) as well as obesity and hyperlipidemia (37-39). CRP levels >3 mg/L can be classified as high risk of cardiovascular diseases, CRP = 1 to 3 mg/L as medium risk, and CRP <1 mg/L (40) as low risk. The levels of CRP have been shown to increase with age (41) and, therefore, the subjects selected for the present study were aged between 35 to 55 years to allow standardization of the sample.

Our findings demonstrated that periodontal treatment decreased the circulating CRP levels in normal-weight patients with periodontitis, and this was in agreement with other studies (36,42,43). Paraskevas et al. (44) also showed that non-surgical periodontal therapy reduced CRP levels in systemic circulation. Al-Zahrani and Alghamdi (45) reported that obesity did not have a negative impact on response to periodontal therapy and, instead, reduced systemic inflammation, measured by serum CRP level. This was in agreement with our results which also showed a decrease in the CRP levels after treatment in obese individuals with periodontitis. Conversely, other studies did not verify significant

alterations in CRP concentrations after periodontal therapy in normal-weight patients (17,46,47) or obese individuals (17). According to Yamazaki et al., the lack of statistical significance in verifying alterations in CRP may be related to the small number of patients or other methodological limitations (47).

Dyslipidemias are often related to obesity, and this could be one of the mechanisms responsible for the relation between obesity and periodontitis (13,14). However, these results must be considered with caution because, in addition to lipids, other mechanisms may be mediating the relation between body weight and periodontal disease, as proposed by Saxlin et al. (15). One limitation of this study was that changes in diet and lifestyle were not measured, and it is known that lipid profile alterations may occur because of this. However, as the obesity condition was maintained up to the end of the study, it can be inferred that such changes did not occur. Further randomized controlled studies are needed in order to better elucidate the mechanisms involved in this relation. Thus, it can be concluded that periodontal treatment was able to improve the periodontal parameters and circulating hs-CRP in obese and non-obese subjects. Lipid profile was modified only in obese patients post-therapy.

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