STUDY ON THE EFFECTS OF CLASSICAL PERIODONTAL THERAPY ON THE LIPID PROFILE IN HYPERLIPIDEMIC AND CHRONIC PERIODONTITIS PATIENTS

Ovidiu NICOLAICIUC1, Irina-Georgeta URSĂRESCU (ŞUFARU)2, Ioana MÂRŢU2, Liliana PĂSĂRIN3, Ana-Maria ZAHARESCU4, Ionuţ LUCHIAN2, Maria-Alexandra MÂRŢU-ŞTEFANACHE2, Silvia MÂRŢU5

1PhD Student, “Gr.T.Popa” UMPh, Iaşi, Department of Periodontology, Romania
2Univ. Assist., “Gr.T.Popa” UMPh, Iaşi, Faculty of Medical Dentistry, Romania
3Lecturer, “Gr.T.Popa” UMPh Iaşi, Faculty of Medical Dentistry, Romania
4Trainee Physician, Endodontics, “Gr.T.Popa” UMPh Iaşi, Romania
5Univ. Prof., “Gr.T.Popa” UMPh Iaşi, Department of Periodontology, Romania
Corresponding author: Irina-Georgeta Ursărescu (Şufaru); e-mail: irina_ursarescu@yahoo.com

Abstract

Aim: The study was conducted to assess the effect of improved periodontal health following periodontal treatment on the metabolic lipid control of patients on anti-lipemic treatment. Materials and methods: The study population consisted of 20 patients aged 34–62 years with diagnoses of hyperlipidemia and chronic periodontitis. All patients used statin to treat their elevated levels of low-density lipoprotein cholesterol. Blood samples were obtained for measurement of serum lipids, fasting plasma glucose, and high sensitive C-reactive protein. Periodontal parameters, including plaque index, gingival index, probing pocket depth, clinical attachment level, and percentage of bleeding on probing were evaluated. All parameters were assessed in each subject at the baseline, after 3 months as a control, and 3 months after the non-surgical periodontal treatment, scaling and root planning included. Results and discussion: All lipid parameters decreased after the periodontal treatment, but only the decreases in total cholesterol and low-density lipoprotein cholesterol levels reached statistical significance compared to the baseline (P = 0.002 and P = 0.003, respectively). Improved periodontal health may influence metabolic control of hyperlipidemia and could be considered as an adjunct to the standard measures of hyperlipidemic patient care. Conclusions: Treatment of periodontitis may result in a potential benefic effect on the metabolic control of hyperlipidemia. Keywords: chronic periodontitis, hyperlipidemia, periodontal treatment.

1. INTRODUCTION

Cardiovascular diseases (CVDs), namely coronary heart disease (CHD), stroke, congestive heart failure and peripheral artery disease, became the leading cause of chronic disease morbidity and mortality in industrialized countries in the twentieth century [1]. CVDs are now a global problem as their incidence is also increasing in the developing countries as a consequence of a better control of infectious diseases such as HIV, malaria and tuberculosis, and also due to obesity and diabetes epidemic [2]. A large body of evidence is available on the beneficial effects of controlling a number of recognized CVD risk factor, including hypercholesterolemia, hypertension, smoking [3] and sodium intake [4] for reducing CVD mortality. However, the incidence of CVD is still increasing [2], as controlling of all recognized risk factors might not be sufficient for reducing the CVD burden on the general population [5].

Inflammation plays a key role in the development of CVD, 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 CVD [6]. A number of potential sources of inflammation have been investigated over the last 30 years, including bacterial and viral infections.

Periodontal disease is an infectious affection which may result in increased spillover of inflammatory cytokines from the gingival tissues into blood circulation, leading to increased mobilization of lipids from the liver and adipose tissue [7]. Lipids may interact directly with the
macrophage cell membrane, interfering with membrane-bound receptors and enzyme systems, and altering macrophage gene expression for essential polypeptide growth factors and pro-inflammatory cytokines, such as TNF-α and interleukin-1 beta (IL-1b) [8], which are thought to be associated with periodontal disease. The interrelationship between periodontitis and hyperlipidemia provides an example of a systemic disease predisposing to oral infection, and once the oral infection is established, it exacerbates the systemic disease. Elevated values of serum lipids may lead to poor periodontal health [9]. The control of periodontal infection results in significant decreases in lipid levels [10].

The purpose of the present study is to evaluate whether the local, non-surgical periodontal treatment influences metabolic control of hyperlipidemia in hyperlipidemic patients receiving a statin group anti-lipemic agent.

2. MATERIALS AND METHODS

The study population consisted of 20 patients aged 34–62 years with diagnoses of hyperlipidemia and chronic periodontitis. The inclusion criteria were: hyperlipidemic patients prescribed statins; patients with at least 1 natural teeth in the mouth, and at least four pockets located on non-adjacent different teeth with probing pocket depth of at least 4 mm.

Exclusion criteria used were any other systemic disease affecting lipid metabolism (impaired glucose tolerance, diabetes mellitus or other endocrine diseases, nephritic syndrome, chronic renal disease, and cardiovascular disease); any current hormone replacement treatment; three-fold elevation in the liver enzymes; patients subjected to any periodontal treatment during the past 6 months, and any systemic antibiotic administration within the last 6 months. Smokers and ex-smokers were also excluded from the study.

All subjects completed the entire study, and no adverse effects were reported. All patients received atorvastatin in dosages of 10 or 20 mg at baseline. At the end of the first month, the lipid levels of subjects were re-evaluated for possible dose adjustment. However, no need to change the statin doses for any of the participants was identified. Thus, statin dosage in the study population was constant throughout the study. Also, no patient complained of problems related to the prescribed statin regimen.

Fasting plasma glucose levels were measured in order to detect the presence of diabetes or prediabetic / metabolic syndrome, exclusive conditions for study participation. Twenty hyperlipidemic patients – 12 females and 8 males aged 34–62 years (mean 49.55± 3.29), who were prescribed a statin drug by the same physician - were included in the study. A lipid-lowering diet and a physical training program were recommended initially, with no further monitoring. After being informed on the purpose of the study and given ample opportunity to ask any questions, the subjects signed consent forms.

All participants were asked to respond to a questionnaire regarding their medical status, current medications, socio-demographic characteristics, and life-style habits. Data related to age, gender, body mass index (BMI) and number of natural teeth present was recorded. The reason for teeth lost was evaluated according to patients’ history. BMI was calculated as body weight, in kilograms, divided by the square value of height, in meters.

Blood samples were collected for the measurement of triglyceride, total cholesterol, low-density lipoprotein cholesterol (LDL), high-density lipoprotein cholesterol (HDL), very low-density lipoprotein cholesterol (VLDL), fasting plasma glucose (FPG) and high sensitive C-reactive protein (hsCRP). The samples were obtained after a 12-h fasting period, from an antecubital vein. Serum lipid levels were determined by routine enzymatic methods. In order to identify subjects with pathological lipid values, the following cut-off points were used, according to laboratory recommendation: Triglyceride >200 mg/dl, total cholesterol >200 mg/dl, LDL >130 mg/dl, HDL <35 mg dl, and VLDL >40 mg/dl. The nephelometric method was used to assess serum hsCRP levels. The lower and upper detection limits for CRP were 0.00 and 1.1 mg/dl, respectively.

All dental variables were assessed at six different sites (mesio-buccal, central-buccal, disto-buccal, mesio-lingual, central-lingual and disto-lingual) of each tooth present, including wisdom teeth. Clinical measurements of
periodontal parameters were recorded on a full-mouth and included plaque index (PI), gingival index (GI), probing pocket depth (PPD), clinical attachment level (CAL) and bleeding on probing (BOP). All assessments were carried out with Williams periodontal probe.

All subjects were reassessed after a 3-month period during which they received statin, but no periodontal care by the same clinician. At the end of the 3-month control period, all subjects received non-surgical periodontal treatment consisting of two appointments of intensive oral hygiene instruction, including plaque disclosing, tooth brushing technique instruction, interdental cleaning, and supragingival scaling and polishing, as well as four appointments during 1 week during which subgingival debridement was completed on a quadrant-by-quadrant basis using hand instruments. One month following root planning, periodontal parameters were recorded to determine any further surgical treatment needs of the study population, and site-specific rescue therapy was provided.

All periodontal parameters and systemic factors were re-examined 3 months after completion of the periodontal treatment, at a 6-month follow-up visit, i.e. after a 6 month statins treatment.

Reproducibility of the examiner was assessed by conducting duplicate clinical periodontal examinations on five patients. Each subject was assessed twice during one visit, within an 1-hour interval. The second set of recordings was carried out “in blind” to the first assessment. Reproducibility of examination was determined by calculating the percentage of examined sites, where the scores were repeated exactly or to an accuracy of ±1 mm. Assessment of the mean difference in the scores (with 85% accuracy) between the two examinations indicated no systematic bias in measurements.

All data are presented as mean values, with standard deviations and range of values. Non-parametric analysis of variance for repeated measurements (Friedman test) was used to evaluate the differences between the three time points: baseline, 3-month follow-up, and 6-month follow-up. A statistical significance threshold of $P < 0.05$ was accepted. Wilcoxon signed ranks test was used for post hoc analyses ($P < 0.021$ was accepted as significant).

### 3. RESULTS

Twenty eligible patients with hyperlipidemia and chronic periodontitis were enrolled in the study. The mean number of sites with probing depths of at least 4 mm was 13.25, with a range of 5–18, and the mean number of different teeth with PPD ≥4 mm was 7.05, with a range of 4–10. The average number of natural teeth was 18.20, with a range of 10–29. The mean number of teeth lost due to self-reported mobility was 3.75, with a range of 0–8.

#### Table 1. Periodontal parameters at each study point: baseline, 3 months after statins only and at 6 months (mean, standard deviation, and range)

<table>
<thead>
<tr>
<th></th>
<th>Baseline (BL) (0 months)</th>
<th>After statins only (3 months)</th>
<th>3 months after periodontal treatment (6 months)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean ± SD</td>
<td>Range</td>
<td>Mean ± SD</td>
</tr>
<tr>
<td>PI</td>
<td>2.92±0.59</td>
<td>0.98–3.73</td>
<td>1.66±0.61</td>
</tr>
<tr>
<td>GI</td>
<td>2.18±0.41</td>
<td>0.68–3.87</td>
<td>1.08±0.40</td>
</tr>
<tr>
<td>PPD (mm)</td>
<td>2.97±0.60</td>
<td>2.26–4.46</td>
<td>2.87±0.58</td>
</tr>
<tr>
<td>BOP (%)</td>
<td>49.02±19.67</td>
<td>15–84</td>
<td>39.90±18.52</td>
</tr>
<tr>
<td>CAL (mm)</td>
<td>3.30±1.63</td>
<td>0.65–6.64</td>
<td>3.14±1.50</td>
</tr>
</tbody>
</table>

3M/BL = comparison of 3 months to baseline (BL), 6M/3M = comparison of 6 months to 3months, 6M/BL = comparison of 6 months to baseline (BL), 3M = 3 months follow-up after baseline (after 3 months with statins only); 6M = 6 months follow-up (after 6 months with statins and 3 months after periodontal treatment); NS = not significant; PI = plaque index; GI = gingival index; PPD = probing pocket depth; BOP = bleeding on probing; CAL = clinical attachment level.
### Table 2. Biochemical parameters at each study point: baseline, 3 months after statins only and at 6 months (mean, standard deviation, and range)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Baseline (BL) (0 months)</th>
<th>After statins only (3 months)</th>
<th>3 months after periodontal treatment (6 months)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean ± SD</td>
<td>Range</td>
<td>Mean ± SD</td>
</tr>
<tr>
<td>Triglyceride (mg/dl)</td>
<td>167.35±120.12</td>
<td>44–618</td>
<td>160.05±100.70</td>
</tr>
<tr>
<td>Total cholesterol (mg/dl)</td>
<td>245.05±49.77</td>
<td>148–363</td>
<td>205.24±32.55</td>
</tr>
<tr>
<td>LDL (mg/dl)</td>
<td>161.35±44.70</td>
<td>80–262</td>
<td>124.38±36.40</td>
</tr>
<tr>
<td>HDL (mg/dl)</td>
<td>51.02±13.02</td>
<td>32–88.20</td>
<td>46.02±10.95</td>
</tr>
<tr>
<td>VLDL (mg/dl)</td>
<td>31.46±13.45</td>
<td>8–119</td>
<td>31.23±12.34</td>
</tr>
<tr>
<td>FPG (mg/dl)</td>
<td>90.75±11.16</td>
<td>70–120</td>
<td>92.15±7.85</td>
</tr>
<tr>
<td>hsCRP (mg/dl)</td>
<td>0.62±1.10</td>
<td>0.01–4.54</td>
<td>0.65±1.19</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>28.30±3.40</td>
<td>22.67–40.63</td>
<td>28.20±1.31</td>
</tr>
</tbody>
</table>

3M/BL = comparison of 3 months to baseline (BL), 6M/3M = comparison of 6 months to 3 months, 6M/BL = comparison of 6 months to baseline (BL), 3M = 3 months follow-up after baseline (after 3 months with statins only); 6M = 6 months follow-up (after 6 months with statins and 3 months after periodontal treatment); NS = not significant; LDL = low-density lipoprotein cholesterol; HDL = high-density lipoprotein cholesterol; VLDL = very low-density lipoprotein cholesterol; FPG = fasting plasma glucose; hsCRP = high sensitive C-reactive protein; BMI = body mass index.

Significant differences in periodontal parameters were recorded between the 3-month evaluation and baseline, except for PPD and CAL (Table 1). Total cholesterol and LDL levels and BMI showed statistically significant decreases at the end of the control period (P = 0.003, P = 0.012, P = 0.019, respectively). There was a slight increase in serum CRP levels at the 3-month evaluation, but not significant (P = 0.615) (Table 2).

PI, GI, PPD and BOP showed significant decreases after 6 months, compared to both baseline and 3 months (Table 1). All lipid parameters also decreased at the end of the study, but only the decreases in total cholesterol and LDL levels reached statistical significance compared to the baseline (P = 0.002 and P = 0.003, respectively). A significant decrease was also found in BMI (P = 0.013) at the end of the study; also, the serum hsCRP levels showed a statistically significant decrease (P = 0.001) compared to the baseline (Table 2).

### 4. DISCUSSION

The association between periodontal health and hyperlipidemia has been discussed in the literature of the field [11]. Although very limited data is reported on the periodontal status of hyperlipidemic patients who underwent medical evaluation, it has been observed that hyperlipidemic patients manifested a poor periodontal status, compared to healthy controls [11]. The findings in these studies seem to conclude that a successful management of periodontal infection may lead to reduction in local periodontal symptoms and may have a beneficial effect on the metabolic control of hyperlipidemia.

Although the study population was relatively reduced, due to the stringent eligibility requirements, involving elimination of individuals with a number of potential confounders, such as impaired glucose tolerance,
diabetes mellitus and other endocrine diseases, nephritic syndrome, chronic renal disease and cardiovascular disease, whose conditions are all believed to be involved in the development of both periodontal disease and hyperlipidemia.

At the beginning of the study, life-style changes, such as diet modification and physical exercise - which are important components of the treatment of lipid disorders - were recommended, in addition to anti-lipemic drug treatment. All patients agreed with physician’s recommendations during the study, but further monitoring was not performed. Also, it was not feasible to measure fat mass during routine medical check-up. Consequently, it was decided to use the BMI as a proxy for changes in body composition. No additional guidance, such as weight loss management, was provided.

To avoid the effects of individual variations and any time-related interference on the results obtained at the end of the periodontal treatment, both periodontal parameters and lipid markers were assessed, again 3 months after the periodontal treatment, a period during which the subjects received no periodontal care. In our study, both periodontal parameters (PI, GI, and BOP) and lipid levels (total cholesterol and LDL) manifested statistically significant reductions after 3 months, compared to the baseline. The significant reductions in the periodontal parameters may be attributed to the role of statins, which have anti-inflammatory pleiotropic effects [12] and also, to some extent, to the influence of the Hawthorne effect, associated with the improvement of oral hygiene as an unintended consequence of research participation [13].

The results obtained 3 months after the nonsurgical periodontal treatment (6 months from the baseline) showed an improvement in lipid profile, even though among lipid parameters only the decreases in total cholesterol and LDL levels reached statistical significance. There were no significant differences in lipid parameters between the 3 and 6 months, however, when expressed as degree of significance levels (P-values), the decreases in total cholesterol and LDL levels are higher at 6 months than after 3 months, compared to the baseline.

Although no significant difference was found in total cholesterol and LDL levels between 3 and 6 months, periodontal treatment as an adjunct to anti-lipemic therapy may increase the impact of statins due to the resolution of gingival inflammation. Periodontitis-induced changes in immune cell function may cause metabolic disregulation of lipid metabolism through a mechanism involving pro-inflammatory cytokines [7].

Our data, obtained in hyperlipidemic patients, agree with other studies [14-17] conducted in normolipidemic subjects with periodontitis, which have shown a positive effect of the periodontal treatment on serum lipid profile. Losche et al. [15] reported that the periodontal treatment led to slight reductions in serum lipids, although no significant changes in the plasma levels of different lipid fractions were observed. In another study, subjects with severe and generalized periodontitis received intensive periodontal treatment, including standard periodontal treatment with adjunctive local delivery of minocycline, which led to decreases in total cholesterol and LDL levels 2 months after the periodontal treatment [14].

CRP, a lipoprotein-associated inflammatory mediator, was also evaluated in our study. Similar to our results, other studies have reported significant decreases in CRP levels following a periodontal treatment [14, 18, 19].

Finally, this study shows that, in subjects with slight to moderate periodontal disease, the decrease in cholesterol levels following periodontal treatment seems to be slightly higher than the decrease recorded after 3 months with only statin treatment but no periodontal treatment, compared to the baseline.

Even if further long-term studies in larger populations with more severe periodontal disease are needed to confirm the effect of the periodontal treatment on serum lipid profiles in hyperlipidemic patients in antilipemic drug treatment, prevention and control of periodontal disease could be considered an integral part of the hyperlipidemic control.

5. CONCLUSIONS

Chronic infections, including periodontitis, may modify the serum lipid profile in a way that
STUDY ON THE EFFECTS OF CLASSICAL PERIODONTAL THERAPY ON THE LIPID PROFILE IN HYPERLIPIDEMIC AND CHRONIC PERIODONTITIS PATIENTS

increases the risk of atherosclerosis. Treatment of periodontitis may result in a potential benefic effect on the metabolic control of hyperlipidemia, thus reducing the risk for cardiovascular diseases.

References


