Non-surgical Periodontal Treatment and Low Level Laser Therapy (LLLT) Outcomes for Patients Suffering from Type 2 Diabetes Mellitus, Obesity and Chronic Periodontitis

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Abstract

To determine the level of hsCRP and HbA1c, Plaque Index (PI), Gingival Index (GI), Clinical Attachment Level (CAL) and general periodontal index, before and after nonsurgical periodontal treatment (NSPT) with additional Low-level laser therapy (LLLT).

96 subjects are included in this study suffering from T2DM, divided into three study groups: underweight, normal weight and obese subjects. Obtained values for PI, GI, CAL and CIPTN will be noted for all participants. LLLT was applied in close contact with gingiva for five consecutive days. For the determination of hsCRP and HbA1c levels blood samples are taken in the beginning of the study and control measurements after 3 months.

There was no significant difference regarding age between groups (F=12.6; p<0.05). As far as tobacco use subjects in normal weight group showed higher number of users compare to other two groups 46.9% (Chi=0.34, p>0.05). Overweight patients in group A showed higher values of PI (2.3±0.5; CV=21.7) and GI (2.2±0.4; CV=18.2). During the first visit and after 3 months moderate correlation between hsCRP and PI (r=0.50, p<0.01), GI (r=0.48, p<0.01) and CAL (p<0.01) was noted.

Keywords: Chronic periodontitis, laser therapy, type II diabetes mellitus, non-surgical periodontal treatment.

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Introduction

Colonization of dental plaque biofilms on tooth surface by invasive oral pathogens represent the initial phase of periodontal infection. Tissue destruction in periodontitis results in breakdown of the collagen fibers of the periodontal ligament, resulting in the formation of a periodontal pocket between the gingiva and the tooth. ‘Pocketing’ is not evident on simple visual inspection, and assessment using a periodontal probe is essential. Periodontitis is a slowly progressing disease but the tissue destruction that occurs is largely irreversible.

In the early stages, the condition is typically asymptomatic; it is not usually painful, and many patients are unaware until the condition has progressed enough to result in tooth mobility.

The pockets deepen as a result of the further destruction of fibers of the periodontal ligament (referred to as attachment loss and the resorption of the alveolar bone that occurs in parallel with the progressing attachment loss. Advanced periodontitis is characterized by gingival erythema and edema, gingival bleeding, gingival recession, tooth mobility, drifting of teeth, suppuration from periodontal pockets, and tooth loss. The condition is very common, with severe periodontitis that threatens tooth retention affecting 10–15% of adults in most population’s studied.¹

Numerous studies have exposed possible link between periodontitis and various systemic disease. Periodontitis has been described as a
potential risk for increased morbidity and mortality for diabetes, insulin resistance, rheumatoid arthritis, Chronic Obstructive Pulmonary Disease (COPD), obesity, osteoporosis, anemia, dialysis patients and complications of pregnancy. Evidence suggests a bi-directional relationship between periodontitis and systemic disease and metastatic extent of infection from the oral cavity as a result of transient bacteremia erasing from the contaminated dental plaque and periodontal socket which can cause immunological injury to the host, in the majority of cases this is confirmed among overweight and obese patients.7

Currently, obesity is considered as important public health problem and represents an huge risk factor which contributes in the development of many chronic disease, including T2DM. The main characteristic of this serious condition is the systemic inflammation which can be evaluated through quantification of the inflammatory markers like C-reactive protein (CRP), high sensitivity C-reactive protein (hs-CRP), TNFα, IL-1, IL-6 and IL-8.8

Diabetes has been unequivocally confirmed as a major risk factor for periodontitis. Diabetes mellitus is a metabolic disorder characterized by hyperglycemia due to defective secretion or activity of insulin.6 In the current classification of this condition, the terms “insulin-dependent diabetes mellitus” and “noninsulin-dependent diabetes mellitus” are not used, in part because they relate to treatment rather than to the diagnosis.9 A conclusive diagnosis of diabetes mellitus is made by assessing glycated hemoglobin levels; in those people with diabetes, sequential fasting plasma glucose levels will be 7 mmol/L or more.10

The causes of type 2 diabetes mellitus range from insulin resistance with relative insulin deficiency to a predominantly secretory defect accompanied by insulin resistance. The onset is generally more gradual than for type 1, and this condition is often associated with obesity. In addition, the risk of type 2 diabetes increases with age and lack of physical activity, and this form of diabetes is more prevalent among people with hypertension or dyslipidemia. Type 2 diabetes has a strong genetic component.11 People with type 2 diabetes constitute 90% of the diabetic population. Conversely, periodontitis is a risk factor for worsening glycemic control in patients with diabetes, and may increase the risk for diabetic complications. While associations between periodontal diseases and several chronic systemic diseases have been demonstrated in recent years, the most consistently supported interaction has been that between periodontal disease and diabetes.9

In recent years, some reports are describing the effects of periodontal treatment and glycemic control. Those reports are concluding that varieties of treatment approaches results in different clinical effects. The quantity of HbA1c is decreased in patients suffering from T2DM which beside conventional therapy have received systemic antibiotics,12 and furthermore there is no significant difference in HbA1c levels regardless the fact if the antibiotic therapy is administered or not, but finally the conservative periodontal treatment by its own results in improved clinical effects.13

C-reactive protein (CRP) and other acute phase molecules are usually present at relatively low levels in plasma, but may be raised dramatically within 72 hrs of tissue injury or with infection. CRP was first reported by Tillett and Francis in 1930 and was named so because it was discovered as a substance in the serum of patients with acute inflammation that reacted with the c-(capsular) polysaccharide of Pneumococcus. CRP opsonizes bacteria for complement-binding and activates complement when complexed. The normal CRP levels vary between populations, with mean values between 1.0 to 3.0 mg/l. However, using ultrasensitive methods, it is possible to detect CRP levels as low as <1.0 mg/l.14

New technologic advances have produced modern therapeutic modalities including LLLT (Low-level Laser Therapy) which in some studies have resulted with positive clinical effects in the treatment of periodontal disease in Type II Diabetes patients.15

LLLT has proven effective in the reduction of inflammation and swelling. LLLT was introduced as a therapeutic modality as early as 1968. LLLT includes wavelengths between 500 and 1,100nm and typically involves a dose of 1–4 J/cm2 using lasers with output powers of 10 – 90mW. The infrared portions of the spectrum (e.g., GaAlAs, 800–900 nm) have been shown to have highly absorbent and unique therapeutic effects in living tissues and seem to provide the best results. LLLT has shown to be effective in the treatment of impaired microcirculation, wound
healing, pain relief, fracture healing, and reduction of inflammation and swelling. 16, 17

The aim of the present study is to evaluate hs-CRP, HbA1c level, plaque index, OHI(s) index, Gingival Index (GI), Clinical Attachment Level (CAL) and Community Periodontal Index of Treatment Needs (CIPTN) index in patients suffering from Diabetes Mellitus Type 2, obesity and chronic periodontitis before and after non-surgical periodontal treatment and low-level laser therapy LLLT.

Materials and methods

Subjects were selected from patients treated at the University Dentistry Clinical Center of Kosovo in Pristina, initially the study group included 120 participants suffering from Diabetes Type II but due to subjective and objective reasons only 96 patients finished the study (from Jan 1st, 2016 until Dec 31st, 2016). All participants suffering from Diabetes Mellitus Type 2 are selected based on the International Classification of Disease, 9th Revision [ICD – 9 – CM] (6E-250.00 code). Patients were divided into three groups, overweight, normal weight and underweight (32 subjects in each group).

Inclusion criteria for participation of potential subjects in this study are:
- patients with Diabetes Mellitus Type 2
- diagnosed chronic periodontal disease
- age 30 – 80, and
- having at least 20 remaining natural teeth were considered for the study.

Exclusion criteria are:
- no past or present history of malignant disease,
- not taking medication known to influence periodontal status,
- not having history of any periodontal treatment in past 6 months.

In the beginning of the study data records for social status, smoking habit and the Body Mass Index (BMI). All patients who had history of smoking were heavy smokers (>20 cigarettes/day). Community Periodontal Index of Treatment Needs (CPITN) as an epidemiological screening procedure for periodontal treatment needs in populations was presented and described by World Health Organization since 1978, named WHO 621 (“Trinity”, with the Score 0 – 4).

In our study we used the Simplified Oral Hygiene Index (OHI-s) 18 with 6 teeth surface scored, four from posterior and two anterior teeth.

Criteria for classifying Debris:
0 - No debris or stain present
1 - Soft debris covering not more than one third of the tooth surface, or presence of extrinsic stains without other debris regardless of surface area covered
2 - Soft debris covering more than one third, but no more than two third, of the exposed tooth surface.
3 - Soft debris covering more than two thirds of the exposed tooth surface.

Loe-Silness Gingival Index (GI) was utilized for four areas of the tooth then summed and divided by four to give the GI for the tooth, later adding the values of each tooth and dividing by the number of teeth examined, to assess the prevalence and severity of gingivitis in populations, groups and individuals.

Score 0 = Normal Gingiva
Score 1 = Mild inflammation - slight change in color, sight edema. No bleeding on probing.
Score 2 = Moderate inflammation – redness, edema, glazing. Bleeding on probing.
Score 3 = Severe inflammation – marked redness and edema, ulceration. Tendency toward spontaneous bleeding.

Clinical Attachment Level (CAL)-measured clinically from the base of the pocket-PD to the cement-enamel junction - CEJ (in millimeters), using the formula PD + CEJ = CAL. Measurements at baseline for OHI-s, GI and CAL are done using dental mirror and scaled periodontal probes. After baseline measurements, clinical parameters are noted and later all participants underwent a supragingival and subgingival full-mouth scaling and root planning (FRP), using hand instruments and ultrasonic devices under local anesthesia (LIGNOSPAN, Lydocaine HCl 2%, Epinephrine 1:100000, Septodont, USA). Pocket irrigation was done with 1% chlorhexidine gel, three times in 10 minutes (Corsodyl 1%, Glaxo Smith Kline, Brentford, Middlesex, United Kingdom). Later, on the gingival part of the affected side LLLT was applied.

LLLT adjusted to (660 nm, 10mW, 8 min/daily, in contact with gingiva); model (Hager&Werken Laser HF "confort" V023-17, Duisburg, Germany) continuously in the next five days.

Blood samples were taken at baseline and at 3-month recall visit. Two milliliters of blood was
collected using 22-gauge needle and 2 ml syringes, and immediately transferred to the University Clinical Center of Kosovo Central Laboratory Department. The hs-CRP estimation was done by latex turbidometric immunoassay in a fully automated analyzer (Hitachi 911 Analyser, Hitachi Medical Corporation, Tokyo, Japan). For qualitative and quantitative analysis of HbA1c values high performance liquid chromatography device was used (Tosoh HPLC Glycohemoglobin Analyzer, Tosoh Medics, Inc., San Francisco, CA).

We re-evaluated clinical periodontal parameters, hs-CRP and HbA1c after 3 months.

The present study used SPSS statistical package (Version 18.0; SPSS Inc., Chicago, IL, USA) for the data analysis. The significance of differences in periodontal indexes on one side and hs-CRP and HbA1c among groups was compared using analysis of covariance (ANOVA) adjusted for the covariate at baseline measures.

**Results**

Regarding the gender distribution between groups, it’s evident that male subjects are dominant X(m)=63; n=96 in all groups (Chi=0.28; p>0.05). There was no significant difference regarding age discrepancy among subjects (F=12.6; p<0.01). Patients group with normal and underweight subjects have more tobacco users compare to overweight/obese group 46.9% (Chi=0.34, p>0.05). Higher average standard discrepancy regarding BMI was observed at the third group compared to other two groups (CV=6.02, p<0.01). (Table 1 and 2)

**Table 1.** Demographic characteristics by BMI groups.

<table>
<thead>
<tr>
<th>Variables</th>
<th>N=32 for each group</th>
<th>Test</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Overall</td>
<td>Underweight</td>
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<td>Gender, n (%)</td>
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<td></td>
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<tr>
<td>Female</td>
<td>12 (37.5)</td>
<td>11 (34.4)</td>
</tr>
<tr>
<td>Male</td>
<td>20 (62.5)</td>
<td>21 (65.6)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>53.3 ± 8.1</td>
<td>62.2 ± 9.5</td>
</tr>
<tr>
<td>Smoking, n (%)</td>
<td>15.20</td>
<td>15.27</td>
</tr>
<tr>
<td>Xb ± SD</td>
<td>3.48</td>
<td>2.79</td>
</tr>
<tr>
<td>Xb-average</td>
<td>3.81</td>
<td>2.59</td>
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</tbody>
</table>

**Table 2.** Dental health by BMI groups.

<table>
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**Table 3.** Pearson Correlation between blood parameters and tooth indexes (r). p<0.01.

Overweight patients represented in group A showed higher values for PI (2.3±0.5; CV = 21.7), GI (2.2 ±0.4; CV = 18.2) and CAL (5.1 ±1.1; CV = 21.6). CPITN values are much higher at obese group compare to other two groups (Chi = 19.5; p<0.05). (Table 2)

Comparative data analysis of our measurements showed that root planning and scaling of periodontal pockets resulted in improved results for PI, GI, CAL after three months.
months – compared to baseline measurement outcomes. Meanwhile, hsCRP and HbA1c levels at baseline and after three months demonstrated weak correlation with periodontal parameters. As far as the impact of baseline measurements, covariance analysis (ANOVA) was utilized to analyze differences in periodontal indexes in all three groups adapted for baseline variables. Differences of PI, GI, CAL and hsCRP values were statistically significant between groups after three months. Whereas, p value <0.05 is considered significant.

There is no correlation between HbA1c and tooth indexes, for both baseline and follow up measurements.

There is evidence that, for baseline measurement, there is moderate correlation between hs-CRP and plaque index (r = 0.50, p <0.01), gingival index (r=0.48, p<0.01) and clinical attachment level (r=0.53, p<0.01). There is weak correlation (between all three groups), for follow up measurement, between hs-CRP and plaque index ( r = 0.35, p <0.01), gingival index(r=0.32, p<0.05), while the correlation is moderate between hs-CRP and clinical attachment level (r=0.49, p<0.01). (Table 4)

**Discussion**

Certain literature data are confirming that presence of periodontal disease in patients suffering from T2DM can be a potential threat for health. Worsened periodontal status have the potential to make worse the primary disease. In some studies there is a positive correlation between obesity and periodontal disease, whereas in some other studies this correlation was weak or absent.

Age, gender, alcohol consumption, tobacco use and BMI are by some means risk factors, but these causes are related to periodontal disease. The most prominent risk factors for periodontal disease are age and tobacco use, but the conjoin effect of tobacco use and BMI are confirmed factors related to periodontal disease. Although smoking and BMI are independent variables, up till now its stated that they represent risk factors that are showing linkage to periodontal disease.

The results of our present study among type 2 diabetes patients suffering from chronic periodontitis after root planning and scaling with additional LLLT for five days demonstrated significant decrease of hs-CRP serum levels (baseline 0.758 mg/dl and after three months 0.403 mg/dl ) and for HbA1c serum levels (baseline 7.9 mmol/mol and after three months 7.1 mmol/mol) in group A (normal weight patients), whereas those values were not significant for other two groups B and C (obese and underweight)-Table 4.

<table>
<thead>
<tr>
<th>Group</th>
<th>Baseline</th>
<th>3 Months</th>
<th>p Value</th>
<th>Baseline</th>
<th>3 Months</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A</td>
<td>7.0 ±1.9 (63±14)</td>
<td>7.1 ± 1.2 (54±9)</td>
<td>0.028*</td>
<td>0.758 ± 0.294</td>
<td>0.403 ± 0.101</td>
<td>0.034*</td>
</tr>
<tr>
<td>Group B</td>
<td>8.3 ± 1.2 (52±8)</td>
<td>8.1 ± 1.4 (51±7)</td>
<td>0.692</td>
<td>0.204 ± 0.09</td>
<td>0.203 ± 0.03</td>
<td>0.387±0.08</td>
</tr>
<tr>
<td>Group C</td>
<td>7.8±2.2 (71±21)</td>
<td>7.2±1.3 (64±13)</td>
<td>0.011</td>
<td>0.387±0.08</td>
<td>0.203±0.03</td>
<td>0.201±0.07</td>
</tr>
</tbody>
</table>

**Table 4.** Correlation between HbA1c and hsCRP values.

Obradović R. et al. evaluated the efficacy of LLLT in diabetic periodontitis through histological analysis, findings of gingival tissue treated with LLLT showed expressed healing, as is evident by the absence of inflammatory cells. Tissue edema could not be seen, and the number of blood vessels was reduced. Therefore, authors concluded that LLLT has shown efficacy in the treatment of periodontitis in patients suffering from diabetes mellitus.

In another study, realized by the same author (Obradović R. et al.) demonstrated the effectiveness of LLLT in the treatment of periodontitis among patients suffering from diabetes type 1 and diabetes type 2. Results obtained from their study, demonstrated that LLLT as an adjunct in periodontal therapy reduces gingival inflammation in patients with diabetes mellitus type 1 & 2 and periodontitis. Results of our study were not similar to those reported by Anna Dongari Bagtazoglu et al., who, in their meta-analysis do not support the hypothesis that periodontal treatment can reduce systemic CRP levels.

Igić et al., conducted a pioneering attempt to demonstrate the events in the gingival cells during inflammation, as well as the changes occurring after LLLT treatment in children. They confirmed that gingivitis can be successfully treated with LLLT as a supplement to basic treatment. Cytomorphometric analysis confirmed that the nuclei of the squamous stratified gingival
epithelium were reduced in size after basic treatment, although not to the size of the nuclei of healthy gingiva.22

Our findings are similar to literature data indicating that adjuvant LLLT therapy reduces gingival inflammation during periodontal treatment and gives better results that basic periodontal treatment alone.23,24,25,26,27

D’Aiuto et al., conducted a pilot study on 94 subjects and assessed serum CRP and IL-6 levels at baseline and at 2 and 6 months following non-surgical periodontal therapy. They found significant reduction in CRP and IL-6 serum levels, along with improvement in all clinical periodontal parameters with therapy.28 Tonetti et al., report from their study that CRP and IL-6 levels did decrease 6 months after therapy in both treatment group, standard periodontal therapy and intensive periodontal therapy, but Tonetti and colleagues suggest that CRP and other markers might not adequately reflect the relevant inflammatory pathways or that the long-term improvements were independent of the systemic inflammatory response.29 Yamazaki et al., report from a study on Japanese that there was no statistically significant difference in IL-6 and hsCRP before and after therapy. They report that this lack of statistical significance may reflect the various contributions made by periodontal disease to the total burden of inflammation in different patients and the relatively small numbers in patients.30

Raman et al., in his study on 40 subjects with type 2 diabetes suffering from diabetes mellitus and chronic periodontitis recorded statistically significant decrease of HbA1c levels three months after NSPT treatment, meanwhile patients who demonstrated ≥50 % reduction of PPD showed significant reduction of HbA1c and hs-CRP levels (p=0.004 and p=0.012).31

Lalla et al., recorded 50% reduction of clinical parameters from baseline, furthermore the authors support the statement that evidences have always indicated that non-surgical periodontal treatment is the gold standard of periodontal treatment and the results of this study concur.32

Meanwhile, Sgolastra et al., conducted a meta-analysis on randomized clinical trials on the effect of periodontal treatment on metabolic control. They reported that NSPT was effective at reducing HbA1c and fasting plasma glucose, it is interesting to note that the control group which received OHI alone also demonstrated reductions in their HbA1c levels (p=0.053, ES=0.495).33

Ismail et al., demonstrated that LLLT decreased clinical parameters of CP. The levels of IL-1α and IL-1β in GCF were decreased (p<0.05), but the level of MMP-9 was increased (p<0.01). After LLLT, the level of IL-1α correlated positively with MMP-9 (p<0.05) and the MMP-9 levels correlated negatively with plaque index (p<0.05) and papillary bleeding index (p<0.01), concluding that whether elevated levels of MMP-9 in GCF might be beneficial for reparation processes.34

HbA1c reductions as high as 17.1% have also been reported by Stewart et al., The reduction in HbA1c levels for the NSPT group concur with findings by Darre et al., who reported a reduction of 0.8% (9mmol/mol) following periodontal therapy.36

In one recent study, which was carried out Meqa et al., they utilized scaling and root planning (SRP), SRP + photodynamic therapy (PDT), SRP + low-level laser-therapy (LLLT) and basic therapy, in all four quadrants. A significant reduction of PPD, CAL, GI and BOP for the PDT treated quadrants, with similar results for LLLT and SRP-treated sites. The PDT group in this study showed significantly higher PPD reduction than the other two study groups after four and eight weeks (P<.01 and P<.001, respectively).37 Results from our study were not in agreement with a study by Llambers et al., reported no concurrent statistically significant improvements in the levels of HbA1c.38

Relevant results were obtained by Engerbretson et al. showing that in general, the non-surgical periodontal therapy did not improve glycemic control in patients with Diabetes Mellitus Type 2 and moderate to advanced chronic periodontitis, and based on their findings authors do not support the use of non-surgical periodontal treatment in patients with diabetes for the purpose of lowering HbA1c.39 Wang et al. in their meta-analysis, exploring nineteen randomized trials showed that adding Doxycycline to non-surgical periodontal therapy does not significantly improve metabolic control in patients with Type 2 Diabetes Mellitus and chronic periodontitis, results also reinforce that diabetes is a risk factor for periodontitis. However, evidence suggests that periodontal therapy itself improves metabolic control.40
Very reliable research completed by bin Zulkeple et al., found that there were no significant differences between participants of the control and test groups in the percentages of sites with the presence of plaque and bleeding on probing (p &gt; 0.05). On the other hand, significant differences were found between both groups in their percentages of sites with clinical attachment loss of 4-6 mm (p = 0.13) and number of missing teeth (p = 0.20). The findings of the present study suggest that postmenopausal women have more severe periodontal destruction compared to premenopausal females. 41

Mirnić J. et al. in their study demonstrated that there was no significant difference between non diabetic and diabetic patient group in the success of metabolic control and periodontal indexes outcomes between baseline and the results obtained after three months. 42

Even though current available literature is very modest regarding the effects of LLLT on periodontal tissue, as far as T2DM patients those information’s are also limited on decreased inflammation of gingival tissue, improved microcirculation and acceleration of healing process, and recovering effect on periodontal complex. 43

Very reliable research completed by bin Ahmed et al., regarding the correlation between menopause and chronic periodontitis utilizing diacerein in the treatment protocol showed that significant change and improvement of all the measured clinical parameters with the reduction of IL-1β and osteocalcin levels especially in the group in which diacerein was given. Diacerein has a playful therapeutic effect in management of chronic periodontitis. 44

Conclusions

Within the limitations of this study, non-surgical periodontal treatment together with Low Level Laser Therapy (LLLT) is associated with improved clinical parameters and decreased levels of hs-CRP and HbA1c in normal weight patients with Diabetes Mellitus Type 2, but there was low impact on those levels for obese and underweight subjects.

There is evidence that, for baseline measurement, there is moderate correlation between hs-CRP and plaque index, gingival index and clinical attachment level.

There is no correlation between HbA1c and tooth indexes, for both baseline and follow up measurements.

Acknowledgments

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Declaration of Interest

The authors report no conflict of interest.

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