The Effect of Periodontal Treatment on Circulating Tumor Necrosis Factor-Alpha and Insulin Resistance in Patients with Type 2 Diabetes Mellitus

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Abstract. The aim of this study is to investigate the effect of periodontal treatment on the relation between inflammation and insulin resistance in patients with type 2 diabetes mellitus. Group I included 15 type-2 diabetic patients with chronic periodontitis; Group II were systemically healthy 15 patients with chronic periodontitis and family history of Type 2 diabetes mellitus; while Group III included 10 Type 2 diabetic patients without chronic periodontitis and was considered as a control group. Circulating TNF-α level, glycated hemoglobin, fasting blood glucose, fasting human serum insulin concentration as well as insulin sensitivity assessed using HOMA-IR were measured before and after 3 months of periodontal treatment that were composed of conventional mechanical treatment with adjunctive systemic doxycycline therapy. Higher levels of the assessed parameters were observed in type 2 diabetic patients with periodontitis compared to those without periodontitis. Circulating TNF-α level significantly was reduced after periodontal treatment. The results indicate that periodontal treatment was effective in improvement of insulin sensitivity and glycemic control in Type 2 diabetics, which could be explained by reduced serum TNF-α with its insulin resistance mediated effect.

Keywords: Diabetes mellitus, Insulin resistance, Periodontitis, Tumor necrosis factor.
Introduction

Diabetes Mellitus (DM) comprises a group of common metabolic disorders that share the phenotype of hyperglycemia. Several distinct types of DM exist and are caused by a complex interaction of genetics, environmental factors, and lifestyle choices. Depending on the etiology of DM, factors contributing to hyperglycemia may include reduced insulin secretion, decreased glucose utilization, and increased glucose production. The metabolic irregularity associated with DM causes secondary pathophysiologic changes in multiple organ systems that impose a tremendous burden on the individual with diabetes and on the health care system[1]. The two most common forms of diabetes mellitus are type-1, formerly insulin dependent diabetes mellitus (IDDM), and type-2, formerly non-insulin diabetes mellitus (NIDDM)[2].

Type 2 diabetes is the most common type of DM, which accounts roughly for 85% of the cases and generally occurs in individuals over 40 years of age. Although, Type 2 is so called multiple risk syndrome, lowered insulin sensitivity; named insulin resistance, is the major pathogenic factor in the etiology of the disease[3,4]. Diabetes mellitus requires continuous lifelong management to reduce the high morbidity and premature mortality caused by its associated complications. These complications can be reduced, if not completely prevented, with early diagnosis and treatment to achieve optimal glycemic control[5].

Insulin resistance (decreased sensitivity or responsiveness to the metabolic action of insulin) is determined by both genetic and environmental factors[6]. Insulin resistance also is a predictor of Type 2 DM development even in individuals with normal glucose tolerance[7], and observed in first degree relatives of patients with Type 2 diabetes[8]. It is also generally accepted that infection results in a state of insulin resistance[9], and accumulating evidences suggest that Type 2 DM is associated with chronic low grade inflammation[10]. Recently, inflammation and inflammatory cytokines have been postulated to be important additional pathogenic factor in development of Type 2 DM[11].

Periodontitis is a chronic destructive inflammatory disease of the tooth supporting tissues. It affects 10-15% of the adult population and represents the major cause of tooth loss[12]. The prevalence of periodontal diseases has been reported as 60% in subjects with Type 2 diabetes and as 36% in patients without diabetes[13]. Periodontitis also
has been reported as one of diabetes complications\textsuperscript{[14]}. Attention has been focused on our understanding of the negative influences of oral chronic inflammation on systemic health\textsuperscript{[15]}. Research has established a strong relationship between periodontal diseases and diabetes. This relation can be seen clinically and more recently on the molecular level\textsuperscript{[16]}. Both diseases are thought to share a common pathogenesis that involves an enhanced inflammatory response that can be observed at the local and systemic levels\textsuperscript{[17]}. The inflamed periodontium is highly vascular and the ulcerated pocket epithelium may serve as a portal to the systemic circulation for the bacterial products and locally produced inflammatory mediators\textsuperscript{[18]}. Furthermore, patients with periodontitis and diabetes were found to have significantly higher levels of local inflammatory mediators, compared to systemically healthy individuals with periodontal diseases\textsuperscript{[19]}.

Tumor necrosis factor-alpha (TNF-α) is a pro-inflammatory cytokine secreted by macrophages, monocytes, neutrophils, T-cells and Natural Killer cells following their stimulation by bacterial products\textsuperscript{[20]}. Studies have reported higher levels of TNF-α in serum of chronic periodontitis patients\textsuperscript{[3,21,22]}. Moreover, in human cross-sectional studies, elevated circulating TNF-α levels are associated with insulin resistance in Type 2 diabetics, as well as in non-diabetic offspring and may predict later impairment in insulin action\textsuperscript{[23-25]}.

The mechanisms by which TNF-α suppresses insulin action have been proposed by several investigators. In 1992, Feingold et al.\textsuperscript{[26]} first suggested that TNF-α produces dysregulation of lipid metabolism, thus release of high levels of free fatty acids (FFA), LDL and triglycerides (TRGs) which thought to induce insulin resistance indirectly\textsuperscript{[27,28]}. TNF-α may also decrease insulin action indirectly by modifying the hypothalamic-pituitary adrenal axis, and increases plasma concentrations of insulin counter-regulatory hormones; adrenocorticotropic hormone, cortisol, adrenaline and glucagons\textsuperscript{[29]}.

TNF-α can suppress insulin action directly by suppressing mRNA stability of Glucose transporter-4 (GluT\textsubscript{4})\textsuperscript{[30]}. Also, it suppresses mRNA encoding for Insulin receptor substrate-1 (IRS-1)\textsuperscript{[31]}. Furthermore, it induces formation of intra-cellular hydrogen peroxide, which directly inhibits the insulin receptor tyrosine phosphorylation\textsuperscript{[32]}. TNF-α has been identified as a potent antagonist to the cell surface insulin receptor substrate\textsuperscript{[33]}. It also interferes with insulin signaling by Serine/threonine
phosphorylation of IRS-1. The serine phosphorylated IRS-1 may block the autophosphorylation reaction in IR\cite{34}, leading to an inhibition of insulin induced tyrosine phosphorylation and insulin action in intact cells\cite{35}. Therefore, TNF-α can be a perfect candidate to study the inflammatory link between diabetes and periodontal diseases at a molecular level.

Additional evidence for the role of periodontal diseases complicating DM comes from studies examining the association between periodontal disease and diabetes metabolic control\cite{36}. It was further illustrated by recent studies demonstrating that effective treatment of periodontitis may actually improve some diabetic complications, and were associated with lower levels of glycated hemoglobin\cite{37}. The reduction in periodontal inflammation may help decrease inflammatory mediators in the serum that are associated with insulin resistance, thereby, improving glycemic control\cite{3,38}.

Therefore, this clinical study was conducted to determine the clinical significance of the relationship between periodontal inflammation and glycemic control, as well as the effect of periodontal treatment on both circulating TNF-α levels and insulin resistance in Type 2 diabetics.

**Subjects and Methods**

**Study Population**

A total of forty patients (25 females and 15 males), aged 35 to 55 years (mean age 45.6 ± 7.9) were selected from the out-patient clinic of the Department of Oral Medicine and Periodontology, Faculty of Dentistry, Ain Shams University.

All patients were screened and selected for non-smokers and free from any systemic diseases using medical questionnaire, guided by Cornell Medical Index\cite{39}, except for Type 2 diabetes mellitus in diabetic groups. Also, for patients who are not receiving any systemic drug at the time of the examination and for at least four weeks prior to the study; except for oral hypoglycemic drugs for the diabetic groups, which was unchanged during and at least 2 months before the start of the study. As well as any patient that reports any changes during study period were excluded. Pregnant females as well as breast feeding mothers, and patients who had contraindications to doxycycline therapy were excluded.
from the study. The proposed nature of the study was explained and informed. Consent was obtained from all patients before starting the study. Both the protocol and consent form were reviewed and approved by the ethical committee of the Faculty of Dentistry, Ain Shams University, Egypt. The study was conducted in accordance with the ethical principles provided by the Declaration of Helsinki and according to the principles of good clinical practice.

Patients were classified into three study groups; Group I included 15 Type 2 diabetic patients with moderate to severe chronic periodontitis (mean probing depth 3.176 ± 0.228 mm and mean clinical attachment loss 4.715 ± 0.703 mm); Group II were 15 systemically healthy patients with moderate to severe chronic periodontitis (mean probing depth 3.179 ± 0.162 mm and mean clinical attachment loss 4.326 ± 0.259 mm) and with a family history of Type 2 diabetes mellitus (two first degree relatives - at least one parent - with type 2 diabetes). While Group III included 10 type 2 diabetic patients without chronic periodontitis and was considered as a control group. Group I and III were the diabetic groups (Table 1).

Table 1. Demographic parameters of the study groups.

<table>
<thead>
<tr>
<th>Gr. I</th>
<th>Age (years)</th>
<th>Gender Distribution</th>
<th>Clinical Parameters</th>
<th>Recalls</th>
<th>Diabetic Status</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>49.7 ± 5.5</td>
<td>5 m/33.3% 10 f/66.7%</td>
<td>7 Y/46.6% 8 N/53.4%</td>
<td>6.2 ± 4.4</td>
<td>100% 1 Y/66% 14 N/34%</td>
</tr>
<tr>
<td>Gr. II</td>
<td>45 ± 6.4</td>
<td>6 m/40% 9 f/60%</td>
<td>15 Y (100%)</td>
<td>Non diabetics</td>
<td>0% 0%</td>
</tr>
<tr>
<td>Gr. III</td>
<td>42 ± 5.3</td>
<td>4 m/40% 6 f/60%</td>
<td>6 Y/60% 4 N/40%</td>
<td>3.2 ± 1.7</td>
<td>100% 0%</td>
</tr>
</tbody>
</table>

Treatment Regimen

Both, Group I and Group II have received the conventional periodontal therapy, which included instructions in self-performed plaque control measures, including tooth brushing with a soft dental brush; interdental cleaning with interdental brush or dental floss, and adjunctive chlorhexidine gluconate (0.2%) mouthwash three times per day for 10 days. As well as full mouth supra, sub-gingival scaling and root planning using ultrasonic scaler and hand instruments, besides the adjunctive systemic doxycycline hyclate 100 mg capsule once per day for 14 days. Recall appointments were done every 2 weeks throughout the study period for professional prophylaxis and oral hygiene reinforcement.
**Periodontal and Laboratory Parameters Assessments**

Both periodontal and laboratory parameters were assessed at baseline and 3 months after treatment, except for the control group that were assessed only at baseline.

Periodontal parameters included; plaque index (PI)\(^{[40]}\), sulcus bleeding index (BI)\(^{[41]}\), probing depth (PD), and clinical attachment level (CAL)\(^{[42]}\). PD and CAL were measured using Ash William’s graduated periodontal probe of 0.8 mm cross-sectional diameter. This was introduced to the depth of the pocket nearly parallel to the long axis of the tooth; four readings were recorded for each tooth: Mesiobuccal, Midbuccal, Distobuccal and Midlingual.

 Patients were instructed to remain fasting for at least 8 hrs. Venous blood samples were withdrawn from radial venipuncture for each patient, and assayed for fasting plasma glucose (FPG) measured with glucose-oxidase-peroxidase method*. The glycated hemoglobin A1c (HbA1c) concentration using (ionic-exchange-chromatographic-spectrophotometric) method¥. Fasting human serum insulin concentration (SIC) and Serum total TNF-α concentration was measured using commercially available Enzyme Amplified Sensitivity Immunoassay (EASIA)#$.

Body Mass Index obtained by \(\frac{\text{Weight (Kg)}}{[\text{Height (m)}]^2}\) was recorded as to exclude the possibility that the changes in parameters after treatment were mediated through weight loss\(^{[43]}\) and based on FPG and SIC. Homeostasis Model Assessment for insulin resistance (HOMA-IR) score was applied as a measure for insulin resistance analysis using the following formula:

\[
\text{HOMA-IR} = \frac{\text{Fasting SIC (µIU/ml) } \times \text{ FPG (mg/dl)}}{405} \tag{[44]}\]

**Statistical Analysis**

One-way statistical analysis of variance (ANOVA) (Procedure of SAS\(^{††}\)), followed by Duncan's multiple range test, were used to test the effect of groups on periodontal and other parameters. Paired \(t\)-test

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\(\ddagger\) SAS version 9.1, SAS Institute, Cary, NC
(Procedure Means of SAS) was used to test the effect of periodontal treatment of periodontal and other parameters. Cross tabulation and Chi-square test (Procedure Frequency of SAS) were run to test the effect of group on the prevalence of different scores as well as the relation between scores. Spearman simple correlation coefficient (Procedure CORR of SAS) was calculated between different parameters before treatment.

**Results**

All patients were committed to treatment protocol throughout the 3 months period of the study, and no one has reported any adverse reactions to systemic doxycycline therapy. There were no significant differences in the mean of BMI -with p-value ≤ 0.05- between the three groups; neither before treatment nor after treatment, also in each group before and after treatment. The mean duration of diabetes was (6.2 years ± 4.4) and (3.2 years ± 1.7) in Groups I and III, respectively.

In all periodontal parameters a highly statistical significant reduction after treatment was observed in Group I, with a mean reduction in PI, BI, PD and CAL (-1.4037 ± 0.268, -1.4037 ± 0.2680, -1.0232 ± 0.5287, -1.5464 ± 0.7915), respectively and in Group II, -1.6010 ± 0.2368, -1.6010 ± 0.2368, -1.1978 ± 0.3130, 1.2584 ± 0.4907, respectively (Table 2).

<table>
<thead>
<tr>
<th>Table 2. Mean of periodontal parameters in different groups before and after periodontal parameters treatment.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Before Treatment</strong></td>
</tr>
<tr>
<td><strong>Group</strong></td>
</tr>
<tr>
<td>PI</td>
</tr>
<tr>
<td>Group I</td>
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<tr>
<td>Group II</td>
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<tr>
<td>Group III</td>
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<tr>
<td>BI</td>
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<tr>
<td>Group I</td>
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<td>Group II</td>
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<tr>
<td>Group III</td>
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<tr>
<td>PD (mm)</td>
</tr>
<tr>
<td>Group I</td>
</tr>
<tr>
<td>Group II</td>
</tr>
<tr>
<td>Group III</td>
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<tr>
<td>CAL (mm)</td>
</tr>
<tr>
<td>Group I</td>
</tr>
<tr>
<td>Group II</td>
</tr>
<tr>
<td>Group III</td>
</tr>
</tbody>
</table>

*** = Significant at p ≤ 0.001, SD = Standard deviation, p = Probability level, dt = Duncan’s Multiple Range Test. Same letter within each column are not significantly different (p ≤ 0.05) NS = Insignificant (p > 0.05).
Based on the mean clinical attachment, loss patients in each group were further categorized regarding the severity of periodontitis; into mild periodontitis (mean CAL 1-2 mm), moderate periodontitis (mean CAL 3-4 mm), and severe periodontitis (mean CAL/ > 5 mm). Group I (91.7%) had moderate periodontitis and (8.3%) had severe periodontitis before treatment while, after treatment all patients had mild periodontitis. In Group II all the patients had changed from moderate periodontitis before treatment into mild periodontitis after treatment (Fig. 1).

There was a reduction of mean FPG in Group I from 213.6 ± 49.924 mg/dl to 208.7 ± 36.648 mg/dl; while in Group II, mean FPG level changed from 96.0 ± 17.807 mg/dl to 86.3 ± 14.057 mg/dl after treatment, compared to the control group, which was 151.1 ± 26.987 mg/dl. Although, not statistically significant. Group II (28.6%) had a range of FPG level between 110-125mg/dl (pre-diabetics), while after treatment the percentage of pre-diabetics in this group became 14.3%.

The mean of SIC in Group I decreased from 21.192 ± 15.998μIU/L to 12.383 ± 8.432 μIU/L, while in Group II changed from 14.357 ± 5.623 μIU/L to 12.264 ± 8.261 μIU/L after treatment, compared to the control group (11.780 ± 1.163 μIU/L).

On HbA1c concentration analysis, no statistically significant differences were found in Group I and II (p < 0.05), although the mean of HbA1c concentration in Group I decreased from (9.200 ± 2.038%) to (8.583 ± 1.755%), and changed from (4.793 ± 0.726%) to (4.600 ± 0.873%) in group II, but the control group was (6.440 ± 1.137%).
Furthermore, the percentage of good controlled diabetics in group one was changed from 13.4% to 40% and no more uncontrolled patients was found after treatment (Fig. 2).

Concerning TNF-α results, the mean baseline TNF-α level was higher in periodontitis Groups I and II (23.197 ± 12.858 pg/ml, 30.210 ± 20.729 pg/ml), respectively, than Group III (12.137 ± 5.731 pg/ml) without periodontitis. The mean of TNF-α level in Group I decreased from 30.210 ± 20.729 pg/ml to 13.231 ± 6.459 pg/ml, while in Group II changed from 23.197 ± 12.858 pg/ml to 17.315 ± 10.799 pg/ml with a statistically significant difference between before and after treatment levels (Fig. 3).
The mean of HOMA-IR Score in Group I decreased from $11.724 \pm 9.857$ to $6.721 \pm 5.059$ after treatment, while in Group II changed from $3.398 \pm 1.531$ to $2.677 \pm 1.910$), compared to HOMA-IR Score in the control group, which was $4.379 \pm 0.793$ (Table 3).

Table 3. Mean of biochemical parameters in different groups before and after treatment.

<table>
<thead>
<tr>
<th>Biochemical Parameters</th>
<th>Before Treatment</th>
<th>After Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group</td>
<td>Mean</td>
</tr>
<tr>
<td>FPG (mg/dl)</td>
<td>Group I</td>
<td>213.6</td>
</tr>
<tr>
<td></td>
<td>Group II</td>
<td>96.0</td>
</tr>
<tr>
<td></td>
<td>Group III</td>
<td>b</td>
</tr>
<tr>
<td>SIC (μIU/L)</td>
<td>Group I</td>
<td>21.192</td>
</tr>
<tr>
<td></td>
<td>Group II</td>
<td>14.357</td>
</tr>
<tr>
<td></td>
<td>Group III</td>
<td>B</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>Group I</td>
<td>9.200</td>
</tr>
<tr>
<td></td>
<td>Group II</td>
<td>4.793</td>
</tr>
<tr>
<td></td>
<td>Group III</td>
<td>B</td>
</tr>
<tr>
<td>TNF-α (pg/ml)</td>
<td>Group I</td>
<td>23.197</td>
</tr>
<tr>
<td></td>
<td>Group II</td>
<td>30.210</td>
</tr>
<tr>
<td></td>
<td>Group III</td>
<td>B</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>Group I</td>
<td>11.724</td>
</tr>
<tr>
<td></td>
<td>Group II</td>
<td>3.398</td>
</tr>
<tr>
<td></td>
<td>Group III</td>
<td>b</td>
</tr>
</tbody>
</table>

Fig. 4. Prevalence of insulin resistant patients in the study groups before and after treatment.
The percentage of insulin resistance patients in Group I before treatment was (100%) and changed to (86.7%) after treatment. While in Group II (93.3%) were insulin resistance and changed to (60%) after treatment (Fig. 4). A positive correlation was found between serum TNF-α and insulin resistance, although, it was statistically insignificant.

Discussion

It has been clear that inflammation is a possible link between diabetes and periodontal disease\textsuperscript{[45]}. Further researches were needed to clarify how inflammatory periodontal disease may affect insulin resistance and glycemic control\textsuperscript{[46]}. Gram-negative bacteria derived LPS are considered a potent inducer of TNF-α from monocytes and macrophages, chronic periodontitis induces prolonged, continuous LPS infusion as well as local and systemic TNF-α production\textsuperscript{[33]}. Furthermore, TNF-α has been implicated as a causative factor in insulin resistance and in Type 2 diabetes through different direct and direct mechanisms, both animal models and in human studies\textsuperscript{[23,47,48]}. Therefore, it can be hypothesized that chronic periodontal infection contributes to state of insulin resistance through chronic up-regulation of TNF-α in response to LPS from subgingival bacteria, which is a possible mechanism contribute to increase diabetes severity and complicate diabetes control\textsuperscript{[37]}.

This study investigated the effect of periodontal therapy on Type 2 diabetes patients with periodontitis by assessing the effect of this therapy on the level of circulating TNF-α and insulin resistance.

It was worth including Group II in this study as first-degree relatives of subjects with Type 2 diabetes demonstrate the insulin resistance before they develop overt diabetes\textsuperscript{[49]}, and because hyperglycemia further impairs both, insulin action and insulin secretion\textsuperscript{[50]}. The study of primary metabolic defects leading to insulin resistance is best undertaken before insulin secretion begins to fail and blood glucose rises\textsuperscript{[51]}. Furthermore, previous studies have examined the relationship between periodontal disease and longitudinal changes in glucose control and circulating TNF-α levels in non-diabetic off-springs of Type 2 diabetics\textsuperscript{[25,52]}. But, to best of our knowledge this is the first study to evaluate the effect of periodontal treatment on both, circulating TNF-α levels and insulin sensitivity in those highly susceptible subjects.
The use of doxycycline as an adjunct to mechanical periodontal treatment in diabetics might have benefit as a broad spectrum antibiotic effective against most of periodontal pathogens. This reaches concentrations in gingival fluid 7 to 10 fold over serum levels, as well as a potent modulator of the diabetic patient's host response to periodontal infection by inhibiting non-enzymatic glycation of extracellular proteins, and possibly, has a similar effect on glycation of hemoglobin as well.

Recent studies have concluded that HOMA-IR is a simple index that is strongly correlated with insulin resistance index assessed by the accurate. However, complex and laborious euglycemic-hyperinsulinemic clamp, "The gold standard method for assessing insulin sensitivity", in both obese and normal range-weight Type 2 diabetic patients, as well as healthy subjects. Similarly, the values of IR obtained by this index can be predictive of the occurrence of diabetes. This index also provides a more reasonable index for insulin sensitivity than fasting serum insulin purse, because in diabetics fasting hyperglycemia is usually accompanied by inadequate insulin secretion. Hence, this problem is overcome by the mathematical model of this score[53-55].

There was no reduction in the mean BMI in any group at the end of the study; therefore, this excludes the possibility that the changes in different parameters after periodontal treatment were mediated through weight loss. In accordance with previous studies, the treatment regimen may help in reduction in bacterial load and local inflammation, which explain significant improvement in all periodontal parameters after periodontal treatment[56-58].

The present results were in accordance with the study done by Iwamoto et al.[3] who showed a significant reduction in FPG by an average (7.45 mg/dl), and in SIC by an average (3.88 μIU/ml) after mechanical periodontal therapy with adjunctive local minocycline. This reduction was explained by decreased need of endogenous insulin to maintain blood glucose homeostasis that may be mediated through improved insulin resistance after treatment. Moreover, these results highlight the possible effect of periodontal treatment on improving insulin sensitivity in those patients.

Furthermore, on comparing baseline mean levels of FPG and SIC in Group II to Group III, the SIC of non-diabetics with periodontitis in Group II (14.357 ± 5.623 μIU/ml) were higher and insignificantly
different from that of diabetics without periodontitis in Group III (11.780 ± 1.163 μIU/ml). Although, the FPG were lower and significantly different in Group II (96.0 ± 17.807 mg/dl) compared to Group III (151.1 ± 26.987 mg/dl). These findings strongly support the previous researches that have observed insulin resistance in first degree relatives of patients with Type 2 diabetes, which was not yet enough to develop fasting hyperglycemia\textsuperscript{[7,8,51]}. Interestingly, these findings support the hypothesis that chronic periodontitis as a subclinical inflammation may have a role in the predisposition of insulin resistance and type 2 DM\textsuperscript{[10,59]}.

The mean change in HbA1c in Group I was -0.7154 ± 1.3428% and -0.1929 ± 0.7995% in Group II, denoting a better glycemic control in both groups with treatment, which are in accordance with other studies\textsuperscript{[60-62]}. Previous investigations of the effect of periodontal treatment on glycemic control of Type 2 diabetics showed great controversy. Early studies have shown that the combination of scaling and root planning with systemic doxycycline therapy was associated with an improvement in periodontal status that was accompanied by a greater significant improvement in glycemic control, compared to mechanical treatment alone\textsuperscript{[60,61]}. Grossi \textit{et al.}\textsuperscript{[62]} who used the same treatment regimen in our study, but with a larger sample size showed at 3 months, significant reductions in mean HbA1c reaching nearly 10% from the pretreatment value.

Several studies also documented significant improvement in HbA1c even in well-controlled diabetics who had mild periodontitis after localized scaling and root planning\textsuperscript{[63,64]}. In a meta-analysis study of 10 intervention trials that included more than 450 patients, found that average decrease in actual HbA1c level was (0.66%) in Type 2 diabetic patients and 0.71% if antibiotics were given to them. However, none was statistically significant\textsuperscript{[65]}.

Contrary to other studies showed no significant improvement in glycemic control despite improvements in patients’ periodontal health\textsuperscript{[66,67]}.

The change in HbA1c concentration in our study after treatment; although, insignificant. However, the mean absolute reduction of 0.7% often are considered to be clinically significant in the practice of medicine\textsuperscript{[46]}.
Since several parameters that could be confound to this glycemic control were explored, including medication change, weight loss or non-dental infection, and no moderating effect was associated with any of these variables. Thus, this reduction, although statistically insignificant, is likely due to the combined effect of mechanical periodontal treatment and possibly, the doxycycline mediated antimicrobial effect and inhibition of glycation process. The statistical insignificance may be due to relatively short follow up period, which was not adequate to register variations in HbA1c levels, and/or the small sample size.

The observed correlation between periodontal attachment loss and circulating TNF-α as well as, subsequent reduction in its level after periodontal treatment was independent of BMI. Thus, more likely to be explained by results from previous studies suggesting that periodontitis may influence plasma TNF-α levels by one of three mechanisms; 1) enhanced production of TNF-α due to hyper-responsiveness of diabetic monocytes to bacterial challenge, 2) endotoxin entering the circulation from the periodontal biofilm, 3) or from a direct cytokinaemia due to translocation of cytokines from the periodontal space into the circulation through ulcerated periodontium[19,68].

A significant decrease was observed in percentage of insulin resistance patients in Group I by 13.3% and more interestingly by 33.3% in Group II, which are not due to change in dose. Due to type of drugs or weight loss, thus, most probably the reduction was in response to improvement in periodontal status after treatment. These results were in accordance with Iwamoto et al.[3] who suggested that improvement in insulin sensitivity after treatment may be mediated by the reduction of circulating TNF-α with its known role in development of insulin resistance. Therefore, target groups for routine complete periodontal examination and effective treatment of periodontal infection should be expanded to include not only Type 2 diabetic patients, but also the genetically predisposed susceptible non-diabetic off-springs.

In conclusion, it’s recommended monitoring local TNF-α level and its relation to serum TNF-α concentration and insulin sensitivity in Type 2 diabetics with chronic periodontitis before and after periodontal treatment. This would be beneficial for further evaluating the effect of periodontal treatment on this group of patients. Furthermore, clinical periodontal research needs to progress rapidly in determining the
adequate treatment protocols for diabetic patients. Hence, as in regard to clinical trials of proper antimicrobial agents (both systemically or locally delivered), or the use of anti-inflammatory agents that would act at any level of inflammatory cascade to diminish the overall burden of increased inflammatory response in these patients.

References


تأثر علاج اللثة على العلاقة بين الالتهابات ومقاومة الإنسولين في المرضى الذين يعانون من مرض السكري من نوع 2

علا عزت، وسوزان سيف الله إبراهيم، و هالة كمال عبد الجابر
قسم طب القدم وعلاج اللثة والتشخيص والأشعة
كلية طب الأسنان
جامعة عين شمس ، القاهرة – جمهورية مصر العربية
و جامعة الملك عبد العزيز
جدة - المملكة العربية السعودية

المستخلص. الهدف من هذه الدراسة التحقق من أثر علاج اللثة والعلاقة بين مقاومة الإنسولين والالتهاب في المرضى المصابين بالسكري نوع 2. الأساليب: الفريق الأول، وشمل 15 مريضاً بالسكري نوع 2 مع التهاب السمحاك الحول سنى المزمن، "الفريق الثاني" 15 مريضاً صحيحًا مع التهاب السمحاك الحول سنى المزمن وتأتي عائلية لمرض السكري النوع 2، بينما الفريق الثالث شمل 10 مرضى بالسكري نوع 2 دون التهاب السمحاك الحول سنى المزمن، واعتبرت مجموعة مراقبة. تم قياس تعميم عامل نخر الورم ألفاً ومستوى الهيموغлюбين جليكوبس، سكر الدم في حالة الصيام، تركيز الإنسولين في مصل الدم البشري في حالة الصيام، وكذلك تقييم حساسية الإنسولين قيست قبل وبعد 3 أشهر من علاج اللثة التي كانت تتكون من المعالجة الميكانيكية التقليدية مع العلاج الدوكي النظامية. النتائج: لوحظت مستويات أعلى من المعايير المقررة في
مرضى السكري نوع 2 مع التهاب السمحاقة الحول سنى مقارنة بتلك التي بدونه. تعميم مستوى عامل نخر الورم ألفا كبرى، خفضت بعد علاج اللثة، خاتمة: تبين النتائج أن علاج اللثة كان فعالاً في تحسين مراقبة حساسية الإنسولين ونسبة السكر في الدم في مرضى السكر النوع-2 التي يمكن أن تفسر بانخفاض تعميم عامل نخر الورم ألفا مع أثر وسادة على مقاومة الإنسولين.