STUDYING THE IMPACT OF NON-SURGICAL PERIODONTAL TREATMENT ON GLYCOSYLATED HEMOGLOBIN LEVEL IN NON-DIABETIC PEOPLE

So-Hyun Son¹, Eun-Sun Lee²*

¹Department of Dental Hygiene, Shingu College, Seongnam 13174, Korea.
²Department of Dental Hygiene, Kyungbok University, Pocheon 11138, Korea. charity340@hanmail.net

ABSTRACT

Non-Surgical Periodontal Treatment (NSPT) is the first recommended approach to prevent periodontal infections. This study aimed to compare the HbA1c level in non-diabetic people with chronic periodontitis with people with healthy periodontium tissue. Also, in this study, the impact of NSPT on the blood sugar control of non-diabetic patients with chronic periodontitis was investigated. In this clinical trial study, patients were divided into two control and intervention groups. The intervention group included 20 non-diabetic patients with chronic periodontitis, and the control group contained 20 non-diabetic patients with healthy periodontitis. Periodontal clinical parameters included: Clinical attachment loss (CAL), Gingival index (GI), Probing pocket depth (PPD), and HbA1c. NSPT was performed for the intervention group. After three months, periodontal clinical parameters and HbA1c were measured and compared with the initial results. Before non-surgical periodontal treatment, the level of HbA1c in the intervention group was higher than in the control group (P < 0.001). In the group of intervention, there was a significant difference in HbA1c levels before and after treatment of non-surgical periodontal (P < 0.001). While in the control group, the HbA1c level before and after does not show a significant difference (P > 0.001). This study found that chronic periodontitis can affect blood sugar control in healthy individuals. Non-surgical periodontal treatment improves periodontal tissue health and lowers HbA1c levels.

Key words: Hemoglobin level, Periodontal treatment, Non-diabetic people, Blood sugar.

Introduction

Chronic periodontitis and diabetes mellitus are among the most common chronic diseases that have a two-way correlation between them and have many common factors in pathobiology. Diabetes mellitus is reported as a risk factor for periodontitis, which helps to increase the prevalence, severity, and disease progression [1, 2]. Periodontal disease is the diabetes sixth complication, which is accompanied by neuropathy, nephropathy, retinopathy, macrovascular disease, and changes in wound healing. Periodontitis appears to be a risk factor for diabetes [3, 4].

Glycosylated hemoglobin (HbA1c) in blood is used as a diagnostic test in diabetes. The increase of HbA1c is important in both diabetic and pre-diabetic patients. In general, HbA1c of 5.7-6.4% is considered as a pre-diabetic condition [5-7]. Chronic periodontitis is an infectious disease that causes the destruction of periodontal tissues and ultimately tooth loss. Periodontitis is reported as a risk factor in the pathogenesis and increased incidence of systemic diseases [8, 9]. Chronic periodontitis increases the inflammatory mediators production, including tumor necrosis factor-alpha (TNF-α), interleukin-6, interleukin-1β, and interferon-gamma, which play a vital role in sugar and fat metabolism. TNF-α has an important effect on fat metabolism and is also an insulin antagonist. Interleukin-6 and interleukin-1β are both insulin antagonists [10].

Although many previous studies have reported more severe periodontal disease in patients with diabetes than in people without diabetes, relatively few researchers have examined the association between periodontitis and blood sugar or glycosylated hemoglobin levels in people without diabetes [11].

Several studies have shown the negative effect of periodontal infection on blood sugar control, as well as the impact of non-surgical periodontal treatment on improving blood sugar control in diabetic patients [12]. However, there are few studies regarding the impact of periodontal infection on the blood sugar level of non-diabetic patients. Nibali et al. [13] reported a significant increase in non-fasting glucose levels in subjects with periodontitis compared to healthy subjects. A few studies suggest that periodontitis may affect glucose metabolism in healthy subjects, albeit to a lesser extent than in diabetic subjects [3]. According to these studies, periodontal infection in non-diabetic people can cause disturbances in their blood sugar regulation [4].

Wolff et al. [3] observed higher mean HbA1c levels in patients with periodontitis than in healthy controls. Large population-based research revealed that the chronic periodontal infection presence at the beginning of the study (baseline) has a positive relationship with alters in HbA1c levels over time [14]. The available evidence shows that the HbA1c test may be used as an objective measure to
determine the risk of diabetes in periodontitis people or to determine the progression and severity of periodontitis in patients with diabetes [4].

Non-Surgical Periodontal Treatment (NSPT) is the first recommended approach to prevent periodontal infections. This study aimed to compare the HbA1c level in non-diabetic people with chronic periodontitis with people with healthy periodontium tissue. Also, in this study, the impact of NSPT on the blood sugar control of non-diabetic patients with chronic periodontitis was investigated.

Materials and Methods

This study was a non-randomized controlled clinical trial in non-diabetic people. According to the results of the study by Perayil et al. [15] and at the confidence level of 95%, the power of the test is 80% and the accuracy is 0.3, the number of 15 patients in each group and with the possibility of dropping 25% of the samples, the number of 20 patients in the two intervention groups (suffering from chronic periodontitis) and control (healthy periodontium) were contained in the study. The age range of the people was 30 to 50 years. The intervention group was selected from the patients referred to the periodontology department and the control group was selected from other departments. The samples were selected by Non-probability Sampling and Convenience Sampling methods.

The criteria for entering the study in the intervention group include: not suffering from systemic diseases, having CAL ≥ 3 mm or PPD ≥ 5 mm in at least 30% of teeth, having at least 20 teeth, having normal fasting blood sugar, having a normal body mass index (18.5 < BMI < 25). In the control group, pain criteria included: no systemic diseases, having at least 20 teeth, normal fasting blood sugar, and having a normal body mass index (18.5 < BMI < 25). Exclusion criteria include history of diabetes mellitus, use of antibiotics, non-steroidal anti-inflammatory drugs, and immunosuppressive drugs for at least one week in the last 3 months, periodontal treatment in the last 6 months, heavy bleeding in the last month, pregnancy and breastfeeding, smoking, alcohol and drug addiction, having a removable prosthesis or long bridge, patient's non-cooperation after treatment (Scaling and Root Planning), having diabetes, systemic disease or conditions that affect glucose or periodontium tissue (so from the implementation of the study).

The aims of the research were introduced to the patients and all of them signed the written consent form. After obtaining a written consent form, a fasting blood glucose test was used to measure blood sugar to enter the study. FBS (fasting blood sugar) of patients was measured with a glucometer (Caresens, Isens, Germany) next to the dental unit. People whose FBS was in the normal range (70-110 mg/dL) were included in the study. To ensure the accuracy of the glucometer device, before the start of the study, three people's blood sugar was measured with the device, and then the next day, these three people were re-checked in their FBS test laboratory. According to the results of the FBS test, the accuracy of the device was evaluated to be above 98%.

In the subjects who were included in the study, before starting non-surgical periodontal treatment, two milliliters of peripheral venous blood was taken from their antecubital vein by a trained medical nurse to check HbA1c using a 5 ml syringe. The blood samples were then transferred to the blood collection tube containing the anticoagulant ethylenediaminetetraacetic acid. After sending the samples to the laboratory, the HbA1c level was measured with a 32ml HbA1c kit using high-performance liquid chromatography. Three months after non-surgical periodontal treatment, patients' HbA1c was measured again. Clinical periodontal parameters were determined before the intervention and 3 months after the treatment by a trained dental student under the supervision of a periodontist in both groups. The reliability of the examiner (Intra-examiner reliability) was confirmed by examining 5 patients in the same way in two sessions with an interval of 24 hours and observing more than 87% accuracy of the measured items, in the range of 1 mm.

PPD (the distance between the gingival margin to the pocket base) and CAL (the distance between the junction of enamel and cement to the pocket base) in six points (mesiobuccal, midbuccal, distobuccal, mesiopalatal, hidiopalatal, and deltopalatal in all Teeth except the third molar and The remaining roots were measured by Williams periodontal probe (Hu-Friedy Chicago, IL, USA).

The GI index (Loe and Silness 1963) was used to study the inflammatory condition of the gums. According to this gingival tissue index, a score of 0 to 3 was given in the margin and interproximal areas separately based on the severity of inflammation. To check the bleeding, the periodontal probe was inserted into the gingival sulcus with gentle pressure and moved slowly in the sulcus.

The people who entered the study were given oral hygiene training, including the use of interdental tools (dental floss or interdental brush) to control microbial plaque by a periodontist. For the intervention group, it was performed in two sessions two weeks apart by a trained dental student under the supervision of a periodontologist. One week after the first session and the reduction of inflammation in the intervention group, hopeless teeth and microbial plaque factors (overhanging repairs and caries adjacent to the gum tissue) were removed from the oral environment. The second session of SRP was completed two weeks after the first session under local anesthesia without a time limit for each patient. The people in the control group did not have any plaque and other microbial plaque factors in the mouth, and their periodontium tissue was healthy, so they were only given oral hygiene education. No additional periodontal treatment was performed in both groups until the end of the
study. For both groups, a monthly program was set up to check oral hygiene to control microbial plaque and check their systemic conditions. No periodontal treatment was performed in these sessions. After three months, periodontal clinical parameters were re-measured by the primary examiner and HbA1c of the subjects in both groups.

Data were entered into SPSS23 software. The Shapiro-Wilk test was utilized to check the data normality. To determine the mean before and after within the data group, if the data were normal, the paired t-test was utilized, and if the data were not normal, the Wilcoxon test was utilized. Non-parametric Mann-Whitney test was utilized to compare the mean of the two groups due to the non-normality of PPD and HbA1C data. Considering the normality of GI data in two groups of Independent t-test was used. P values less than 0.05 were reported significant.

**Results and Discussion**

In this study, 40 people participated in two control and intervention groups. There were 12 women and 8 men in the intervention group and 11 women and 9 men in the control group. The results of the chi-square test showed that the gender distribution was similar in the two groups (p = 0.75). The mean ± SD of the age of the intervention group was 39.28 ± 1.88 years and the control group was 38.70 ± 1.86 years, which was a significant difference based on the Mann-Whitney test (P = 0.015). The mean and standard deviation of BMI in the intervention group was 23.81 ± 1.56 and in the control group was 23.42 ± 1.34, which was not statistically significant (P = 0.94). The average changes in HbA1C following non-surgical periodontal treatment were 0.22% ± 0.13% in the intervention group and 0.01% ± 0.05% in the control group, which indicated a significant difference between the two groups (Table 1) (P < 0.001).

### Table 1. The mean ± SD of HbA1C before and after intervention in two groups.

<table>
<thead>
<tr>
<th></th>
<th>Intervention group</th>
<th>Control group</th>
<th>Test result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before</td>
<td>5.45 ± 0.62</td>
<td>5.12 ± 0.33</td>
<td>P-value** = 0.66</td>
</tr>
<tr>
<td>After</td>
<td>5.23 ± 0.69</td>
<td>5.11 ± 0.32</td>
<td>P-value** = 0.058</td>
</tr>
<tr>
<td>Differences</td>
<td>0.22 ± 0.13</td>
<td>0.01 ± 0.05</td>
<td>P-value** &lt; 0.001</td>
</tr>
<tr>
<td>Test result</td>
<td>P-value* &lt; 0.001</td>
<td>P-value* = 0.66</td>
<td></td>
</tr>
</tbody>
</table>

**Mann-Whitney U non-parametric test; *Wilcoxon non-parametric test**

The analysis of periodontal parameters in the intervention group showed that all these parameters showed a significant decrease after treatment (Tables 2 and 3). Thus, GI decreased by 0.57 in the group of intervention and 0.01 in the group of control (P < 0.001), and the reduction in PPD was 0.54 mm in the group of intervention and 0.03 mm in the group of control (P<0.001).

### Table 2. The mean ± SD of GI after and before intervention in two groups.

<table>
<thead>
<tr>
<th></th>
<th>Intervention group</th>
<th>Control group</th>
<th>Test result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before</td>
<td>2.42 ± 0.22</td>
<td>0.63 ± 0.20</td>
<td>t**** = 28.61</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>df = 38</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>P-value &lt; 0.001</td>
</tr>
<tr>
<td>After</td>
<td>1.85 ± 0.30</td>
<td>0.62 ± 0.18</td>
<td>t**** = 15.19</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>df = 38</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>P-value &lt; 0.001</td>
</tr>
<tr>
<td>Differences</td>
<td>0.57 ± 0.24</td>
<td>0.01 ± 0.08</td>
<td>P-value** &lt; 0.001</td>
</tr>
<tr>
<td>Test result</td>
<td>t*** = 10.59</td>
<td></td>
<td>P-value* = 0.56</td>
</tr>
<tr>
<td></td>
<td>df = 19</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>P-value &lt; 0.001</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**** Independent parametric t test; *** Paired t parametric test; **Nonparametric Mann-Whitney U test; *Nonparametric Wilcoxon test

### Table 3. The mean ± SD of PPD before and after intervention in two groups.

<table>
<thead>
<tr>
<th></th>
<th>Intervention group (mm)</th>
<th>Control group (mm)</th>
<th>Test result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before</td>
<td>3.38 ± 0.34</td>
<td>2.33 ± 0.49</td>
<td>P-value** &lt; 0.001</td>
</tr>
<tr>
<td>After</td>
<td>2.84 ± 0.38</td>
<td>2.30 ± 0.46</td>
<td>P-value** &lt; 0.001</td>
</tr>
<tr>
<td>Differences</td>
<td>0.54 ± 0.27</td>
<td>0.03 ± 0.06</td>
<td>P-value** &lt; 0.001</td>
</tr>
</tbody>
</table>
The findings of this research revealed that in non-diabetic people with periodontitis, the level of HbA1c is higher than in people with healthy periodontium tissue, and NSPT reduces HbA1c in the short term. Periodontal disease is called the diabetes sixth complication, which is accompanied by macrovascular disease, neuropathy, nephropathy, retinopathy, and changes in wound healing [3]. It has also been shown that periodontitis is a risk factor for poor blood sugar control in diabetic patients due to the presence of bacteria and their by-products in infected periodontal pockets and their secretion into the systemic circulation [13]. In addition, inflammatory cytokines, especially IL-1β and TNF-α, are secreted from periodontal infectious tissue and enter the blood circulation, which can reduce insulin sensitivity [3, 10].

In this research, it was observed that the level of HbA1c in the intervention group was significantly higher than in the control group. In the present study, all systemic factors affecting blood sugar were excluded from the study. So there is a possibility that the higher level of HbA1c in the intervention group than in the control group is related to the infection caused by chronic periodontitis. The findings of this study are consistent with many other studies. Banjar et al. [4] reported that patients with periodontitis were similar to have undiagnosed hypoglycemia than patients with healthy periodontium. They reported that there is a direct relationship between the severity of periodontitis and increased HbA1c, and the relationship between mean HbA1c levels and periodontal disease is more evident in severe periodontitis. Taylor et al. [16] stated that severe periodontal infection may change glycemic control in diabetic patients. Wolff et al. [3] reported a significant increase in blood glucose levels in patients with systemic healthy periodontitis, which indicates that these patients have impaired blood sugar control and are in a prediabetic state.

Demmer et al. [17] reported that the risk of developing diabetes is doubled in people with moderate periodontal disease. In a recent systematic study, Graziani et al. [18] showed that glycemic control is endangered in non-diabetic patients with periodontitis. Unlike most studies, Kebede et al. [19] in a long-term study found no association between diabetes incidence and periodontitis during an 11-year follow-up period. Ghalaut et al. [20] compared glycosylated hemoglobin levels with the severity of periodontitis and could not report a significant difference between these two variables. Due to the infectiousness of periodontal pockets and also the secretion of inflammatory mediators, especially IL-1β and TNF-α from infected periodontal tissues, which cause dysfunction of insulin receptors and thus reduce insulin sensitivity [3, 10, 21]. Accordingly, periodontal treatment may improve blood glucose control by reducing the release of proinflammatory mediators [3, 10].

In this study, the impact of NSPT on the blood sugar control of patients using the HbA1c test was done after three months. HbA1c is a suitable alternative to FBS for screening diabetic patients. In 2011, the WHO approved HbA1c as a diagnostic test in diabetic patients [4]. Because glucose in the blood irreversibly binds to hemoglobin, HbA1c reflects the level of blood glucose in a period of 30 to 90 days and is not affected by daily blood sugar fluctuations [3, 21, 22]. NSPT is an efficient method to remove plaque and microbial plaque adhering to the tooth root surface. NSPT reduces gingival inflammation, and pocket probing depth and improves clinical adhesion level. Although research has shown that the effect of NSPT may last up to one year, the maximum improvement is within the first 3 months [23]. Due to the opening of dentin tubules in SRP, pathogens invade inside the tubules, which can act as a re-infection source after 3-4 months [24]. Therefore, in this study, periodontal clinical parameters were re-examined three months after NSPT.

Considering that all periodontal clinical parameters were significantly reduced after the treatment, there is a possibility that the reduction of HbA1c in the intervention group is due to the elimination of inflammation and chronic infection, which is seen in these people. Several studies have investigated the impact of NSPT treatment on periodontal clinical parameters and blood HbA1 levels during three months and concluded that all these parameters decrease, which is in line with our study [17, 21, 22]. Cruz et al. [25] stated that non-surgical periodontal treatment improves plaque control and inflammatory conditions of the gingival tissue in patients with chronic periodontitis with or without diabetes. Dag et al. [26] reported that SRP decreased HbA1c levels only in subjects with controlled diabetes. Smith et al. [27] reported that periodontal mechanical treatment alone is not effective in controlling blood sugar in diabetic patients. Periodontitis causes a subclinical inflammatory condition Systemic (subclinical) through periopathogens and inflammatory mediators. Systemic inflammation affects pancreatic β-cells and alters insulin signaling. The reduction of HbA1c level after periodontal treatment may be related to the reduction of insulin resistance and insulin sensitivity improvement by reducing the inflammatory cytokines and pathogenic bacteria number [28].

<table>
<thead>
<tr>
<th>Test result</th>
<th>$t^{***} = 10.59$</th>
<th>$df = 19$</th>
<th>P-value* = 0.02</th>
</tr>
</thead>
</table>

*** Paired t-parametric test; **Nonparametric Mann-Whitney U test; *Nonparametric Wilcoxon test
The finding of this study supports the evidence obtained from former observational researches that show that non-diabetic patients with periodontitis have higher glycemic levels than people without periodontitis, and non-surgical periodontal treatment reduces the blood sugar of these people at the same time as reducing periodontal parameters. It confirms the theory of a two-way relationship between periodontitis and diabetes.

Conclusion

This study found that chronic periodontitis can affect blood sugar control in healthy individuals. Non-surgical periodontal therapy improves periodontal clinical parameters and decreases blood HbA1c levels within three months. Small sample size, measurement of only FBS to confirm the non-diabetic status of the participants, short follow-up period of three months, lack of assessment of serum or gingival crevicular fluid (GCF) levels of pro-inflammatory mediators including CRP, IL 6-IF-γ, IL-1β, and TNF-α, and lack of adjustment for confounding factors such as race and ethnicity are the limitations of this research. Future studies should determine the relationship between serum or GCF levels of various pro-inflammatory mediators and HbA1c levels.

Acknowledgments: None

Conflict of interest: None

Financial support: None

Ethics statement: None

References

18. Graziani F, Gennai S, Solini A, Petrini M. A systematic review and meta-analysis of epidemiologic...