

# The effect of non-surgical periodontal therapy on glycemic control and C1-reactive protein levels among type 2 diabetic patients with periodontitis: A clinical trial

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## Abstract

It suggests that non-surgical periodontal therapy without systemic antibiotic therapy may not achieve a significant improvement in glycemic control and systemic inflammation in diabetic patients. However, it is important to highlight that the decision of whether or not to use antibiotics to treat periodontitis. Thus this study aimed to evaluate over 3 months the consequence of non-surgical periodontal treatment without systemic antibiotic therapy on serum levels of HbA1c and C-reactive protein (CRP). Forty-two participants with type 2 diabetes mellitus (DM) and moderate periodontal disease were randomized into intervention (IG) and control (CG) groups. The IG received non-surgical periodontal therapy in the form of full-mouth scaling and root planing. Participants were followed up for 3 months. The CG received non-surgical periodontal therapy after 3 months. Clinical parameters, including plaque index (PI), gingival bleeding index (GBI), probing pocket depth (PPD), clinical attachment level (CAL), and HbA1c and CRP levels, of all patients were recorded at baseline and after 3 months. A p-value less than 0.05 considered significant. At the end of 3 months, IG showed improvement in all the clinical parameters compared to CG. There were no significant differences in HbA1c and CRP after 3 months when compared to the baseline level in both groups. Clinical parameters were significantly improved by the employment of non-surgical periodontal treatment without systemic antibiotic therapy, but HbA1C and CRP levels were not significantly affected.

**Keywords:** Antibiotics, Diabetes, Non-surgical periodontal treatment, Periodontal Disease

## 1. Introduction

Diabetes is a chronic disease that affects 8.5% of the world's population. It is estimated that by 2040, the number of people with the disease will increase to 642 million worldwide. Based on the epidemiological studies it is estimated that in the year 2030 nearly 9.2 million Iranians likely to have diabetes [1].

It has been described that periodontal disease is the sixth complication of diabetic patients after

diabetic nephropathy, neuropathy, retinopathy, vascular disease, and delayed healing [2]. Periodontitis is a chronic inflammatory disease that causes progressive damage of periodontium and leading to tooth loss. It is associated with an undesirable impression on the patient's quality of life [3]. The production of pro-inflammatory mediators such as and C-1 reactive protein (CRP) in patients with periodontitis is increased. All these mediators can

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cause insulin resistance and also alter the lipid and glucose metabolism [4]. Glycosylated haemoglobin (HbA1c) forms by irreversible binding of glucose to haemoglobin. HbA1c levels represent glycaemic control over the previous 1-3 months [5]. Thus, periodontal disease can affect HbA1c and CRP levels in diabetic patients [4].

One of the most common therapy that used for the treatment of periodontitis is scaling and root planing. Although scaling and root planing improves the periodontal status in the majority of patients, it is usually insufficient to alter the bacterial profile followed by periodontal status [6]. The aim of systemic periodontal antibiotic therapy is to killing subgingival pathogens that remain after conventional mechanical periodontal therapy to support mechanical periodontal therapy and the host defense system [7]. It suggests that in patients with a long history of diabetes, the conventional periodontal therapy alone cannot achieve a significant improvement in glycemic control and systemic inflammation [7-9]. However, it is important to highlight that improper administration of antibiotics can lead to side effects of various intensities, and their indiscriminate use might lead to the tolerance to the antibiotics [10]. Therefore, the need to use or not to use these agents by dentists can be a challenge. Thus, this study aimed to evaluate the consequence of non-surgical periodontal therapy without systemic antibiotic treatment on serum levels of HbA1c and CRP over 3 months.

## 2. Materials and Methods

### 2.1 Study population

This study received ethics approval by Guilan University of Medical Sciences (Approval code: IR.GUMS.REC.1398.307). Also, the clinical trial protocol was registered (IRCT registration number: IRCT20190721044287N1) and available online. The study population consisted of 42 participants with type 2 DM (HbA1c  $\geq$  7%). Inclusion criteria included the following: 1) Patients with chronic periodontitis who received no periodontal treatment in the past 6 months; 2) Receiving periodontal and antibiotic treatments during the last 6 months; 3) Patients with at least 14 teeth in the mouth and a pocket depth (PD)  $\geq$  5 mm in at least four areas and 4  $\geq$  clinical attachment level (CAL)  $\geq$  3 mm in at least four areas; 4) Diabetes diagnosed by a physician for the past 6 months; 5) Patients with unchanged diabetic

medication for the past 3 months. Exclusion criteria included: 1) Patients with advanced diabetic problems (macrovascular and microvascular); 2) Chronic pulmonary disease; 3) Kidney and liver diseases; 4) Malignancies; 5) Heart disease (coronary artery disease); 6) Transplanted patients; 7) History of infection and trauma; 8) Alcoholic and smoker patients; 9) Pregnant women; 10) Patients with severe periodontitis.

### 2.2 Groups

In this study, using a computer program, participants were randomized into two groups of 21 each: the intervention group (IG) and the control group (CG). All the patients received health education using toothbrush and toothpaste with a modified bass method twice a day, and dental floss and chlorhexidine mouthwash (0.12%) twice a day. The IG received non-surgical periodontal therapy in the form of full-mouth scaling and root planing in two sessions, 1 week apart, with the use of slim instruments, under local anesthesia. Participants were followed up for 3 months. The CG received non-surgical periodontal therapy after 3 months.

### 2.3 Follow up

During 3 months of follow up, patients with the following criteria were excluded from the study: 1) Patients with diabetic diet changes during the study period; 2) Patients with problems requiring emergency treatment; 3) Patients who changed their diets or medications or used antibiotics during the study.

### 2.4 Data collection

Clinical parameters, including plaque index (PI), gingival index (GI), gingival bleeding index (GBI), probing pocket depth (PPD), CAL were examined at baseline and after 3 months. Patients' blood samples were obtained from the Razi Laboratory at 8.5-11 A.M. to assess their HbA1c and CRP levels at baseline and after 3 months.

### 2.5 Statistical analysis

Data was compiled and analyzed through SPSS version 24. Quantitative variables like HbA1c and CRP were presented as mean  $\pm$  SD. The Pearson test was used to test the correlation of the periodontal parameters with HbA1C and CRP levels, and the

correlation of serum level of HbA1C with CRP level. Differences among all variables from baseline to the 3-month visit were analyzed using the Wilcoxon Mann-Whitney U test because it was not normally distributed. The linear regression test was used to evaluate the effect of age and gender on the HbA1C and CRP levels. A p-value <0.05 considered significant.

### 3. Results

HbA1c and CRP levels in the CG and IG at baseline and after 3 months are shown in Table 1 and Table 2, respectively. Table 3 showed HbA1c and CRP levels changes between baseline and after 3 months. Based on the results of the present study, the two groups did not differ significantly in the HbA1C (Table 1) and CRP (Table 2) levels at baseline. Also, the results indicated that age and gender did not significantly affect the HbA1C and CRP levels at baseline.

The results indicated that all periodontal parameters measured (PI, GI, GBI, PPD, and CAL) showed improvement after 3 months of non-surgical periodontal treatment in the IG compared to the CG (Table 4).

Based on the result of the present study, the relation between HbA1C (Table 5) and CRP (Table 6) with periodontal parameter changes was not statistically significant.

Table 1. HbA1c level in the control group (CG) and intervention group (IG) at baseline and after 3 months

Group	Subgroup	Number	Mean	SD	
Baseline	CG	>9 HbA1c	15	8.07	0.46
		≤9 HbA1c	6	9.76	0.54
	IG	>9 HbA1c	15	7.85	0.64
		≤9 HbA1c	6	10.35	1.15
After 3 months	CG	>9 HbA1c	15	7.91	0.78
		≤9 HbA1c	6	9.6	0.35
	IG	>9 HbA1c	15	7.92	0.80
		≤9 HbA1c	6	10.06	11.90

Table 2. CRP level in the control group (CG) and intervention group (IG) at baseline and after 3 months

Group	Number	Mean	SD	
Baseline	CG	21	3.60	2.36
	IG	21	3.04	2.10
After 3 months	CG	21	3.61	2.38
	IG	21	2.43	2.09

Table 3. HbA1c and CRP levels changes between baseline and after 3 months in control group (CG) and intervention group (IG)

Parameter	Group	Subgroup	Number	Mean	SD
HbA1C	CG	>9 HbA1c	15	-0.13	0.54
		≤9 HbA1c	6	-0.23	0.47
	IG	>9 HbA1c	15	0.17	0.57
		≤9 HbA1c	6	-0.55	0.56
CRP	CG	-	21	0.004	0.67
	IG	-	21	-0.60	0.70

Table 4. Differences of periodontal parameters in intervention group (IG) compared to control group (CG) after 3 months

Periodontal parameter	Group		Statistic	P value
	CG (Mean Difference ± SD)	IG (Mean Difference ± SD)		
PI	16.89 ± -4.95	8.16 ± -40.62	4.70	<0.001
GI	0.12 ± 0.08	0.28 ± -0.88	5.61	<0.001
PD	0.15 ± 0.07	0.55 ± - 1.10	5.60	<0.001
CAL	0.15 ± 0.03	0.31 ± - 0.50	5.24	<0.001
GBI	8.41 ± 0.19	19.01 ± -46.24	5.04	<0.001

Plaque index (PI), Gingival index (GI), Pocket depth (PD), Clinical attachment level (CAL), Gingival bleeding index (GBI)

Table 5. Relationships between periodontal parameters and HbA1c serum level changes in the control group (CG) and intervention group (IG) after 3 months

Group	Subgroup	PI	GI	PD	CAL	GBI
CG	>9 HbA1c	r = 0.06 p = 0.820	r = -0.26 p = 0.342	r = 0.04 p = 0.869	r = -0.23 p = 0.39	r = 0.23 p = 0.410
	≤9 HbA1c	r = 0.47 p = 0.340	r = -0.25 p = 0.633	r = 0.24 p = 0.641	r = -0.61 p = 0.191	r = 0.69 p = 0.125
IG	>9HbA1c	r = - 0.36 p = 0.182	r = -0.23 p = 0.409	r = 0.05 p = 0.851	r = -0.27 p = 0.329	r = -0.06 p = 0.831
	≤9 HbA1c	r = -0.50 p = 0.313	r = 0.51 p = 0.313	r = 0.01 p = 0.984	r = -0.58 p = 0.222	r = -0.19 p = 0.718

Plaque index (PI), Gingival index (GI), Pocket depth (PD), Clinical attachment level (CAL), Gingival bleeding index (GBI)

Table 6. Relationships between periodontal parameters and CRP serum level changes in the control group (CG) and intervention group (IG) after 3 months

Group	PI	GI	PD	CAL	GBI
CG	r = -0.20 p = 0.383	r = - 0.32 p = 0.158	r = 0.10 p = 0.679	r = - 0.04 p = 0.876	r = 0.007 p = 0.976
IG	r = -0.23 p = 0.318	r = - 0.24 p = 0.299	r = -0.20 p = 0.381	r = -0.20 p = 0.393	r = 0.36 p = 0.109

Plaque index (PI), Gingival index (GI), Pocket depth (PD), Clinical attachment level (CAL), Gingival bleeding index (GBI)

## Discussion

Based on the result of the present study, non-surgical periodontal therapy without systemic antibiotic therapy could improve the periodontal status of patients with type 2 DM. Similar to the result of the present study, Vaghani *et al.* showed scaling, and root planing is associated with significant reductions in the GI, Oral Health Index (OHI-S), PPD, and CAL levels of patients with periodontitis [4]. These findings are similar to a study done by Obeid *et al.*, which showed the effectiveness of scaling and root

planing in improving the periodontal status of patients with periodontitis [11].

Based on the results of the present study, non-surgical periodontal therapy without systemic antibiotic therapy did not affect the serum level of HbA1C. Similarly, a study done by Aldridge *et al.* reported a significant improvement in periodontal parameters after scaling and root planing without systemic antibiotic therapy but did not found any improvement in HbA1c levels in 22 patients with type 1 diabetes and severe periodontitis [9]. Grossi *et al.*

indicated that that topical antimicrobial and systemic doxycycline along with mechanical therapy (100 mg/day for 14 days) resulted in a significant gain in attachment level and a reduction of almost 1% in the levels of HbA1c at 3 months after treatment [12]. Another study conducted by Singh *et al.* showed that non-surgical periodontal treatment followed by systemic doxycycline is associated with improved glycaemic control in type 2 diabetic patients [10]. This may be due to their antimicrobial effects.

Based on the results of the present study, non-surgical periodontal therapy without systemic antibiotic therapy did not affect the serum level of CRP. Similarly, in a study, non-surgical periodontal therapy without systemic antibiotic therapy did not affect the serum level of high-sensitivity C-reactive protein (hsCRP) in Sixty participants with type 2 DM and moderate to severe periodontal disease [8]. Also, Katagiri *et al.* evaluated the effects of periodontal treatment simultaneously on both A1c and CRP levels in DM [13]. In that study of 49 participants, scaling and root planing plus topical treatment with minocycline ointment showed no effect on hsCRP levels after 6 months.

It seems that the clinical beneficial results achieved with non-surgical periodontal treatment in the short-term are frequently not maintained in the long term, particularly in more advanced cases [6] or in those associated with risk factors, such as smoking [14] and diabetic patients [15], because of tolerance to the treatment observed in the case of smokers, or due to the higher prevalence of severe periodontitis observed in patients with diabetes mellitus [5, 15]. For this reason, it has been suggested that the administration of systemic antibiotics can be used together with scaling and root planing.

The limitations of the study were the small sample size. Also, serum levels of pro-inflammatory mediators such as TNF- $\alpha$ , IL-1  $\beta$ , IL-6 were not measured. In conclusion, there is a need for more randomized controlled clinical trials with larger sample sizes, long-term follow-ups, and strict adjustments for confounding factors, such as age, gender, body mass index (BMI), race/ethnicity, and smoking status to confirm the findings of this study

Despite the improvement of clinical parameters after three months of non-surgical treatment due to no change in important serological markers associated with inflammatory disease and there is a possibility of

disease progression and re-alteration of clinical parameters, it is suggested that antibiotic therapy should be used as adjunctive therapy.

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### Author Contributions

All authors contributed equally in conceptualization, methodology, software, validation, formal analysis, investigation, resources, data collection, writing original draft, visualization, supervision, and project administration.

### Conflicts of Interest

The authors declare no potential conflicts of interest.

### Ethical declarations

This study received ethics approval by Guilan University of Medical Sciences (Approval code: IR.GUMS.REC.1398.307). Also, the clinical trial protocol was registered (IRCT registration number: IRCT20190721044287N1) and available online.

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