Original

The clinical and systemic effects of periodontal treatment in diabetic and non-diabetic obese patients

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Abstract: The purpose of the present study was to evaluate the response to periodontal management in obese individuals with poorly controlled diabetes mellitus (DM) and obese individuals without DM. Changes in clinical and biochemical parameters were also investigated. Seventeen obese patients with poorly controlled DM and 14 obese non-DM patients with generalized chronic periodontitis were enrolled. The anthropometric measurements, periodontal parameters, and serum levels of lipid (triglyceride, high-density lipoprotein cholesterol, total cholesterol, low-density lipoprotein cholesterol) and glucose (fasting plasma glucose [FPG], insulin, insulin resistance [IR], hemoglobin [Hb]A1c) metabolism, pro-inflammatory mediators (high-sensitivity C-reactive protein, tumor necrosis factor- α [TNF- α] and Pentraxin-3), and interleukin-6 were measured before and at 3 months, and 6 months after full-mouth scaling and root planing (FM-SRP) together with full-mouth disinfection (FMD). A significant reduction in TNF- α ($P < 0.001$) values was observed in both groups following periodontal healing. However, significant changes in FPG ($P < 0.05$), HbA1C ($P < 0.05$), and the homeostasis model assessment of IR (HOMA-IR; $P < 0.05$) were only observed after 3 months in the DM group. Our findings suggest that obesity with or

without DM does not seem to be a modifying factor for the clinical outcome of FM-SRP and FMD. (J Oral Sci 58, 523-531, 2016)

Keywords: obesity; periodontal therapy; chronic periodontitis; diabetes; cytokines.

Introduction

Diabetes mellitus (DM) is a known risk factor for hyperinflammation in response to periodontal pathogens (1) and the progression of periodontal disease. DM impairs the connective tissue repair mechanism and decelerates the resolution of inflammation, which causes severe periodontal destruction (2). Increasing evidence suggests that obesity is a direct and indirect risk factor for periodontal disease because it affects glycemic control indirectly and induces the secretion of pro-inflammatory mediators from adipose tissue which affects the influence of dental plaque on the periodontal condition (3).

Periodontitis may negatively influence glycemic control, which can be improved by conventional periodontal management, and lowers the risk of a diabetic co-morbidity, thereby generating a two-way relationship. Moreover, it has been proposed that periodontitis prompts an inflammatory alteration in adipose tissue, which is associated with obesity, DM, and periodontal sickness (4).

Obesity, increased waist circumference (WC), and weight gain may be risk factors for periodontitis (5). However, obesity does not seem to affect the outcome of periodontal treatment (6). The purpose of the present study was to evaluate the clinical response to full-mouth

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Table 1 Demographics, oral hygiene, and anthropometric status of the patients at baseline

	Diabetic group	<i>P</i> values	Non-diabetic group
Age (years) (mean $\pm$ SD) (range)	51.3 $\pm$ 8.6 33 to 63	NS	49.2 $\pm$ 9.2 30 to 62
Female/male (<i>n</i>)	14/3	NS	9/5
Frequency of brushing teeth (<i>n</i>)			
Once a day	16	NS	12
Twice a day	1		2
Interdental cleaning (<i>n</i>)	2	NS	1
Weight (kg) (mean $\pm$ SD) (range)	87.5 $\pm$ 7.0 79 to 105	NS	88.5 $\pm$ 7.0 78 to 100
WC (cm)			
Females (mean $\pm$ SD) (range)	108.4 $\pm$ 11.3 96 to 137	NS	106.2 $\pm$ 8.4 95 to 120
Males (mean $\pm$ SD) (range)	113.6 $\pm$ 8.5 104 to 120		112.4 $\pm$ 7.4 104 to 120
BMI (kg/m ²) (mean $\pm$ SD) (range)	34.1 $\pm$ 1.9 31.6 to 39.3	NS	34.1 $\pm$ 3.7 30.8 to 42.8
Class I (BMI of 30 to 34.9 kg/m ²) (<i>n</i>) (%)	11 (64.8)	NS	10 (71.4)
Class II (BMI of 35 to 39.9 kg/m ²) (<i>n</i>) (%)	6 (35.2)		3 (21.4)
Class III (BMI of $\geq$ 40 kg/m ²) (<i>n</i>) (%)	–		1 (7.2)

NS: non-significant difference, SD: standard deviation, WC: waist circumference, BMI: body mass index.

scaling and root planing (FM-SRP) in obese patients with poorly controlled DM and without DM. This was done to determine whether periodontal treatment had a systemic effect on the biochemical parameters in obese individuals with poorly controlled DM or without DM.

Material and Methods

Case definitions

Chronic periodontitis (CP) was clinically determined based on the following criteria described by Savage et al. (7): presence of ≥ 5 teeth with ≥ 1 sites with a probing depth (PD) ≥ 5 mm, clinical attachment loss (CAL) ≥ 2 mm, and presence of bleeding upon probing (BOP). Patients with a body mass index (BMI) of ≥ 30 kg/m² and a WC of >88 cm (females) and >102 cm (males) were diagnosed as obese. Obesity was subcategorized as follows: class I, BMI 30–34.9 kg/m²; class II, 35–39.9 kg/m², and class III, ≥ 40 kg/m². Type 2 DM was diagnosed according to the diagnostic criteria of the American Diabetes Association (8).

Study groups

Study participants were categorized into two groups: obese patients without DM and obese patients with DM. Patient characteristics are shown in Table 1. Assessments for eligibility and patient assignment into study groups were done by a clinician (CAG) who was not involved in the clinical proceedings.

Inclusion criteria were as follows: CP, obesity, at least 15 natural teeth, >25 years of age, and type 2 DM (in the

DM group). Exclusion criteria were defined as follows: antibiotic or anti-inflammatory drug use within the previous 6 months, pregnancy or lactation, periodontal therapy within the previous 6 months, smoking or history of smoking, alcohol consumption, and use of lipid-lowering medications.

Between January 2015 and October 2015, 72 obese patients were enrolled at the Department of Periodontology, Erciyes University, Kayseri, Turkey. Forty-one patients were excluded from the study, (25 did not meet the inclusion criteria and 16 refused to participate). As a result, 31 participants (8 males and 23 females; age range, 30–63 years; mean age, 50.4 $\pm$ 8.9 years) were included in the present study. Two participants in the DM group withdrew participation at 6 months due to loss of contact. Twenty-nine participants completed the study (Fig. 1).

The study details were explained to all participants, and then written informed consent was provided by each patient before initiation of the study protocol. This clinical study was approved by the Erciyes University, Faculty of Medicine Ethics Committee (Decision Number: 2014/606).

Clinical examinations

The following parameters were evaluated at baseline, 3 months, and 6 months (the end of the study): plaque index (PI) (9); gingival index (GI) (10); PD; percentage of sites with BOP; and clinical attachment loss (CAL). In addition, the percentage and number of deep sites were also calculated. The Decay-Missing-Filling Index (DMFT)

Fig. 1 Flow chart of study procedure.

was recorded. Clinical examinations were repeated 3 and 6 months following periodontal management. All clinical dimensions were obtained from the six sites (mesio-buccal, mid-buccal, disto-buccal, mesio-lingual, mid-lingual, and distolingual) of each tooth using a 15 mm periodontal probe (Ψ) at baseline and at 3 and 6 months following treatment. All periodontal clinical measurements were made by the same investigator (FOT).

Panoramic and periapical radiographs were obtained to confirm the diagnosis of CP, as well as the diagnosis of various pathological conditions.

To assess the reliability of clinical measurements, ten randomly selected individuals were re-evaluated at baseline and during the treatment period. The reliability of the continuous variables was calculated as the standard deviation of the differences divided by two. The range of the mean error for PD was 0.11–0.16, and this indicated reliable measurements were obtained during the evaluation periods. Cohen's kappa (κ) was used to describe the reliability of discrete (GI) and BOP values. Based on duplicate measurements, the κ values of GI and BOP were 0.89 ± 0.04 and 0.91 ± 0.05 , respectively.

Serum sampling and biochemical analysis

At baseline, 3 months, and 6 months after treatment, 20 mL fasting venous blood samples were collected from the antecubital fossa by an experienced nurse. All blood samples were obtained in the morning between 8:00 and 8:30 am. Blood samples were centrifuged immediately

after collection and separated serum samples were stored at -80°C until analysis.

Lipid (triglyceride, high-density lipoprotein cholesterol, total cholesterol, low-density lipoprotein cholesterol), inflammatory factors (interleukin-6 [IL-6], tumor necrosis factor- α [TNF- α], high-sensitivity C-reactive protein [hsCRP], pentraxin-3 [PTX3]), and glucose (fasting blood glucose, insulin, hemoglobin [HbA1c]) parameters were measured in the serum samples. Moreover, the homeostasis model assessment of IR (HOMA-IR) was calculated as $\text{FBG} \times \text{fasting serum insulin level}/405$. A score >2.7 was considered IR.

TNF- α (Invitrogen, Waltham, MA, USA), IL-6 (Invitrogen), and PTX3 (Shanghai Yehua, Shanghai, China) serum levels were measured using a commercial solid-phase enzyme-linked immunosorbent assay (ELISA) kit according to the manufacturer's instructions. The plates were read with an Epoch microplate spectrophotometer (BioTec Winooski, VT, USA). The values were expressed as ng/mL (PTX3) and pg/mL (TNF- α and IL-6); the variation coefficients were: TNF- α , 4.4%; IL-6, 6.2%; and PTX3, $<10\%$. All biochemical analyses were performed at Erciyes University in the Department of Biochemistry, Faculty of Medicine.

Periodontal treatment

All participants received periodontal treatment 2 h after breakfast following the blood sampling. After local infiltration, FM-SRP was performed by the same investigator (ZT) with manual instruments and ultrasonics. Periodontal therapy was completed within 24 h during two consecutive visits. The FMD protocol was performed as previously described by Quirynen et al. (11).

At baseline, the participants in both groups were instructed in standard oral hygiene, including plaque control using toothbrushes/interdental brushes and brushing the dorsum of the tongue twice a day. Oral hygiene instructions were repeated at each session. During the periodontal management sessions, obligatory tooth extractions were performed, and referrals for dental treatments were made as soon as periodontal treatment was completed.

Statistical analyses

The sample size was calculated according to our previous study (12) using data relative to the mean difference and standard deviation (SD) between the HOMA-IR and HbA1c levels of the obese patients during the experimental period. It was estimated that 11 individuals per group would be sufficient to detect a decrease of 1.3 in HOMA-IR levels (SD, 1.00; α error, 0.05; β error, 0.2).

Table 2 Periodontal parameters of the patients

	Diabetic group	Between groups	Non-diabetic group
PI			
Baseline	2.2 (2.0 to 2.4) ^a	NS	2.4 (1.8 to 2.5) ^a
3 months	1.1 (0.8 to 1.4) ^b	NS	1.2 (0.9 to 1.4) ^b
6 months	0.4 (0.4 to 0.8) ^c	NS	0.5 (0.4 to 0.6) ^c
Within the group	<0.001		<0.001
GI			
Baseline	1.5 (1.1 to 1.7) ^a	NS	1.6 (1.4 to 1.8) ^a
3 months	0.9 (0.7 to 1.0) ^b	NS	0.7 (0.7 to 0.8) ^b
6 months	0.4 (0.3 to 0.5) ^c	NS	0.4 (0.3 to 0.5) ^c
Within the group	<0.001		<0.001
PD (mm)			
Baseline	3.1 ± 0.5 (2.6 to 4.9) ^a	NS	2.9 ± 0.3 (2.6 to 3.8) ^a
3 months	2.6 ± 0.2 (2.3 to 3.0) ^b	NS	2.6 ± 0.2 (2.0 to 2.9) ^b
6 months	2.2 ± 0.2 (1.9 to 2.7) ^c	NS	2.2 ± 0.1 (2.0 to 2.7) ^c
Within the group	<0.001		<0.001
BOP-positive (%)			
Baseline	60.0 ± 15 (14 to 89) ^a	NS	62.8 ± 15 (28 to 84) ^a
3 months	38.2 ± 12 (10 to 47) ^b	NS	34.2 ± 6 (19 to 54) ^b
6 months	28.3 ± 10 (9 to 42) ^c	NS	27.2 ± 6 (13 to 41) ^c
Within the group	<0.001		<0.001
CAL (mm)			
Baseline	3.7 ± 0.8 (2.8 to 5.4) ^a	NS	3.6 ± 0.5 (2.7 to 4.6) ^a
3 months	3.4 ± 0.7 (2.4 to 5.1) ^b	NS	3.3 ± 0.5 (2.5 to 4.4) ^b
6 months	3.0 ± 0.7 (2.0 to 4.6) ^c	NS	3.0 ± 0.4 (2.5 to 4.1) ^c
Within the group	<0.001		<0.001
Distributions of the PD (%)			
Baseline			
<3 mm	76.1	NS	76.4
4-6 mm	22.6	NS	22.8
>6 mm	1.3	NS	0.8
3 months			
<3 mm	85.7	NS	91.1
4-6 mm	13.6	NS	8.6
>6 mm	0.7	NS	0.3
6 months			
<3 mm	96.3	NS	98.6
4-6 mm	3.7	NS	1.4
>6 mm	0		0
Number of teeth (<i>n</i>)			
Baseline	25.8 ± 2.6 (18 to 28)	NS	25.9 ± 1.8 (22 to 28)
3 months	24.8 ± 2.3 (18 to 28)	NS	25.3 ± 1.9 (22 to 28)
6 months	24.1 ± 2.5 (18 to 28)	NS	24.2 ± 2.4 (20 to 28)
Within the group	NS		NS
Number of decayed teeth (<i>n</i>)			
Baseline	3.8 ± 2.5 (0 to 10) ^a	NS	3.7 ± 1.8 (0 to 8) ^a
3 months	2.3 ± 2.3 (0 to 8) ^b	NS	2.6 ± 1.9 (0 to 6) ^b
6 months	1.2 ± 2.6 (0 to 5) ^c	NS	1.4 ± 1.8 (0 to 5) ^c
Within the group	<0.001		<0.001
DMFT index			
Baseline	10.7 ± 5.0 (3 to 18)	NS	10.5 ± 5.7 (1 to 22)
3 months	10.8 ± 5.1 (3 to 18)	NS	10.6 ± 5.7 (1 to 22)
6 months	11.2 ± 5.3 (3 to 18)	NS	10.5 ± 5.7 (1 to 22)
Within the group	NS		NS

Different superscript letters (a, b, c) within columns differ significantly. NS: non-significant difference, PI: plaque index, GI: gingival index, PD: probing depth, BOP: bleeding upon probing, CAL: clinical attachment loss, DMFT: decay-missing-filling index.

In addition, the estimated minimum number for detecting a decrease of 2.1 in the HbA1c levels (SD, 1.4; α error, 0.05; β error, 0.2) was ten patients per group.

Normality of the data was tested using the Kolmogorov-Smirnov test. The Student's *t*-test was used to analyze the baseline parametric data, including age, weight, WC, and

BMI. Comparisons were made using the Chi-square test and the exact method analysis for categorical variable samples.

The repeated measures two-way analysis of variance (ANOVA) test was utilized for both groups to analyze the repeated measurements. In addition, results were

Table 3 Lipid and glucose levels in patient subjects

	Diabetic group	Between groups	Non-diabetic group
HDL			
Baseline	50.1 ± 14.2 (33.1 to 77.7)	NS	49.4 ± 15.6 (25.0 to 78.6)
3 months	52.3 ± 13.3 (25.4 to 74.0)	NS	46.5 ± 12.2 (27.0 to 70.3)
6 months	48.0 ± 10.8 (29.0 to 67.0)	NS	45.4 ± 14.1 (22.0 to 71.5)
Within the group	0.068		0.059
LDL			
Baseline	138.3 ± 39.1 (31.6 to 190.5)	0.017	102.6 ± 27.4 (60.5 to 147.4)
3 months	142.6 ± 45.8 (36.8 to 213.6)	NS	117.4 ± 34.4 (69.2 to 190.2)
6 months	135.0 ± 38.0 (41.0 to 199.9)	NS	111.4 ± 36.5 (48.5 to 179.6)
Within the group	0.824		0.074
TC			
Baseline	221.5 ± 46.0 (125 to 305)	NS	192.5 ± 31.4 (134 to 243)
3 months	230.9 ± 52.7 (121 to 300)	NS	200.2 ± 35.2 (147 to 275)
6 months	215.8 ± 40.6 (136 to 280)	NS	192.7 ± 37.6 (127 to 260)
Within the group	0.148		0.412
TRG			
Baseline	167.8 (127.7 to 200.0)	NS	166.4 (116.5 to 212.0)
3 months	178.5 (117.0 to 228.6)	NS	157.9 (120.0 to 220.1)
6 months	169.0 (104.0 to 215.0)	NS	167.5 (73.0 to 213.6)
Within the group	0.762		0.136
HgA1c			
Baseline	7.4 (6.9 to 8.4) ^a	<0.001	5.3 (5.2 to 5.6)
3 months	7.3 (5.8 to 8.3) ^b	<0.001	5.2 (5.1 to 5.4)
6 months	7.4 (5.7 to 8.6) ^{a,b}	<0.001	5.2 (5.1 to 5.5)
Within the group	0.020		0.639
Insulin			
Baseline	14.5 (10.6 to 22.0)	NS	18.3 (10.7 to 22.6)
3 months	14.0 (7.8 to 18.5)	NS	14.7 (7.8 to 18.6)
6 months	14.0 (6.8 to 18.1)	NS	17.1 (8.5 to 23.4)
Within the group	NS		NS
Glucose			
Baseline	142.0 (128.0 to 162.0) ^{a,b}	<0.001	86.5 (80.5 to 92.2)
3 months	138.0 (116.0 to 185.0) ^a	<0.001	91.5 (78.5 to 96.5)
6 months	153.0 (121.0 to 218.0) ^b	<0.001	90.5 (78.5 to 97.5)
Within the group	0.023		0.845
HOMA-IR			
Baseline	5.35 (4.21 to 8.8)	<0.001	3.93 (2.25 to 5.06)
3 months	4.5 (2.31 to 8.22)	0.001	3.0 (1.8 to 4.18)
6 months	5.4 (2.20 to 6.57)	0.003	3.87 (2.05 to 5.37)
Within the group	NS		NS

Different superscript letters (a, b, c) within columns differ significantly. NS: non-significant difference, HDL: high density lipoprotein, LDL: low density lipoprotein, TC: total cholesterol, TRG: triglyceride, HgA1c: hemoglobin A1c, HOMA-IR: homeostatic model assessment-IR.

adjusted for age and sex to obtain the corrected *P* values. Moreover, we performed log transformation of variables that were not normally distributed. Bonferroni correction was used for post hoc comparisons. Missing values were attributed using the last observation carried forward method. A commercial statistical software (SPSS Statistics V21, IBM, Chicago, IL, USA) was used for analyses with the significance level set at *P* = 0.05.

Results

There were no significant differences in the demographic characteristics, oral hygiene habits, and anthropometric status between the groups. During the evaluation period, none of the participants reported changes in their lifestyle or eating habits, and no alterations were observed in the anthropometric measurements for both groups (Table 1).

No patients took anti-inflammatory and/or antimicrobial medication during the evaluation period.

Periodontal parameters were similar at baseline for both groups. None of the patients had any complaints following periodontal treatment. There were no significant differences between groups in the follow-up period. However, intra-group analysis revealed significant improvements at the 6-month follow-up. The numbers of decayed teeth were similar for both groups at all evaluations, these were significantly reduced in both groups after restorative dental treatments following periodontal therapy (Table 2). In addition, patients in both groups were in good health when they completed the study. No adverse effects were reported for periodontal treatment.

No significant differences were observed in the lipid profiles and insulin levels between the study groups

Table 4 Values of inflammatory parameters in patient subjects

	Diabetic group	Between groups	Non-diabetic group
TNF- α			
Baseline	14.6 (12.0 to 17.3) ^a	NS	12.8 (10.5 to 15.0) ^a
3 months	10.9 (6.3 to 12.4) ^a	NS	11.3 (7.2 to 16.1) ^a
6 months	5.1 (4.1 to 6.4) ^b	NS	3.8 (2.6 to 6.4) ^b
Within the group	<0.001		<0.001
IL-6			
Baseline	2.32 (1.72 to 4.7)	NS	2.23 (1.8 to 4.6)
3 months	2.04 (1.8 to 2.4)	NS	2.13 (1.8 to 3.0)
6 months	2.00 (1.8 to 2.4)	NS	2.04 (1.8 to 2.4)
Within the group	NS		NS
PTX-3			
Baseline	4.38 (3.7 to 6.1)	NS	4.76 (3.1 to 7.9)
3 months	4.31 (3.0 to 5.1)	NS	4.50 (3.0 to 6.9)
6 months	4.43 (3.7 to 5.6)	NS	4.62 (3.0 to 6.8)
Within the group	NS		NS
HsCrp			
Baseline	3.6 (3.4 to 10.2)	NS	3.4 (3.4 to 5.4)
3 months	3.4 (3.4 to 10.7)	NS	3.3 (3.2 to 5.4)
6 months	3.6 (3.2 to 8.2)	NS	3.3 (3.2 to 8.2)
Within the group	NS		NS

Different superscript letters (a,b,c) within columns differ significantly. NS: non-significant difference, TNF- α : tumor necrosis factor-alpha, IL-6: interleukin-6, PTX-3: pentraxin-3, HsCrp: high sensitive C-reactive protein.

(Table 3). However, HbA1c levels were significantly higher in the DM group ($P < 0.001$) than the non-DM group in all examinations. In addition, HbA1c levels were significantly reduced at the 3-month follow-up in the DM group ($P = 0.02$). HOMA-IR was reduced at the 3-month follow-up in both groups ($P = 0.042$), but HOMA-IR levels were significantly ($P < 0.01$) higher in the DM group than the non-DM group (Table 3).

No differences were observed in inflammatory parameters using inter-group or intra-group analyses, except for TNF- α levels. TNF- α levels were significantly reduced at the 6 month follow-up visit in both groups ($P < 0.001$) (Table 4).

Discussion

We made several important observations during our study. Firstly, DM did not affect the clinical response to periodontal treatment. Secondly, only levels of TNF- α and HbA1c were significantly altered in the diabetic group, and no changes in lipid parameters were observed in both groups.

SRP is an effective method for treating CP. The addition of FMD to FM-SRP or quadrant SRP (Q-SRP) is effective (13,14) and does not cause any obvious discomfort or change in one's quality of life (15). Moreover, based on a recent meta-analysis, FMD, FMS, and Q-SRP all effectively manage CP. Comparison of FMD and Q-SRP revealed that FMD was moderately better than Q-SRP in reducing probing depth and increasing clinical attachment level (13). Therefore, we used FMD and FM-SRP as the treatment of choice to restrict the cumulative effect of

bacteremia and avoid repeated acute inflammation during treatment (16,17). As a result, significant improvements were observed in all periodontal parameters throughout the study period in both groups.

It can be argued that only poorly controlled DM patients can be compared with systemically healthy non-obese patients as the control group. However, evidence suggests that obesity is the main factor for controlling DM (18,19). The prevalence of obesity has not been associated with DM in the Turkish population, but Daousi et al. (18) reported that 86% of DM patients were overweight or obese. We designed the present study based on these findings.

Recent studies evaluating the effect of periodontal treatment on inflammatory mediators in obese patients (BMI ≥ 30 kg/m²) reported a significant reduction in circulating pro-inflammatory cytokines (20-22). Gonçalves et al. (23) reported less of a decrease in TNF- α levels in obese patients compared with non-obese patients following non-surgical periodontal treatment. We have previously demonstrated (12) a significant decrease in TNF- α levels in non-DM obese patients and IL-6 levels in obese non-DM and healthy individuals. However, in this study, only TNF- α levels were significantly reduced after 3 months.

Although previous results are inconsistent with ours (12,23,24), IL-6 and hsCRP levels are generally reduced in diabetic and obese patients following periodontal treatment. Other inflammatory mediators (IL-6, hsCRP, and PTX-3) were not significantly different in the inter-group or intra-group analysis in our study. This could be

explained by the inclusion of patients with moderately severe periodontal problems and mostly class I obesity (BMI of 30-34.9 kg/m²). The magnitude of systemic inflammation in these individuals could be lower compared with more severely obese patients (25).

PTX-3 is an early marker of innate immunity and inflammatory responses in diabetic patients. It is structurally linked to short pentraxins, including hsCRP, and is strongly expressed in atherosclerotic lesions and in patients with chronic kidney disease (26). PTX-3 is synthesized by several cells and tissues, including macrophages, fat tissue, and vascular endothelial cells, unlike hsCRP, which is only produced by hepatocytes (27).

Various cross-sectional studies have been published (28-30), however only one study (31) has investigated alterations in PTX-3 levels after 1 month of periodontal treatment. This makes it difficult to interpret our results in relation to the findings of previous studies. Mathew et al. (31) reported a significant decrease in PTX-3 levels after 1 month of periodontal therapy. However, we did not find any significant changes in PTX-3 levels throughout this study. Clinically, this is a very early stage to evaluate altered PTX-3 levels. In addition, PTX-3 and HsCrp belong to the same family; therefore, it is not unexpected that PTX-3 levels did not change (32). This result may also be explained by the inclusion of patients with moderate periodontitis.

Periodontal treatment reduced HbA1c levels 3-4 months after treatment (33,34). These reports support our findings that FM-SRP with FMD reduced HbA1c levels in diabetic patients after 3 months. However, the effect we observed at 3 months was no longer significant after 6 months, which is also in agreement with results reported in another study (35).

The effect of periodontal disease on DM may be caused by a systemic increase in pro-inflammatory mediators that exacerbate IR (1,12). Successful periodontal management appears to have positive effects on the metabolic control of type 2 DM (1,36,37). Type 2 DM is a multiple-risk-factor syndrome, but decreased insulin sensitivity, or IR, is essential to the development of this metabolic disease (36). The pro-inflammatory cytokine TNF- α is produced by adipose tissues in obese individuals and is a predominant player in inducing IR (38,39). Therefore, the improvement in metabolic control of DM via enhanced insulin sensitivity due to a decrease in peripheral TNF- α concentration can be achieved by periodontal treatment.

HOMA-IR levels were significantly different between the groups at all follow-up examinations. Only the diabetic group showed a significant reduction in intra-

group analysis for HOMA-IR value in our study. We compared the obese group in the present study with an obese group from a previous study, where periodontal therapy reduced HOMA-IR by approximately 26% after 3 months (12). Although we observed a reduction in HOMA-IR after 3 months, the reduction ratio was lower. However, the baseline values in the previous study were higher than in the present study (4.9 vs. 3.9) and the reduction of HOMA-IR by periodontal therapy was higher than our 3-month value (3.6 vs. 3.0). The HOMA-IR levels reported here were better than the previous study at baseline and after 3 months (12). Similar to our findings, Sun et al. (40) reported that periodontal therapy reduced HOMA-IR levels in diabetic patients. However, different methodologies were used and we should compare these findings with caution. Sun et al. (39) evaluated only diabetic patients and obesity was an exclusion factor.

Only TNF- α values were significantly reduced in both groups. Therefore, we partially concluded that periodontal treatment has no systemic effect on the tested parameters. However, the alterations in FPG ($P < 0.05$), HbA1C ($P < 0.05$), and HOMA-IR ($P < 0.05$ after 3 months) were only observed in the DM group.

There were some limitations in the present study. First, although we calculated that 12 patients per group was sufficient to obtain significant results, the high variability among the individuals may have resulted in the observed discrepancies. Second, the inflammatory parameters were evaluated only in serum samples and not in gingival crevicular fluid. Third, our study population consisted mostly of class I obese patients, so obesity subgroups could not be compared. Fourth, we did not analyze any patients with severe periodontitis.

Within the limits of this prospective study, we concluded that the clinical periodontal response to FM-SRP and FMD was successful and that TNF- α levels were significantly reduced. In addition, HbA1C and HOMA-IR were altered in obese DM patients at the 3-month evaluation.

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Conflict of interest

The authors declare that there is no conflict of interest concerning the contents of the study.

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