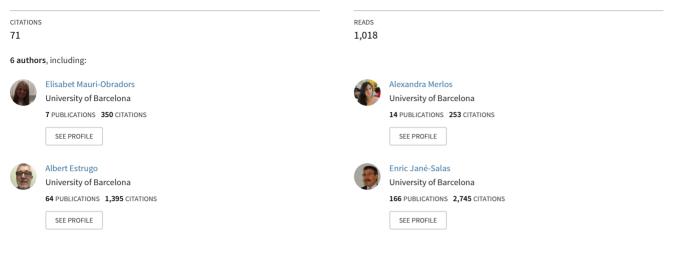
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Benefits of non-surgical periodontal treatment in patients with type 2 diabetes mellitus and chronic periodontitis: A randomized controlled trial

Article *in* Journal Of Clinical Periodontology · December 2017 DOI: 10.1111/jcpe.12858



Article type : Randomized Clinical Trial

Benefits of nonsurgical periodontal treatment in patients with type 2 diabetes mellitus and chronic periodontitis: a randomized controlled trial

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Running title: Periodontal treatment and glycemic control

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This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/jcpe.12858

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Abstract:

Background: Periodontitis and diabetes are highly prevalent conditions whose association has long been recognized.

Objective: To evaluate the effect of nonsurgical periodontal treatment on serum HbA1c (hemoglobin A1c or glycated hemoglobin) levels in patients with type 2 diabetes.

Research Design and Methods: This was a 6-month, single-masked, randomized clinical trial based on 90 patients (HbA1c: 7.7% (61 mmol/mol) \pm 1.13%) who were randomly assigned to either the treatment group (oral hygiene instructions + scaling and root planning using ultrasound and Gracey curettes) or the control group (oral hygiene instructions + supragingival removal of plaque and calculus using ultrasound). Pocket depth, gingival index, and plaque index were assessed at baseline and after 3 and 6 months together with determinations of fasting plasma glucose, HbA1c, and bacterial counts.

Results: Treatment significantly improved the periodontal and metabolic parameters (p<0.05) whereas in the control group no improvement was observed. These results were consistent with the bacteriological results in most but not all cases.

Conclusion: Non-surgical periodontal treatment resulted in a better glycemic status of type 2 diabetes patients and demonstrated the importance of oral health in their general health.

Keywords: glycosylated hemoglobin, periodontal disease, type 2 diabetes mellitus, scaling and root planning, PCR.

Inflammatory periodontal diseases are the most common chronic inflammatory condition, with up to 90% of the world's population affected. The association of periodontitis with diabetes mellitus has been largely recognized (Preshaw et al. 2012; Pihlstrom et al. 2005).

Inflammation of the periodontum starts by the formation of a subgingival biofilm, being major risk factors smoking and diabetes (Preshaw et al. 2012). The increased risk of periodontitis for diabetic patients depends on the glycemic control, as in other complications.. Thus, patients with well-controlled glycated hemoglobin (HbA1c) (~7% (53 mmol/mol)) have a risk of periodontitis low increasing exponentially as glycemic control declines (Al-Khabbaz 2014).

Mechanisms by which diabetes influences the periodontium, by altering the host immune, inflammatory, and wound-healing responses, promoting the accumulation of advanced glycation end products, and inducing high levels of pro-inflammatory cytokines have been

are not fully understood; the roles of inflammation, immune function, neutrophil activity, and cytokines are well-established (Taylor et al. 2013). Pro-inflammatory cytokine levels increase with the severity of periodontitis being interleukin 6 (IL-6) a predictor of successful treatment Shyu et al. (2015). Strong association between diabetes and apical periodontitis, specifically, between glycemic control and periapical inflammation has been reported (López-López et al. 2011, Segura-Egea et al. 2012). Conversely, periodontal treatment improves glycemic control. A mean difference of HbA1c before and after periodontal treatment of 0.40% (95% CI -0.77 to -0.04%, P = 0.03) in favor of treatment groups has been shown (Teeuw et al. 2010). Despite periodontal therapy seems to improve metabolic control, evidence is not enough to support significant association between periodontal therapy and metabolic control in diabetic patients. More evidence is needed (Mauri-Obradors et al. 2015, Wang et al. 2014). The aim was to determine whether 6 months of non-surgical periodontal therapy can lead to a

The aim was to determine whether 6 months of non-surgical periodontal therapy can lead to a reduction in HbA1c levels in patients with type 2 diabetes and generalized chronic periodontitis.

reported (Mealey et al., 2006). Although the mechanisms linking diabetes and periodontitis

Research Design and Methods

Study design

This 6-month, single-blind, randomized trial was a prospective, longitudinal comparing two groups (n=90). Participants and their dentist were obviously aware of the group assignment: treatment (TG) or control (CG) while the single examiner was not. Randomization was achieved by computer program. Ethical approval was from the Medical Ethics Board, University of Barcelona (ref: 367). The study was conducted in accordance with Helsinki Declaration (1975), following CONSORT guidelines (Schulz et al. 2010).

Study participants

Written informed consent was obtained. Inclusion criteria were: type 2 diabetes (diagnosed at least 1.5 years prior the study) and generalized chronic periodontitis (Armitage 1999) at least 9 teeth present and >30% of the probed gingiva with a depth and clinical attachment level \geq 4 mm. Exclusion criteria were antibiotic treatment during the previous 15 days or for periods >10 days during the last 3 months. non-surgical periodontal treatment within the past 6

months, pregnancy, significant changes in diabetes medication during the course of the study, and evidence of other serious systemic disease (ASA III or IV).

Sample size calculation

Up to a 0.80% improvement of HbA1c levels was expected in the TG and a 0.45% in the CG (response to hygiene control and dental intervention). With a power of 80% and an α -error of 5%, and accepting an α -risk 0.05 and a β -risk of <0.2 in a bilateral contrast, 36 patients would be needed in each group to detect statistically significant differences. An estimated rate of 20% loss of patients during follow-up was considered. Thus a total of 48 patients were assigned to CG and the rest (42) to the TG.

Periodontal examination

Patients underwent full periodontal assessment at baseline and at 3 and 6 months. Clinical examination included: (i) plaque index (PI) and (ii) gingival index (GI) of each tooth; and (iii) the probed pocket depth (PPD), at six sites per tooth with a standard manual periodontal probe of 1.5 mm diameter (Figure 1). In the first visit Clinical Attachment level (CAL) was calculated as follows: (i) in the patients having recession of the gingival margin, by adding the probing depth to the gingival margin level; (ii) in patients with gingival margin covering the corona, CAL was calculated by subtracting the gingival margin level from the probing depth and finally (iii) in patients whose gingival margin was at the normal level, CAL was coincident with PD.

Periodontal intervention

All study participants were instructed in oral hygiene using the modified Bass technique. Periodontal 4 was performed at baseline by removal supragingival deposits (plaque and calculus) using an ultrasonic scaler (SATELEC P5 Newtron XS, Acteon, Merignac, France). In addition, TG patients were treated by full mouth debridement, which consisted of scaling and root planning (SRP). Loss of periodontal health, defined as a PPD >2 mm and periodontal attachment loss of >2 mm in >30% of the evaluated sites were considered as criteria of withdrawing from CG, none of patients satisfy these criteria. Control visits were conducted at 3 and 6 months, HbA1c value was recorded at baseline and at 6 months-visit, oral hygiene instructions were repeated, and mouth debridement was conducted for individuals in the TG when needed (presence of points of bleeding and/or increased PPD).

Measurement of metabolic parameters

HbA1c and fasting plasma glucose (FPG) data were obtained from a blood analysis within the period of 30 days before baseline and at the last visit (6 months). HbA1c was determined using high-performance liquid chromatography. Values were from the databases of endocrinology control performed to all diabetic patients in Spain.

Bacterial strains and growth conditions

Aggregatibacter actinomycetemcomitans (Aa) DMS 11122, Prevotella intermedia (Pi) DMS 20706, Porphyromonas gingivalis (Pg), and Tannerella forsythia (Tf) ATCC 43037 were used as controls.

Aa was grown in TGY (30g/L trypticase soy broth, 6g/L yeast extract, 8g/L glucose) at 37°C , 5% CO₂ 24-48 h. Pi, Pg, and Tf were grown in Fastidious Anaerobe Broth (Lab M, Lancashire, UK) at 37°C in anaerobic atmosphere (85% N₂, 5% H₂, 10% CO₂).

Specimen collection of plaque samples

Supragingival plaque was removed prior sampling. Two paper points (size 45) were inserted into the deepest periodontal pockets of both the upper and the lower teeth for 30 s. The points were then collected into microcentrifuge tubes containing 1 ml of phosphate buffer (80 g NaCl; 2 g KCl; 14.2 g Na₂HPO₄; 2.7 g KH₂PO₄; 1 L distilled water; final pH 7.4) and stored at -80°C until use. The treatment performed in both upper and lower arch was identical; thus specimens from tips coming from the same patient were pooled to allow comparison between individuals.

DNA was extracted from cultured bacteria and plaque samples using the DNeasy blood & tissue kit (Qiagen, Germany). Briefly, tubes containing the paper point samples were thawed and vortexed intermittently for 90 s, centrifuged (8,000 rpm, 5 min), suspended in 180 µl ATL buffer with 20 µl of proteinase K added, and incubated at 56°C for 90 min. Two hundred µl of AL buffer and 200 µl of 96% ethanol were added to the samples, which were then placed into the column and centrifuged at 8000 rpm for 1 min. Flow-through was discarded and 500 µl of AW1 buffer was added, followed by the addition of 500 µl of AW2 buffer and centrifugation at 14000 rpm for 3 min. The flow-through was again discarded. Finally, the DNA was eluted in 150 µl of elution buffer.

Purified DNA of the controls was obtained from 1-ml overnight culture. To obtain standard curves, ten-fold dilutions were prepared from a starting point of 300,000 copies of the target gene. The primers and sequences targeting the species-specific DNA regions used for the analyses in this study are listed in Table 1

Real-time quantitative PCR.

Genome-copy levels were considered numerically equivalent to bacterial cell levels, assuming that each cell contained a single genome copy. Standard dilutions were subsequently used to generate the amplification profile.

Real-time qPCR was performed using the SensiFast SYBR® Hi-ROX kit (Bioline, London, UK). The 20- μ l reaction mixture contained 10 μ l of 2× SensiFast SYBR® Hi-Rox Mix, 400 nM of forward and reverse primers, and 5 μ l of extracted DNA. Polymerase activation was achieved at 95°C for 3 min, followed by 40 cycles of denaturing (95°C, 5 s), annealing (60°C, 10 s), and extension (72°C, 20 s). All amplifications and detections were carried out in an ABI 7900 HT thermocycler (Applied Biosystems) in a 384 multi-well plate. Amplification was monitored as fluorescence generated by the double-stranded DNA-SYBR complexes. Dissociation curves were constructed within a temperature range of 60–95°C. Data were analyzed using SDS2.4.1 software (Applied Biosystems). A bacterial load of <200 cells was considered negative.

Data analysis

Standard curves were constructed by plotting the Cq values generated from the qPCR and total cell concentrations (log CFU/mL). The correlation between the Cq values and CFU/mL was automatically generated.

All assays were developed with a linear quantitative detection range established by a slope of 3.2-3.7 cycles/log decade, r2 >0.994, and an efficiency range of 1.8-2.0.

Statistical analysis

A descriptive analysis of the measures of central tendency (mean, median) and dispersion (standard deviation, interquartile range) was performed for quantitative variables with a normal distribution (Kolmogorov-Smirnov test, p>0.05). Qualitative variables were described

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according to frequency (n) and percentage. The bivariate analysis was based on independent data according to normality in Student's t test or an ANOVA. The Mann Whitney U test and the Kruskal-Wallis test were used to compare qualitative and quantitative variables, respectively, with two or more categories; A χ^2 test was used to compare qualitative variables, and a Pearson or Spearman correlation analysis to compare quantitative variables, depending on the normality criteria (Kolmogorov-Smirnov test, p>0.05). Paired data were subjected to a bivariate analysis using Student's t test. Variables that were statistically significant (p<0.05), did not interact with each other, or were clinically relevant were considered in the multivariate linear regression analysis. All tests were two-tailed. A p-value <0.05 was considered to indicate statistical significance. The statistical analyses were carried out using the statistical package SPSS 18.0 for Windows (Statistical Package for the Social Sciences, 2009). Data from all 90 patients were included in the statistical analysis. Data from patients lost to the 3- or 6-month evaluation or who quit the study before its end were included in the statistical analysis as "intention to treat."

Clinical characteristics are summarized in Table 2. At baseline, the two groups had similar mean values for medical parameters, age, sex, medications, duration of diabetes, toothbrushing frequency, interproximal brush use, habit variations, weight, and medications, but more patients in the TG were smokers. The absence of differences in changes in habits, diet, diabetic treatment, and weight variations minimized the influence of external variables on the

Periodontal parameters

After SRP, an improvement in periodontal parameters was observed in the TG whereas the changes in response to the control regimen were minimal (Figure 3). In addition, a comparison of the PI and GI values of the two groups indicated a significant improvement in TG patients at 3 and 6 months (p=0.000) but not in CG patients (p=0.487) (Figure 3).

Metabolic parameters

The similarity between the mean HbA1c values 6 months before the study and at baseline indicated that in the absence of treatment HbA1c levels remain roughly constant. At baseline, the average FPG was also similar between CG and TG patients: 151.7mg/dl (SD 41.90) and 168.73mg/dl (SD 49.54), respectively (p=0.093). However, the difference in the glycemic levels of the two groups after 6 months was significant (p=0.022), decreasing significantly in the TG (18.71 mg/dl, SD 50.35) and increasing in the CG (16.25 mg/dl, SD 54.73). Thus,

glycemic improvement differed significantly between the two groups (p=0.019). Only the variable "group" influenced HbA1c improvement (p=0.019) (Figure 3).

Pearson and Spearman correlation analyses indicated that HbA1c was not influenced by age, height, weight, BMI, time of diabetes evolution, PPD, PI, or GI .The absence of a correlation between PPD and a change in the HbA1c level during the study showed that a heterogeneous initial PPD does not affect the results of treatment. In addition, HbA1c improvement was not related to smoking, body mass index (BMI), frequency of mouthwash use or tooth-brushing, the PI, or the GI, as concluded from the ANOVA (Figure 3).

Sensitivity analysis

The robustness of our conclusions was assessed in a substudy excluding patients with extreme PPD values (>3.5 mm and <2.5 mm) There were no significant differences in the PPD values of the 20 TG and 27 CG patients (3.09 mm and 2.94 mm, respectively, p=1.29). A sensitivity analysis confirmed the greater improvement in HbA1c levels in TG than in CG patients. The Δ HbA1c values (mmol/mol) were -0.51% and -0.06%, respectively (p=0.023). A clear reduction in bacterial counts was determined in some but not all patients, with improvements in the counts of only some bacterial species (Figure 2). This was welldemonstrated in patient #1 of the CG, in whom there was a drastic reduction only in Aa; all other bacterial counts remained high; moreover, the clinical evaluation showed a significant reduction in the HbA1c level (-1.20%). By contrast in others, like patient 20 (TG) there were no significant modifications in the bacterial counts, although declining HbA1c levels were accompanied by decreases in PPD. This suggested that even if treatment had no effect on bacterial counts it leads to an improvement in the clinical condition of the patients and a reduction in PPD (-1.18 mm and -1.28 mm at 3 and 6 months, respectively). The results also indicated that neither Aa nor Pi is directly responsible for the periodontal pathology. Similarly, Pg and Tf counts remained high during the observation period. Moreover, the microbiological data for patients 6 and 46 were almost identical but whereas patient 6 was treated patient 46 was not; thus, despite the careful molecular microbiology analyses, our data demonstrate that the counts of periodonto-pathogenic bacteria correlate poorly with the clinical evolution of diabetic patients, suggesting the need for revised assessment methods.

This study evaluated the effect of nonsurgical periodontal treatment on glycemic control in patients with type 2 diabetes and chronic generalized periodontal diseaseas also done in previously published studies (Kiran et al. 2005, Rodrigues et al. 2003). Treatment

significantly improved HbA1c levels (0.47%), in agreement with similar clinical trials in which HbA1c levels improved by 0.4–0.8% for patients receiving SRP (Kiran et al. 2005, Chen et al. 2012, Koromantzos et al. 2011).

Our study population was larger than those in most published studies investigating the relationship between periodontal health and HbA1c levels (Kiran et al. 2005, Rodrigues et al. 2003, Koromantzos et al. 2011, Al-Mubarak et al. 2002, Lin et al., 2012, Katagiri et al 2009). To detect a difference of 0.4% in a study with a power of 90% and a type 1 error of 5%, a minimum of 19 patients per group is needed (Teeuw et al. 2010). Jones et al. 2007 when evaluating 165 patients, most of whom obese (mean BMI of 32) did not find significant improvement. The metabolic control was very poor, since in most the HbA1c level was >8.5% [69 mmol/mol; mean HbA1c 10% (86 mmol/mol), SD 1.3). Another study also failed to detect a benefit of periodontal treatment on glycemic control (Engebretson & Kocher 2013), the population was also overweight/obese (average BMI of 35). These results suggest that obesity and uncontrolled HbA1c limit the effect of periodontal treatment on the reduction of systemic inflammation. By contrast, our patients were moderately overweight, which is considered normal in diabetic patients. The mean BMI of the patients in our study was similar to that in the series of Koromantzos et al. 2011 and Kaur et al. (2015) and the mean HbA1c level was also significantly lower [-7.7% (61mmol/mol)]. The patients in our study had moderate generalized chronic periodontitis, assessed according to the criteria of Armitage (1999) and also followed by Navarro-Sanchez et al. (2007), and Santos et al. (2009). The average PPD in our study was 3.28 mm, similar that in the populations evaluated by Santos et al. (2009) and Engebretson et al. (2013). Moreover, metabolic control in our patients was moderate (mean 7.7% (61mmol/mol)), as in Koromantzos et al. (2011).

A worse response to periodontal therapy in smokers than in non-smokers has been reported (Türkoğlu et al. 2016). Although our TG patients included more smokers than in the CG, the differences in periodontal and metabolic improvement were significant. Patients in the CG had a slightly lower PPD (2.97 mm) than those in the TG, as reported previously (2.29 mm) (Kiran et al. 2005). This result suggests that differences in PPD do not influence the effects of periodontal treatment. Significant improvements in the periodontal parameters of the CG, by the mere act of proper plaque removal by the patients themselves, was observed in other studies, but these improvements were not as quick or extensive as in the respective treated groups (Raman et al. 2014, Lee et al. 2009). In fact, Raman et al. (2014) found no significant differences between treated and control patients with respect to any of the evaluated

periodontal parameters, nor in their HbA1c or C-reactive protein levels assessed during months 2 or 3 of the study; however, changes in the plaque index at 2 months post-treatment were attributable to calculus removal (in TG), which reduced the amount of plaque retention. Correa et al. (2010) observed improvements in all periodontal and inflammatory parameters but not in the HbA1c levels in patients treated with SRP. Other studies similarly reported major improvements in treated patients (Koromantzos et al. 2011).

Numerous recently conducted randomized clinical trials have examined the effect of periodontal treatment on the glycemic control of patients with type 2 diabetes. Most showed a reduction in HbA1c after 3–4 months of follow-up (Kiran et al. 2005, Koromantzos et al. 2011, Kaur et al. 2015, Engebretson & Kocher 2013, Gay et al. 2014) and an association between mechanical periodontal treatment and a ~0.4% reduction in HbA1c levels at 3 months, equivalent to adding a second drug to a diabetes drug regimen in terms of the clinical impact (Chapple & Genco 2013). A consistent finding of several other systematic reviews and meta-analyses (Teeuw et al. 2010; Liew et al 2013; Sgolastra et al. 2012) is that periodontal treatment is associated with ~0.4% reduction in HbA1c (Teeuw et al. 2010). In their meta-analysis, Liew et al. (2013) determined a -0.41% improvement in HbA1c% in treated vs. control patients. Sgolastra et al. (2012) demonstrated a 0.65% improvement between the two groups.

These studies are confirmed by our results, which also are in agreement with those of Teshome & Yitayeh (2016). In a systematic review and meta-analisis Teshome & Yitayeh (2016) found a significant reduction of HbA1c in the treated group when compared with a control (mean differences of 0.48 and 0.53 at 3 and 6 months respectively). They show significant reduction in the first three months' period although no significant differences were seen between three and six months. Although modest, the difference is of significant clinical impact, because any reduction in glycosylated hemoglobin is associated with a decrease in the long-term complications (Stratton et al. 2000; Genuth et al. 2003; Unger 2008). In fact, 1% reduction in HbA1c is associated with a 21% reduction in the number of deaths related to diabetes, a 14% reduction in myocardial infarction, and a 37% reduction in the microvascular complications (Stratton et al. 2000). This highlights the importance of periodontal treatment in patients with diabetes, as it will contribute to HbA1ccontrol and therefore to a reduction in complications (Casanova et al. 2014). A recent cohort study reported that in type 2 diabetes patients, periodontitis progression is associated with increases in HbA1c. This reinforces the hypothesis that the periodontal treatment improves glycemic control (Costa KL et al. 2017). On the other hand, the meta-analysis conducted by Grellmann et al. (2017), supports the

additional effect of the use of systemic antibiotics in periodontal treatment. Although, antibiotic prescription should be restricted to particularly complicated clinical scenarios

The significant decrease in FPG in our TG patients at 6 months is consistent with other studies reporting a change in FPG levels in the intervention group (Kaur et al. 2015; Rohlfing et al. 2002). The combination of plasma glucose and HbA1c levels serves as a good indicator of diabetes control (Telgi et al. 2013). Periodontal evaluation is essential for individuals with diabetes, who should be aware of their increased risk of periodontal disease. Thus, dentists play a critical role in the management of diabetes patients, identifying those at high risk of diabetes and helping them to control their periodontal disease and therefore their metabolic status. In addition, periodontal therapy could lead to cost savings in patients with type 2 diabetes, thanks to its effect on the metabolic control of these patients (Solowiei-Wedderburn et al. 2017).

Conclusion

The main finding was the improved periodontal status and the significant improvement in metabolic control 6 months after nonsurgical periodontal treatment. No changes in lifestyle of nor in the medical treatment could have influenced these results. Moreover, the periodontal status and metabolic control in the CG, remained unchanged.

Acknowledgements: This study was partially funded by a research grant from SEPA, and by a research grant from the University of Barcelona. We appreciate the collaboration of the endocrinology service of the *Hospital of Bellvitge* for providing us with the results of the analytics of the study patients. We would thank the Catalan association of people with diabetis (ACD) for aiding in participant recruitment for this study. Guarantors: Jose López-López and Miguel Viñas.

Clinical relevance

Scientific Rationale for Study to explore whether 6 months of non-surgical periodontal therapy can lead to a reduction in HbA1c levels in type 2 diabetes patients having generalized chronic periodontitis by means of a randomized clinical trial. *Principal Findings*, nonsurgical periodontal treatment during 6 months is associated with significant improvement in metabolic control. Bacteriological analysis of periodontal microbiota by PCR should be revised since association is actually poor. *Practical Implications* the role played by dentists

in the management of diabetes by identifying those at high risk of diabetes and contributing to the control of periodontal disease and metabolic status is crucial.

Source of funding

No external funding, apart from the support of the authors' institution, was available for this study

Disclosure

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

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Figure legends

Fig 1.

Flow Chart of the study. In the GC there were 4 dropouts: 1 change of address, 1 personal reasons and 2 diseased (Ictus and angina). In the GT there were 7 dropouts: 4 diseased (Ictus, psychiatric disease, kidney failure and trauma) 1 job change, and 2 personal problems. Baseline visits started September 2013, interventions finished February 2015.

Fig 2.

Mean evolution of periodontopathogenic bacterial counts obtained by RTqPCR.

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Table 1. Description of the species-specific primers used in this study, based on the variable regionsof the 16S rRNA gene sequence.

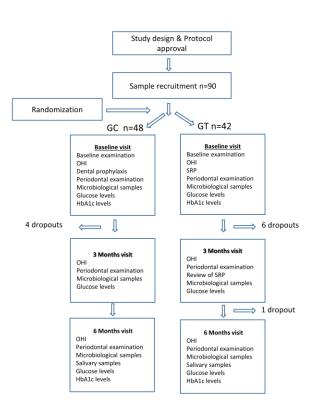
Target	Oligonucleotide Sequence (5'- 3')	Reference
Agreggatibacter actinomycetemcomitans	F: TTACCTACTCTTGACATCCGAA R: ATGCAGCACCTGTCTCAAAGC	Maeda et al. [41]
Prevotella intermedia	F: AATACCCGATGTTGTCCACA R: TTAGCCGGTCCTTATTCGAA	Suzuki et al. [42]
Porphyromonas gingivalis	F: CTTGACTTCAGTGGCGGCAG R: AGGGAAGACGGTTTTCACCA	Maeda et al. [43]
Tannerella forsythia	F: GCGATGGTAGCAATACCTGTC R: TTCGCCGGGTTATCCCTC	Kuboniwa et al. [44]

Accepted

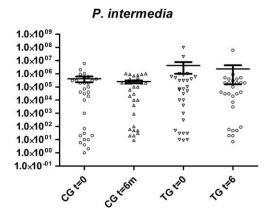
		Group		
		CG n (%)	TG n (%)	p-value
Age; Mean (SD)		62 (10)	61 (11)	0.798
Height; Mean (SD)		1.65 (0.08)	1,65 (0.10)	0.980
Weight; Mean (SD)		80 (15)	79 (13)	0.700
BMI; Mean (SD)		29.39 (4.38)	29,04 (3.91)	0.691
Diabetes duration, years; Median (IQR)		11 (12)	10 (10)	0.068
Sex	Male	20 (41.7)	17 (40.5)	0.909
	Female	28 (58.3)	25 (59.5)	
	0	45 (93.8)	27 (64.3)	0.02*
Smoking	1-9	1 (2.1)	6 (14.3)	
(nº/day)	10-19	0 (0)	3 (7.2)	
	≥20	2 (4.2)	4 (14.3)	
	Never	23 (47.9)	14 (33.3)	0.002*
Smoking	Current	3 (6.3)	15 (35.7)	
	Former smoker	22 (45.8)	13 (31%)	
	0	5 (10.4)	4 (9.5)	0.433
Daily brushing habit	1	16 (33.3)	21 (50)	
(times/day)	2	18 (37.5)	12 (28.6)	
	3	9 (18.8)	5 (11.9)	
	0	32 (66,7)	25 (59.5)	0.579
Daily mouthwash habit	1	12 (25)	12 (28.6)	
(times/day)	2	3 (6.3)	5 (11.9)	
	3	1 (2.1)	0 (0)	
Diabetic treatment	Oral hypoglycemic	20 (41.7)	21 (50)	0.182
	Insulin	10 (20.8)	3 (7.1)	
	Both	18 (37.5)	18 (42.9)	

 Table 2. Clinical characteristics of patients of treatment and control groups at baseline.

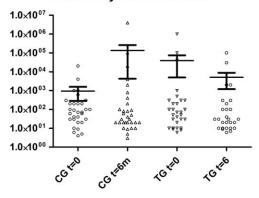
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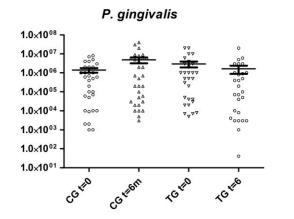


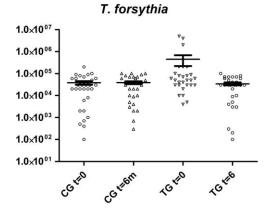




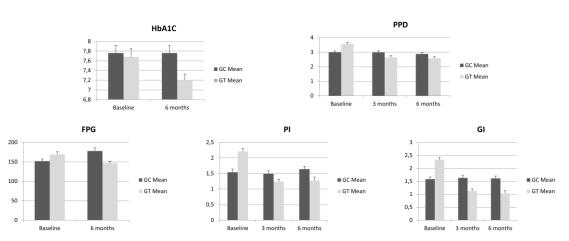
A. actinomycetemcomitans







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