Nonsurgical Periodontal Care for Diabetes Patients: A Case-Control Study

Moya-Villaescusa María José , Sánchez-Pérez Arturo * , Arráez-Monllor Marta , Portillo-Ortega Paloma , Mateos-Moreno Bibiana

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Article

Nonsurgical Periodontal Care for Diabetes Patients: A Case-Control Study

Moya-Villaescusa María José [1], Sánchez-Pérez Arturo [1,*], Arráez-Monllor Marta [2], Portillo-Ortega Paloma [2] and Mateos-Moreno Bibiana [1]

[1] Department of Periodontology, Faculty of Medicine and Dentistry, Universidad de Murcia, 30008, Spain; mjm.villaescusa@um.es (M.M.J.); arturosa@um.es (S.A.); bibimateos@um.es (M.B.)
[2] Department of Endocrinology, Virgen de la Arrixaca Hospital, 30120, El Palmar, Murcia, Spain; martaarraez@gmail.com (A.M.); paloma80es@hotmail.com (P.P.)
* Correspondence: arturosa@um.es (S.A.); Tel.: +34 968888594

Abstract: Background: Diabetes mellitus (DM) and periodontitis are two chronic diseases that are interconnected. The coexistence of these conditions leads to increased severity of periodontitis and challenges in controlling blood glucose levels in diabetic patients. Objectives: The aim of this study was to evaluate both the influence of periodontal disease and its treatment in patients with DM in terms of a reduction in glycosylated hemoglobin levels at 3 and 6 months after treatment. Methods: A sequential, nonprobabilistic, controlled, prospective and longitudinal case–control study was carried out at the University Dental Clinic of the Morales Meseguer Hospital in Murcia, Spain. Thirty diabetic patients were divided into two groups: patients with periodontitis (test group) and patients without periodontitis (control group). The periodontal and endocrine-metabolic variables were measured at baseline and at 3 and 6 months after periodontal treatment for both groups. Results: Statistically significant differences were found at 3 and 6 months after periodontal treatment with respect to HbA1c levels in the group of periodontal patients. However, these differences were not observed in the control group. Conclusion: The presence of periodontal disease increased HbA1c levels in patients with DM. Nonsurgical periodontal treatment significantly decreased the degree of periodontal inflammation and the HbA1c level at 3 and 6 months after treatment.

Keywords: periodontitis; glycosylated hemoglobin; glycemic control; nonsurgical periodontal therapy; periodontal disease

1. Introduction

Periodontal diseases (PDs) are pathologies that affect a large part of the population. These diseases are caused by biofilms, and their main clinical manifestations are gingivitis and periodontitis [1].

Several factors may be involved in the onset and progression of PDs. These include tobacco smoking, genetic factors, hormonal changes, stress, medication, diabetes mellitus, dietary deficiencies, and systemic diseases, among others. In general, all of these conditions can influence the immune response [2].

On the other hand, PD, especially in advanced stages of periodontitis (stages III and IV), can trigger or aggravate several systemic conditions, including preeclampsia and preterm birth [3], cardiovascular events [4], respiratory conditions [5], renal diseases [6], rheumatoid arthritis [7], and particularly diabetes mellitus (DM) [8,9], among others.

In brief, a bidirectional relationship between PD and DM has been suggested [10].

The mechanism linked to the altered immune response in patients with DM and PD appears to be associated with advanced glycation end products (AGEs) and the presence of their receptors (RAGEs) [11].

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This interaction has direct effects on the endothelium, neutrophil function, cytokine activation (particularly TNFα), and collagen synthesis and degradation, hindering reparative processes [12]. One way to assess the AGE level is through glycosylated hemoglobin (HbA1c), which measures the average level of glycosylated glucose in the blood over the last three months.

On the other hand, the persistence of poorly controlled periodontitis has been reported to contribute to systemic inflammatory response syndrome (SIRS), which leads to the development of glucose intolerance [13]. In addition, in severe cases, this condition complicates glycemic control [14,15].

Periodontal treatment has been shown to be highly effective at controlling periodontal disease [16]. The initial step in this treatment is motivation, involving plaque control by the patient and nonsurgical periodontal treatment (NSPT), followed by supportive periodontal treatment (SPT) [16–19]. Some authors consider NSPT to be effective at achieving glycemic control, comparable to the effect of adding a second oral antidiabetic drug [20]. Therefore, the control of periodontal disease by NSPT could play a crucial role in the production of AGEs and the management of DM.

The aim of this case–control study was to ascertain whether NSPT, when compared to no treatment, has an equivalent influence on the level of glycosylated hemoglobin (HbA1c) as the primary outcome variable. The plaque index (PlI), bleeding on probing (BOP), periodontal probing depth (PPD), and clinical attachment level (CAL) were included as secondary variables.

2. Materials and Methods

2.1. Ethical Approval

This study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Ethics Committee of the Virgen de la Arrixaca Hospital (ID: 141/2013, March 3, 2013) in Murcia, Spain. This was a case–control study.

This study followed the **Strengthening the Reporting of Observational studies in Epidemiology** (STROBE) statement for case–control studies.

2.2. Sample Size

A sample size of 15 patients in each group was estimated considering an α=0.05 [95% confidence interval] and β=0.2 [80% power]. These data were entered into the online calculator available at the following web address: https://www.questionpro.com/es/calculadora-de-muestra.html. The following formula was used: Sample Size $=n = \frac{Z^2 * p * (1-p)}{c^2}$

where Z = a confidence level of 1.96 (95%), p =.05 and c = the margin of error (.25%).

The formula substituted with actual values was as follows: (3.8416*(0.19208*0.95))/0.0625 = 11.213

The dropout rate during monitoring was assumed to be 30% = 3.363.

This sample size was in agreement with that in the study by Raman et al. [21].

2.3. Sample Distribution

Thirty diabetic patients (15 periodontal and 15 nonperiodontal patients; 8 women and 22 men; 5 smokers and 25 nonsmokers) with a mean age of 55 years were included in this study. Regarding the type of diabetes, 24 patients had type II DM, 6 patients had type I DM, and the mean duration of diabetes was 19 years. The patients were referred by the endocrinology service of the Virgen de la Arrixaca University Hospital in Murcia (Spain) to the University Dental Clinic of the Morales Meseguer Hospital in Murcia (Spain) for periodontal clinical examination by the same qualified person (B.M-M.). This person was trained and calibrated until the data obtained during the periodontal examination reached significant reliability, with a kappa coefficient close to 0.97.

2.4. Inclusion Criteria

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The inclusion criteria were as follows: diabetes mellitus patients of legal age with an HbA1c level >5.5 or <11 who signed the consent form to participate in this study.

2.5. Exclusion Criteria

The exclusion criteria were as follows: patients previously diagnosed and treated for periodontal disease; pregnant or lactating patients; individuals who had taken antibiotics, antiseptics, or medications that could affect the host response during the month prior to the periodontal assessment; and patients who did not sign the informed consent form.

2.6. Clinical Periodontal Examination

Once the patients were informed of the nature of this study and signed the informed consent form, the trained person proceeded to take a complete clinical history and a periodontogram. All periodontal recordings were performed with a manual periodontal probe (CP-15, Hu-Friedy Manufacturing Co., LLC, Chicago, USA). In addition, the examination was completed via orthopantomography to determine the periodontal status of the patient.

2.7. Blood Samples and Biometric Data

Endocrine-metabolic variables such as the type of DM, duration of disease, body mass index (BMI) and biochemical markers such as LDL, HDL, TG and HbA1c levels were determined by an endocrinologist at the Virgen de la Arrixaca Hospital in Murcia. No changes in diabetes treatment were made during the conduct of this study.

2.8. Group Assignment

The sample was divided into two groups: patients with periodontitis (test group) and patients without periodontitis (control group). Periodontitis was diagnosed in patients who presented with attachment losses due to inflammatory problems greater than or equal to 2 mm at the interproximal level or greater than or equal to 3 mm at the buccal or lingual/palatal level in two or more nonadjacent teeth.

All the samples were reviewed at 3 and 6 months after treatment, and all the periodontal and endocrine-metabolic variables mentioned above were noted.

2.9. Statistical Analysis

The data obtained were analyzed with SPSS statistical software (Statistical Package for the Social Sciences), version 25.0 (SPSS, Chicago, IL, USA). A descriptive and inferential analysis of both groups (test and control groups) was carried out to assess the existence of statistically significant differences between the groups. Student's t test for paired samples was used to determine the existence or absence of statistically significant differences within the same group (test and control groups) regarding the HbA1c level at 3 and 6 months. A p value <0.05 was considered to indicate statistical significance.

3. Results

No individuals dropped out during this study, either at 3 months or 6 months.

3.1. Distribution and Characteristics of the Sample

The resulting groups (test and control) were homogeneous with respect to the following variables: sex, age, type of DM, duration of DM, BMI and biochemical markers (LDL, HDL, TG, and HbA1c levels) at baseline (Table 1).

Table 1. Distribution and characteristics of the sample. (BMI: body mass index; HDL: high density lipoprotein; LDL: low density lipoprotein; TG: triglycerides; HbA1c: glycosylated hemoglobin).SD:

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standard deviation; Min: minimum value; Max: maximum value Non statistically significant differences p >.05.

	TEST GROUP: DM + PERIODONTITIS				CONTROL GROUP: DM + NO PERIODONTITIS			
	Mean	**SD**	**min**	**Max**	**Mean**	**SD**	**min**	**Max**
Age (years)	55.59	10.64	33.37	66.94	54.97	8.60	40.00	66.30
Time of Evolution (years)	18.13	10.1	4	39	18.87	12.70	4	42
BMI	29.24	4.32	20.52	34.19	30.52	3.74	25.82	38.10
HDL	55.67	24.18	-1	93	50.13	10.24	33	71
LDL	84	37.74	-1	124	100.47	29.64	44	159
GT	129.73	112.96	33	464	126.73	58	51	218
HbA1c	8.21	1.23	5.90	10.80	7.87	0.68	6.8	9.2

3.2. Evolution of Periodontal Variables

3.2.1. Clinical Attachment Level (CAL)

The mean periodontal attachment loss in the test group was 4.47 mm (SD: 1.09), with a minimum value of 2.85 and a maximum value of 7.38 mm. Three months after periodontal treatment, the CAL improved, reaching a mean value of 3.16 mm (SD: 1.22), with a minimum value of 1.95 mm and a maximum value of 6.52 mm. These values remained stable 6 months after treatment [mean CAL: 3.24 ±0.85 (1.97; 5.34)].

3.2.2. Gingival Bleeding Index (GBI)

The mean baseline GBI of the periodontal patients was 41%, and the GBI decreased to 7% and 13% at 3 and 6 months after periodontal treatment, respectively. In the control group, the mean baseline GBI was significantly lower (mean 12%, p <0.0001) than that in the test group, and although it decreased to 2% at 3 months after periodontal treatment, it was equal to that in the test group at 6 months after treatment (13%).

3.2.3. Hygiene Index (HI)

Although the HI was slightly greater in the periodontal patient group than in the control group at the beginning (87% versus 72%) and at 3 (62% versus 53%) and 6 months after treatment (63% versus 45%), the differences were not statistically significant.

3.2.4. Evolution of the Endocrine-Metabolic Variable HbA1c

Significant differences were observed at 3 (p=0.039) and 6 (p=0.025) months after periodontal treatment with respect to the HbA1c level in the group of periodontal patients. However, these differences were not found in the control group at 3 (p=0.352) or 6 (p=0.379) months after periodontal treatment (Figures 1 and 2 and Tables 2 and 3).

Table 2. HbA1c values, baseline, at 3 and 6 months of treatment in periodontal patients.

HbA1c	N	Mean	SD	Minimum	Maximum
Basal	**15**	**8,21**	**1,23**	**5,9**	**10,8**
3m	**15**	**7,91**	**1,27**	**5,6**	**10**

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6m	**15**	**7,59**	**1,13**	**6,1**	**9,6**

Table 3. HbA1c values, baseline at 3 and 6 months of treatment in control group.

HbA1c	N	Mean	SD	Minimum	Maximum
Basal	**15**	**7.87**	**0,68**	**6,8**	**9,2**
3m	**14**	**7,76**	**0,89**	**6,2**	**9,9**
6m	**12**	**7,77**	**0,67**	**6,7**	**9,1**

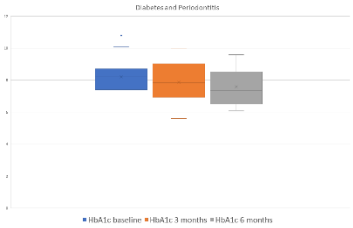

Figure 1. Changes in HbA1c levels in periodontal patients after periodontal treatment.

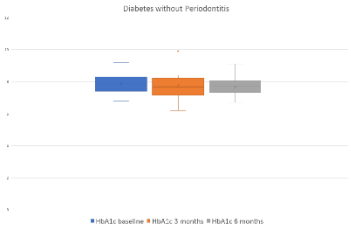

Figure 2. Changes in HbA1c levels in control patients after periodontal treatment.

In the test group, the HbA1c level decreased by 0.264% ± 0.11 [weighted mean difference (WMD) -0.264, 95% confidence interval (CI) = -0.156, -0.513, p= 0.039] at 3 months and by 0.571% ± 0.226 [WMD -0.571%, 95% CI = -0.083, -1.060, p= 0.025] at 6 months after periodontal treatment.

4. Discussion

4.1. Advanced Glycation end Products (AGEs) and Inflammation

A bidirectional relationship between DM and PD has long been suggested [22–24]. On the one hand, the persistence of an infection involving mostly gram-negative bacteria seems to amplify the proinflammatory response via cytokines, leading to SIRS [25,26]. On the other hand, increased AGEs are associated with increased destruction of periodontal tissues [11,12,21,23], thus creating a vicious cycle.

The accumulation of AGEs can lead to changes in the extracellular matrix and inflammatory responses in diabetic patients with periodontitis [11,12]. These findings suggest that AGEs may play a role in the pathogenesis of periodontitis, contributing to periodontal destruction [25]. The interaction of AGEs with their receptors, RAGEs, can lead to increased secretion of proinflammatory cytokines, further intensified by the presence of specific bacteria [26].

On the other hand, the accumulation of AGEs may promote the development of more aggressive subgingival flora, resulting in increased periodontal destruction and elevated levels of proinflammatory cytokines [10]. AGE inhibitors could mitigate these effects, offering a promising avenue for periodontal treatment in diabetes patients.

4.2. Primary Outcome

In our study, HbA1c levels decreased by 0.264% at 3 months and by 0.571% at 6 months after periodontal treatment; therefore, the values improved over time. These data are consistent with the results obtained in various systematic reviews [27,28], in which reductions of 0.27-0.56% were shown

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at 3-4 months after periodontal treatment. In another review of randomized controlled clinical trials, very similar reductions in HbA1c levels were observed at 3 and 6 months after periodontal treatment, with values of 0.514% and 0.548%, respectively [29].

In other studies [30], the statistically significant reduction in HbA1c levels at 3 or 4 months after periodontal treatment was not maintained over time and ceased to be significant at 6 months after treatment. In line with this study, in a recent review [31], the authors found significant reductions in HbA1c levels at 3 and 6 months after NSPT, but the levels decreased over time, from 0.49% at 3 months to 0.38% at 6 months.

Other studies [32–36] have not shown statistically significant differences in the HbA1c levels of periodontal patients with DM after periodontal treatment.

In the present study, both the test group and the control group underwent a hygiene education program and tartar removal. However, this treatment did not yield any improvements in terms of HbA1c levels in the control group. Although the HI improved, decreasing from 72% to 53% at 3 months after treatment and further to 45% at 6 months after treatment, these changes did not have a statistically significant impact on the HbA1c level in the control group. These findings align with those of Chen et al. [37], who indicated that patients with a lower degree of periodontal damage did not experience improvements in HbA1c levels.

Therefore, we believe that, in our study, meticulous SPT played an important role in achieving and maintaining low HbA1c levels even at 6 months.

4.3. Secondary Outcomes

As in other studies, there was total uniformity in that the outcome of NSPT was effective in both diabetic and nondiabetic patients in our study [16,22,38–41]. All clinical variables associated with periodontitis showed marked improvement after NSPT and were maintained with adequate SPT.

Because both groups were initially similar, the only variable that could aggravate periodontal disease was the HbA1c level, which was greater in the group of periodontal patients (mean = 8.21%; SD =1.23%) than in the control group (mean = 7.87%; SD = 0.68%). The U.S. National Health and Nutrition Examination Survey showed that people with elevated glycosylated hemoglobin levels have a greater risk of developing severe periodontal disease [42].

Regarding the GBI, before periodontal treatment, there was significantly more bleeding in the group of diabetic patients with periodontitis than in the control group. However, these differences disappeared after periodontal treatment and remained stable at 3 and 6 months after treatment. These findings show that NSPT is effective at reducing bleeding in diabetic patients with periodontal disease in the same way as it is in nondiabetic periodontal patients [16].

Our study presented a result similar to that reported by Raman et al. [21] in their meta-analysis. The decrease in the bleeding rate was very significant at 3 months and was equal to the decrease in the bleeding rate in the control group at 6 months. The modification of maintenance visits based on a patient's risk profile plays a fundamental role in inflammation control. In our study, the baseline bleeding rate ranged from 41% to 7% at 3 months and 13% at 6 months.

There was a slight relapse after 6 months, which we attributed to relaxation in the patients' hygiene habits. These data highlight the importance of regular maintenance visits within the SPT protocol.

In the group of periodontal patients, a clinical attachment gain of more than 1 mm was observed three months after periodontal treatment, and this gain remained stable at six months post-treatment. These results are consistent with those obtained in periodontal patients without any systemic disease [16]. A less favorable outcome has been reported, with a clinical attachment gain of only 0.22 mm observed three months after treatment [43].

4.4. Alternative Periodontal Treatment Options

Other nonsurgical periodontal treatment options include photodynamic treatment and/or the use of antibiotics. A recent meta-analysis [44] suggested that NSPT combined with photodynamic therapy and doxycycline achieves the best efficacy in reducing HbA1c levels. However, Taylor and

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Borgnakke [24] showed that there was insufficient scientific evidence to support the recommendation of NSPT combined with local or systemic antibiotics. Currently, due to the problem of bacterial resistance emerging from the use of antibiotics, joint antibiotic administration with nonsurgical periodontal therapy is recommended only for young patients with advanced-stage disease [45].

Finally, we must emphasize the importance of motivation in the maintenance of oral hygiene. It has been noted that, compared to individuals with better brushing efficiency, individuals with insufficient brushing efficiency have greater plaque levels, leading to increased levels of glycosylated hemoglobin [21,22].

4.5. Limitations

This study has several limitations. First, this study had a small sample size. Determination of our sample size was based on the agreement of patients to participate in this study, and a total of 30 patients agreed to participate. Our sample size is consistent with that of other similar studies; for example, Moeintaghavi et al. [46] included 40 patients, Raman et al. [21] included 32 patients, and Telgi et al. [47] included 40 patients. Conversely, the study with the largest number of patients was conducted by Engebretson et al. [40], who involved a total of 514 patients. This is noteworthy because, as mentioned by Li et al. [48], small samples may detect statistically significant differences, whereas large samples may not. We believe this discrepancy could be attributed to variations in HbA1c levels at the beginning of the study, differences in the stages of periodontitis and, most importantly, challenges in maintaining adequate patient control with close professional follow-up.

Second, selection bias was present: nonrandom sampling is associated with the risk of selecting individuals who are not representative of the broader population. This can lead to inaccurate conclusions. Furthermore, this study had self-selection bias. In some cases, participants may have self-selected themselves for this study, introducing bias if those who chose to participate differed systematically from those who did not.

Third, the generalizability of the findings is limited: a small sample may not accurately represent the broader population from which findings are drawn.

Fourth, as a consequence of the above, an increase in variability occurred: smaller samples are more susceptible to random variations, making it difficult to establish the true underlying trends or patterns.

Finally, the follow-up time was limited; therefore, insight into the long-term effects of the treatment is limited. Studies with short follow-up times may miss important long-term effects or trends.

4.6. Future Research Directions

Additional studies are needed to determine both the influence of the different degrees of severity of periodontal disease in diabetic patients and the impact of different HbA1c levels on the severity of periodontal disease.

5. Conclusions

Nonsurgical periodontal treatment significantly decreased the degree of periodontal inflammation and the HbA1c level at 3 and 6 months after treatment. Therefore, due to the repercussions for public health and the costs associated with the treatment of DM, periodontal examination and nonsurgical treatment should be considered part of the medical treatment of patients with DM.

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Institutional Review Board Statement This study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Ethics Committee of the Virgen de la Arrixaca Hospital (ID: 141/2013, March 3, 2013) in Murcia, Spain.

Informed Consent Statement Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: The data of this study are available to readers in Excel upon request to the corresponding author (arturosa@um.es).

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Conflicts of Interest: The authors declare no conflicts of interest.

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