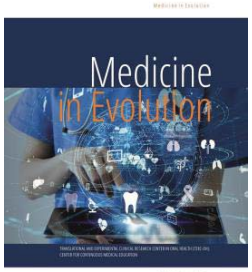
# Evolution of periodontal disease in patients with type 2 diabetes in the context of initial therapy - systematic review

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## Abstract

Periodontal disease and diabetes are two conditions with an increased prevalence in most populations around the world. Diabetic patients present particular manifestations in the oral cavity, mainly determined by the frequent presence of infectious processes, which may be due to: alteration of oral microbial flora, alteration of neutrophil function and/or microangiopathies.

The protocol of this review was developed following the principles of PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyzes) and was structured to cumulate the results of clinical trials based on the effects of non-surgical therapy on periodontal status of patients with type 2 diabetes.

**Keywords:** periodontal disease, hyperglycemia, type 2 diabetes, initial therapy

## INTRODUCTION

The frequency of type 2 diabetes mellitus (DM), a chronic metabolic condition, has been continuously rising worldwide. Diabetes is a metabolic disorder characterized by chronic hyperglycemia and altered metabolism of carbohydrates, lipids and proteins. The cause of this condition can be either a defect in insulin secretion or inadequate action of insulin on target cells in the body or a combination of both.

Regarding the clinical forms, they are represented by: type I diabetes (insulin-dependent diabetes), specific to children and young adults and represent approximately 10% of all patients with diabetes; type II diabetes (non-insulin-dependent diabetes) generally affects subjects over 40 years and type III diabetes, a very rare form that occurs secondary to pancreatic diseases, genetic syndromes, hormonal or drug manifestations (gestational diabetes, iatrogenic, senile, malignant diseases).

Chronic hyperglycemia is generally associated with long-term damage, dysfunction and even insufficiency of various organs such as eyes, kidneys, nervous system, heart and blood vessels [1]. Additionally, diabetic individuals exhibit unique oral symptoms that are mostly brought on by the frequent occurrence of infectious processes that may result from changes in the oral microbial ecology, altered neutrophil function, or microangiopathies. The first clinical signs in the oral cavity may be: frequent candidiasis, persistent gingivitis, periodontitis, polychaete, dry mouth, delayed tissue scarring, acetone-smelling breath, tongue hypotonicity, salivary hyperviscosity and increased tartar formation. The severity of these symptoms differs depending on the type of diabetes and its duration and the evolution can be unpredictable.

Periodontal disease and diabetes are 2 conditions with an increased prevalence in most populations around the world. The association between these two conditions has been recognized and discussed over the years by many dental professionals. About 30-50% of diabetics suffer from a form of periodontal disease, mild or moderate-severe form while the prevalence of severe periodontitis in diabetic adults is 9-11% of cases [2]. Epidemiological studies have identified that diabetes is a major risk for periodontal disease, increasing the risk of it occurring three times compared to non-diabetic individuals, especially if it is associated with inadequate glycemic control [3].

Some patients, especially those with type 2 diabetes, are asymptomatic in the first years after the onset of the disease. Other diabetic patients, especially children with absolute insulin deficiency, may have marked hyperglycemia, polyuria, polydipsia, polyphagia, weight loss, and blurred vision. Untreated, diabetes can even lead to death due to installed ketoacidosis or, in rare cases, due to non-ketotic hyperosmolar syndrome [4].

### *Aim and objectives*

The purpose of this systematic review is to follow the evolution of the periodontal disease in patients with diabetes in the context of initial therapy such as non-surgical treatment, in articles with randomized clinical trials.

## MATERIAL AND METHODS

The protocol of this review was developed following the principles of PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyzes) and was structured to cumulate the results of clinical trials based on the effects of non-surgical therapy on the periodontal status of patients with type 2 diabetes.

***Search strategy***

The search and analysis of the literature were performed in the following databases: PubMed, Cochrane and Clinical Trials.

The literature was researched using a combination of the terms:

- periodontal disease / periodontitis and Diabetes mellitus
- periodontal disease / periodontitis and Type 2 diabetes
- periodontal disease / periodontitis and non-surgical treatment on diabetes mellitus
- periodontal disease / periodontitis and initial therapy on diabetes mellitus

These keywords were used to analyze the literature from the most important databases, with scientific articles in English. Additional search filters were also used to optimize results such as: articles published in the last 10 years and randomized clinical trials.

Inclusion criteria were defined according to the PICOS model:

- Population (P) - adult subjects with type 2 diabetes
- Intervention (I) - non-surgical therapy of periodontal disease
- comparison (C) - periodontal status before and after non-surgical periodontal treatment (initial therapy)
- result (O) - periodontal status assessment
- type of study (S) - randomized controlled clinical trials

Thus, the question based on which the research of clinical studies was conducted was formulated: "What are the effects of non-surgical treatment on periodontal status in patients with type 2 diabetes?"

The criteria for including the articles in the analysis were: only those that reported randomized clinical trials; sample of subjects with type 2 diabetes; definite diagnosis of diabetes patients; evaluation of periodontal indices at the beginning and end of the study; at least 2 treatment groups in each study; at least 10 participants in each group and the adult population.

Exclusion criteria in choosing studies for types of diabetes other than type II; lack of details regarding the evaluation of periodontal status; articles older than 10 years; studies without clear results; languages of international circulation other than English.

Following the research of the specialized literature, a number of 52 scientific papers were identified in 3 databases (PubMed, Clinical Trials, Cochrane) of which 31 were evaluated in detail, after excluding duplicates, from which were excluded review and studies in other languages of international circulation. After evaluating them in terms of inclusion-exclusion criteria, a number of 6 studies were eligible for inclusion in this review. Figure 1 shows the selection diagram of the articles.

The search protocol was performed to include in the analysis, randomized clinical trials with at least two groups of subjects, with at least one study group to which non-surgical treatment was applied.

For the evaluation of the periodontal status, it was aimed that the clinical studies include the evaluation of periodontal indices such as: plaque index (PI), loss of attachment (PA), bleeding index (IS) and periodontal pocket depth (APP).

***Data extraction***

The data were extracted in an Excel table to obtain a count of the most important information. Data such as:

- name of the main author
- year of study
- country of study and type
- data on participants (number, age, sex)

- the periodontal status necessary for the eligibility to participate in the study
- measurements made to examine periodontal status
- the treatment administered and any medicinal substances where appropriate
- data on diabetes mellitus (Type and laboratory tests performed)
- main results

No information was included on the exclusion criteria for periodontal eligibility for each individual study and no information was included on drug treatment for diabetes or diabetes-related eligibility criteria (blood glucose, glycosylated hemoglobin, etc). Also, no information was presented regarding patients such as the presence of risk factors such as smoking, diet, etc.

## RESULTS

### *Data presentation*

The main data were presented in tables 1 and 2 which briefly present the main aspects of the 6 evaluated studies.

Table 1. Brief presentation of the 6 clinical trials analyzed

| No. | Reference | Type of study | Country | Characteristics of the participants | | | Periodontal status | Periodontal status measurements |
|---|---|---|---|---|---|---|---|---|
| | | | | No. | Age | Gender | | |
| 1 | Raman 2014 | randomized clinical trial | Malaysia | 40 | 30-70 | M-F | At least 12 teeth present, 5 or more periodontal pockets of at least 5 mm and loss of attachment of at least 4 mm in at least 2 different quadrants that bleed on probing | • bacterial plaque index<br>• gingival bleeding index<br>• depth of periodontal pockets<br>• loss of attachment |
| 2 | Lopez 2013 | randomized controlled trial | Chile | 52 (26 with diabetes and 26 without diabetes) | 45-70 | M-F | Minimum 15 teeth, periodontal pocket depth of at least 4 mm and attachment level larger than 3 mm | |
| 3 | Auyeung 2012 | randomized controlled trial | Taiwan | 100 | 50-65 | 61M-39F | A loss of attachment of at least 1.5 mm was considered a case of periodontal disease | |
| 4 | Kaur 2015 | randomized controlled trial | India | 100 (52 with poor glycemic control, 48 with good glycemic control) | 45-60 | M-F | Minimum 12 teeth present, attachment loss of at least 4 mm, periodontal pocket depth of at least 5 mm | |
| 5 | Lin 2012 | randomized controlled trial | Taiwan | 28 (14 with standard treatment and 14 with standard treatment + Minocycline) | 40-80 | M-F | Minimum 20 teeth, 5 or more teeth with periodontal pocket greater than or equal to 5 mm | |
| 6 | Chen 2012 | randomized clinical trial | China | 134 | 38-81 | 68M-66F | Minimum 16 teeth, attachment loss larger than 1 mm | |

Table 2. Brief presentation of the 6 analyzed studies (continued)

| No. | Reference | Type of study | Therapeutic approach | 1. Diabetes | 2. Evaluation | Pharmaceutical treatment | Duration | Results |
|---|---|---|---|---|---|---|---|---|
| 1 | Raman 2014 | randomized clinical trial | all patients - dental education. non-surgical therapy group - scaling and root-planing treatment with chlorhexidine 0.12% | Type 2 | HbA1c, CRP | Chlorhexidine 0,12 % | May 2010 - April 2011 | Reduced plaque index in patients with non-surgical therapy. Both groups showed a decrease in HbA1c, CRP |
| 2 | Lopez 2013 | randomized controlled trial | emergency extractions and restoration of carious lesions where necessary. Both groups benefited from dental education, subgingival scaling and crown polishing. | Type 2 | HbA1c | Absent | 9 months | Professional dental prophylaxis significantly improves periodontal status in patients with diabetes. No patients with a progression of periodontal disease were detected. |
| 3 | Auyeung 2012 | randomized controlled trial | instructions on dental hygiene both groups, gingival and subgingival scaling, plaque removal performed at 3,6,9,12 months - treatment group. | Type 2 | HbA1c | Absent | 1 year | Significant improvements in the population with moderate to severe cases of periodontal disease. Patients with mild cases did not show significant improvements. |
| 4 | Kaur 2015 | randomized controlled trial | The patients in the treatment group received dental education at the beginning of the study and 4 sessions of scaling and root-planing for a maximum period of 2 weeks. | Type 2 | HbA1c | Absent | 6 months | Significant improvements in periodontal parameters in groups that received non-surgical treatment. |
| 5 | Lin 2012 | randomized controlled trial | Scaling and root-planing, dental hygiene instructions for both groups. | Type 2 | HbA1c | 14 patients minocycline gel 2% | 6 months | Both groups showed a significant decrease in periodontal pockets and bleeding at probing. |
| 6 | Chen 2012 | randomized clinical trial | group 1 - descaling and root-planing at the beginning and subgingival descaling at 3 months, group 2 - descaling and root- | Type 2 | HbA1c, CRP, triglycerides, FPG, total cholesterol | Absent | 6 months | In the groups that received treatment, the plaque index and bleeding at probing decreased significantly. The depth of the periodontal pockets decreased. |

| No. | Reference | Type of study | Therapeutic approach | 1. Diabetes | 2. Evaluation | Pharmaceutical treatment | Duration | Results |
|---|---|---|---|---|---|---|---|---|
| | | | planing + subgingival prophylaxis at 3 months. control group - no treatment. | | | | | |

***Data analysis***

Of the 6 studies analyzed for this review, Auyeung et al [5] and Lin et al [620] conducted studies on the Taiwanese population, both of which were randomized controlled trials. The Auyeung et al study [5] was performed on a larger sample of patients (100) while Lin et al was performed on a smaller sample (28).

In Auyeung et al [5], patients with periodontal disease were evaluated at 3, 6, 9 and 12 months both in terms of periodontal indices and metabolic parameters (glycosylated hemoglobin) and inflammatory parameters (interleukin-1β and C-reactive protein). Patients were divided into 2 groups, those with a mild stage of periodontal disease and those with a moderate-severe stage. Patients received indications for oral hygiene and supra and subgingival descaling using ultrasonic and manual instruments. Subgingival descaling was performed under local anesthesia [5].

At 3, 6, 9 and 12 months after the initial post-therapy, the patients benefited from scaling and root planing as well as retraining on the rules of dental hygiene. The evaluation of glycosylated hemoglobin was also performed to evaluate the influence of periodontal treatment on diabetes. At the end of the study, a significant decrease in periodontal indices was obtained, such as plaque index, gingival bleeding index and periodontal sac depth in the group with moderate-severe disease [5].

Also, Lin et al [6] studied the evaluation of periodontal parameters in patients with periodontal disease and type 2 diabetes in the context of non-surgical treatment. They used the same initial treatment methods as Auyeng et al [5] but unlike Auyeung et al [5], they also used drug treatment in their study. They divided the patients into 2 groups of 14 patients, one of whom received treatment in the form of scaling and root-planing and the second group in addition to this treatment also received subgingival administration of antibiotic-minocycline. Minocycline was administered as a 2% gel administered at the subgingival level. The administration of minocycline was performed both at the beginning of treatment and in the next 3 weeks, once a week. Also, all patients received dental education [5].

Periodontal parameters such as the depth of the periodontal pocket, the gingival bleeding at the sites, the plaque index, the loss of attachment were analyzed. In addition, they were followed by interleukin 6 (IL-6) - for the evaluation of inflammation, glycosylated hemoglobin and C-reactive protein - for the evaluation of diabetes both at the beginning of the study and after 3 and 6 months of treatment as a secondary objective of study [6].

Both groups of patients showed a significant reduction in the depth of the periodontal pockets, which ranged from 1.7 to 2.02 mm at 3 and 6 months. There were no significant differences between these 2 groups between these parameters. Gingival bleeding was also reduced in both groups. In addition, both groups showed a decrease in the degree of attachment loss. However, the values for the 2 groups were similar, not noticing otherwise a difference between the 2 types of treatment [6].

The Raman et al study [7] evaluates the effects of initial therapy in contrast to the effects of health education in patients with periodontal disease and type 2 diabetes. Of the 40 patients, 20 were divided into the control group and 20 into the experimental group. Both groups received dental education and a toothbrush, interdental brushes and dental floss. The

group that received the non-surgical treatment benefited from scaling and root planing using Gracey curettes and ultrasonic descaling device.

In addition, patients in the non-surgical treatment group also received 0.12% chlorhexidine mouthwash, which they used 3 times / day for a period of 13 days. The control group did not receive any dental treatment except for dental education and motivation from the evaluators [7].

The results obtained showed that the plaque index showed differences between the two groups at the 2-month control but by the end the difference was no longer significant. Also, there were no significant differences between the 2 groups in the gingival bleeding index. The reduction in plaque index is evident in the group that received non-surgical treatment both at 2 months and at the end, which is why we can emphasize the improvement of the periodontal status of these patients. The reduction in plaque index was also present in patients in the control group. All patients also had an improvement in the gingival bleeding index, but in the control group this index increased by the end of the study [7].

The depth of the periodontal pocket in the non-surgical therapy group decreased to less than 2 mm at the final visit, a decrease that also occurred in the control group by at least 50% and even more until the end. The average loss of attachment decreased from 3.35 mm to 2.73 at the end in the non-surgical therapy group and in the control group decreased from an average of 2.79 to 2.56 (statistically significant but lower). Glycosylated hemoglobin and C-reactive protein were also evaluated in the 2 groups of patients to evaluate the effect of these interventions on glycemic control [7].

Similar to Raman et al, the study by Chen et al [8] assessed the effect of initial therapy on a control group that did not receive non-surgical treatment. Chen et al [8] followed the evolution of periodontal factors in 2 groups of patients who received non-surgical treatment compared to a control group who did not receive any treatment. 134 patients selected for this study with type 2 diabetes and periodontal disease were divided into 3 groups, treatment group 1 received scaling and root-planing at first and then subgingival descaling 3 months after the first treatment, the group for treatment 2 received only scaling and root-planing at the beginning of the study and at 3 months only supragingival prophylaxis without any intervention in the periodontal pockets [8].

Group number 3, the control group, did not receive any treatment or dental education from the beginning to the end of the study. Periodontal treatment was performed for a period of 24 hours without the use of antibiotics and antifungals, using standard rigid periodontal curettes and ultrasonic instruments. Both groups who received treatment had a significant improvement in plaque index and gingival bleeding, an improvement that was maintained until the end of the study. Also, the percentage of periodontal pockets with depths of 4-5 mm or more than 6 mm decreased significantly in both treatment groups compared to the control group where a decrease was not highlighted [8].

In the study by Lopez et al [9], a parallel of non-surgical treatment was made comparing 26 patients with type 2 diabetes and 26 patients without diabetes, all of whom had periodontal disease. The extraction of teeth that could not be repaired was performed and the restoration of the other teeth affected by carious lesions was performed urgently. All participants received dental education to perform brushing 3 times a day using the Charter technique and to perform daily dental floss cleaning.

Also, all patients underwent supragingival descaling and crown polishing. In this case, the descaling was done with an ultrasonic descaling device. Participants were monitored 3, 6 and 9 months after the initial treatment when a new series of prophylaxis treatments was performed. None of the patients included in the study had a worsening of periodontal status [9].

Patients with diabetes showed a significant improvement in the size of periodontal pockets, bleeding index and plaque index. Similar changes were present in patients without diabetes except for the depth of the periodontal pockets which did not decrease significantly compared to the initial assessment. In contrast, the group with diabetes had significant results at both 6 and 9 months. Both groups completed the study without achieving a significant increase in attachment. There were no significant differences in the periodontal status between the 2 groups analyzed. No significant change in glycemic control was also observed in terms of the evaluation of glycosylated hemoglobin [9].

In the the group that had a mild form of the condition (early stage), only the value of the depth of the periodontal pocket showed a significant reduction. A significant difference in the value of the plaque index was observed between the 2 groups [9].

The Kaur study [10] et al divided the population with diabetes and periodontal disease (100 patients) into 2 subgroups, those with good glycemic control (48 patients) and those with inadequate glycemic control (52 patients). Each subgroup was subsequently divided into half in patients who received non-surgical treatment for periodontal disease - scaling and root-planing or patients who did not receive any treatment. In addition to these subgroups, a subgroup of non-diabetic patients with periodontal disease was analyzed. Periodontal treatment was performed using a Gracey ultrasonic scaler and curette.

Patients were evaluated at 3 and 6 months for periodontal indices as well as for their glycosylated hemoglobin levels. Changes in periodontal parameters were significantly greater in patients receiving treatment than in others. It was also observed that non-surgical therapy led to a significant reduction in all periodontal parameters in all diabetic and non-diabetic patients [10].

All the studies included in this review had in common the evaluation of the periodontal status according to periodontal indices such as: gingival bleeding, periodontal sac depth, plaque index and loss of attachment. The evaluation was also performed in patients with a specific diagnosis of type 2 diabetes. Parameters for the evaluation of diabetes included glycosylated hemoglobin (HbA1C) and C-reactive protein. Also, all studies used in this review used non-surgical therapy and evaluated periodontal changes at both the beginning and end of the study [10].

## DISCUSSIONS

The evaluated studies followed the evolution of patients with type 2 diabetes and periodontal disease who underwent initial non-surgical therapy. They were evaluated at the beginning of treatment according to various periodontal indices such as plaque index, periodontal pocket depth, bleeding at probing, etc. The aim was to evaluate the periodontal status at different time periods after the first treatment in terms of evaluating the same periodontal indices.

Non-surgical therapy involves multiple procedures in order to control the infection that causes pathological lesions in the periodontal tissue. The realization of scaling and root planing, combined with rigorous control measures of the supragingival plate is very effective because it alters the subgingival ecology by disturbing the microbial biofilm, reducing the amount of pathogenic bacteria and suppressing inflammation. The instrumentation used consists of: curettes - used for descaling and subgingival scaling and supragingival ultrasonic instruments [11].

Diabetes and periodontal disease are 2 chronic conditions that have long been considered biologically connected. In fact, diabetes is one of the primary risk factors for periodontal disease. Cross-sectional and longitudinal studies have identified that the risk of periodontal disease is approximately 3-4 times higher in people with diabetes than in non-

diabetic individuals. Patients with type 2 diabetes also have a higher risk of developing periodontal disease than non-diabetics.

A study of African-American patients found that 70.6% of patients with type 2 diabetes had moderate periodontitis and 28.5% had a severe form of the disease. This percentage is 10.6% higher than in a control group with patients without diabetes. There is a direct link between glucose levels and the severity of periodontal disease. The ratio between patients with diabetes with periodontal destruction compared to non-diabetics is 1.97, 2.10 and 2.42 in diabetics with well-controlled, moderately controlled and poorly controlled blood glucose [12].

The mechanism linking diabetes and periodontal disease is not fully elucidated but involves issues such as inflammation, immunity, neutrophil activity and cytokine biology. Diabetes increases inflammation in periodontal tissue with an increase in inflammatory mediators such as interleukin-1β (IL-1β) and tumor necrosis factor alpha (TNF-α) [3].

Regardless of the degree of glycemic control, the prevalence of periodontal disease is higher in men than in women. Also, the total loss of natural dentition is more common in people with diabetes and prediabetes between the ages of 45 and 64, but it is not as common in those over 65. Also, total loss of dentition is more common in those with an elevated level of glycosylated hemoglobin compared to the control group. And in the case of those with only a part of the missing dentition, it was observed that the number of missing teeth is higher in those with diabetes [13].

The study by Lopez et al [9] showed that occupational dental prophylaxis significantly improves periodontal status in patients with moderate-severe periodontal disease with or without type 2 diabetes. Repeated dental prophylaxis was maintained at 3 and 6 months. improvement of the periodontal status that was maintained until the evaluation of 9 months. Also, no patient showed a worsening of periodontal status. These data support the data presented in other studies performed on patients with diabetes in which the control of supragingival plaque performed by professional cleaning of the oral cavity has favorable effects in stopping the evolution of periodontal disease.

Chen et al [8] note that in order to prevent the recurrence and progression of periodontal infection, periodontal maintenance therapy should be performed at regular intervals. However, in the absence of clinical evidence, the recommendations for proper oral hygiene and subsequent visits to the dentist vary greatly depending on the country and the health system. Thus, the need to standardize an optimal maintenance regime is outlined, especially in patients such as diabetics who may have severe complications if not seen in time at the dentist. The authors note that appropriate periodontal therapy decreases intraoral bacterial levels and reduces the effects induced by oral bacteria. This could also have a positive impact on systemic inflammatory status and metabolic control in patients with diabetes.

Lin et al [6] also note the link between glycemic control and periodontal status. This study concludes that patients with adequate blood glucose control who benefit from well-controlled initial periodontal therapy show an improvement in long-term periodontal status. They also mention that significant results appear in the case of combining non-surgical therapy with surgical therapy. However, poor blood glucose control produces less favorable results in the context of initial therapy performed at regular intervals, especially in patients who are more prone to frequent recurrence of deep periodontal pockets.

Kaur et al [10] observed a statistically significant increase in periodontal variables in patients who did not receive periodontal treatment for 6 months but this increase was not large enough to be clinically relevant. Periodontal progression was observed in both untreated groups but was more significant in the group with poor blood glucose control. And

from this study we can point out again the importance of diabetes as a risk factor for periodontal disease in terms of assessing glycemic levels.

There was a significant decrease in the depth of periodontal pockets less than 3 mm deep and a significant increase in the depth of periodontal pockets greater than 7 mm in the group that did not receive initial treatment, indicating a significant decrease in healthy areas and an increase of those affected. The authors believe that this aspect could occur due to the defect of immune cell function that leads to an inhibition of bactericidal activity in periodontal pockets. This defect affects the severity of periodontal disease and influences its progression [10].

A separate branch of the study from Auyeung et al [5] is the evaluation of the effect of non-surgical treatment on blood glucose control, but this study did not have favorable results in connection with this hypothesis. In the case of Kaur et al [10] a decrease in glycosylated hemoglobin is mentioned but it is mentioned that this aspect is predominant depending on the initial level - a decrease in glycosylated hemoglobin is even greater the higher its value at the beginning of non-surgical treatment. Chen et al [8] also note the possibility of obtaining such results but due to the small population on which they conducted the study they consider that they cannot form an appropriate conclusion on this topic. In order to be able to say for sure what the effect of non-surgical therapy is on blood sugar control, a much larger population is needed to conduct a study.

## CONCLUSIONS

In conclusion, evaluating the results of clinical trials analyzed in this review we can say that the initial therapy in the treatment of periodontal disease in patients with type 2 diabetes is very useful in stabilizing and also in improving periodontal status. In the absence of this treatment, a rapid evolution of periodontal disease can be observed, which can initially lead to systemic damage and worsening of general health.

Also, frequent assessment of blood glucose status and visits to the dentist at regular intervals to assess periodontal status can be extremely useful in treating diabetic patients and also in avoiding the evolution of periodontal status.

In a world where the prevalence of these two diseases, diabetes and periodontal disease is so high and the association between these two diseases is extremely widespread, prevention could be key. In the absence of prevention, initial non-surgical treatment is the gold standard for the treatment of periodontal disease, in both the diabetic and non-diabetic populations.

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