### DIABETES AND PERIODONTAL DISEASE: A BIDIRECTIONAL RELATIONSHIP

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**Summary**. Periodontal disease (PD) and diabetes mellitus (DM) hold a consistent relationship. DM not only increases the risk of having PD and with that its prevalence, but it also augments the progression of more aggressive and quickly defining signs. There is a bidirectional relationship between DM and PD. The treatment of periodontitis in diabetic patients favors a reduction in mediators responsible for the destruction of periodontal tissue and decreases with it, a resistance to insulin. PD is characterized by low grade chronic inflammation that may remain silent in diabetics causing damage that is not locally limited but may extend systemically.

Key words: Periodontal disease, loss of glycemic control, low grade chronic inflammation

### Introduction

Periodontal disease is chronic inflammatory disease of the tissues that support and attach the teeth to the jaws (1). They are caused by gram-negative bacterial infections and are, for the most part, asymptomatic, although much of the actual destructive tissue changes observed clinically are result of the inflamatory host response.

Periodontal disease (PD) is the second main cause of oral cavity disorders affecting the population due to its high prevalence (2). It is more frequent in adults in contrast to cavities which are more common and much more frequent in children.

As per Socransky's (3) definition, PD is a mixed endogenous infection caused by microorganisms that colonize the sub-gingival dental-bacterial plaque, in a structure known as a biofilm. Biofilms are bacterial communities that adhere to oral surfaces. Until now, 700 bacterial species capable of colonizing the mouth have been described. This number competes only with the flora found in the colon. A person may store over 150 different species.

Diverse studies carried out by the WHO confirm that the prevalence and severity of PD tends to be on the rise in the adult population compared to younger groups (4).

Persons with diabetes mellitus (DM) are at greater risk of developing PD. PD is now considered the sixth complication of DM (5). Not only is it more prevalent in this population, but also the progression of symptoms, in a more aggressive and more rapidly setting mode. The main reasons for this situation are the scarce information on the importance of oral hygiene, poor metabolic control and the irregularity in visiting dentists, among others (6).

PD conditions the loss of dental organs, making chewing food difficult, causing pain and as a result, inadequate nutrition (7). In addition, frequently persons with DM have a much more difficult time in tolerating false dentures due to total bone loss and the sensitivity of the alveolar mucosa.

The participation of a physician is relevant in the opportune detection of PD as a health provider for diabetics and whom a patient comes into more contact with.

This article reviews the literature analyzing the bidirectional relationship between diabetes mellitus and periodontal disease, as well as the effects of periodontal treatment on glycemic control with the aim of providing physicians and health personnel the basic elements supporting this relationship and which contribute to their active participation in the diagnosis and opportune referral (8).

# **Effects of Diabetes Mellitus** on the Periodontal State

The function of immune cells, including neutrophils, monocytes and macrophages is often altered in cases of diabetes. Neutrophilic adherence, chemotaxis and phagocytosis are changed, inhibiting an adequate defense against bacteria in the periodontal pouch and significantly increasing the destruction of the periodontal membrane (9). Although neutrophil function is decreased in diabetics, the monocyte/macrophage cell line may be hyper-responding when faced with the bacterial antigenic contact. This hyper-response results in a greater production of pro-inflammatory cytokines (10).

Peripheral monocytes in diabetic patients produce high levels of the tumor necrosis factor- $\alpha$  (TNF-  $\alpha$ ) in

response to the *Porphyromonas gingivalis* antigens compared to the monocytes of non-diabetic patients (11). The level of inflammatory cytokines in the crevicular fluid is also related to glycemic control. Egebretson (12) reported that diabetic patients with periodonitis, whose  $HbA_{1c}$  levels were over 8%, had approximately twice the amount of interleukin-1 $\beta$  (IL-1 $\beta$ ) in their crevicular fluid in comparison to patients with indexes below 8%. The net effect of these changes in the immune response of diabetics is an increase in periodontal inflammation, a loss of epithelial insertion and alveolar bone.

The gingival sulcus (13) is a labile site for the body to present a hermetic closure to the external environment. In this space, the crevicular fluid increases in the presence of inflammation. The increase in the loss of periodontal insertion and the alveolar bone (14) in diabetic patients is associated with changes in the metabolism of connective tissue where there is a lack of response in resorption and formation. The effect of the hyperglycemic state includes the inhibition of osteoblastic proliferation (15) and collagen production resulting in a reduction in the formation and decrease in mechanical properties of the newly formed bone (16-17).

The changes mentioned above may contribute to the pathogenicity of periodontal disease and changes in healing since collagen is the predominating structural protein in the gums. In addition, collagen is susceptible to degradation due to the action of MMPs as collagenases found to be in high amounts in tissues of diabetics, including the periodontal tissue.

## **Effects of Periodontal Disease** on the State of Diabetes

Periodontal disease may have a significant impact on the metabolic state of diabetes. The presence of PD increases the risk of worsening glycemic control in time. Taylor (18), in a cohort study of patients with diabetes with severe PD for two years, found a relative risk six times more the probability of worsening glycemic control in comparison to periodontally healthy diabetics.

Our research group found an association in the increase of  $HbA_{1c}$  values to the severity of periodontal disease in pre-gestational type 2 diabetic women (19) (Fig. 1).

Periodontal disease may induce or perpetuate an elevated inflammatory state not only locally (20), but has also been associated to severe periodontitis with the risk of mortality due to cardio-renal disease (21).

Several studies suggest that patients with periodontitis, particularly those colonized with Gram negative bacteria such as *P. gingivalis*, *Tannerella forsynthesis*, and *Prevotella intermedia*, have greater inflammatory serum markers such as C-reactive protein (CRP), IL-6, and fibrinogen than patients without periodontitis (22-23).

Similarly, there is an increase in resistance to insulin decreasing glycemic control.

The above explains why periodontitis can increase the risk of poor glycemic control and how this improves with periodontal treatment (24).

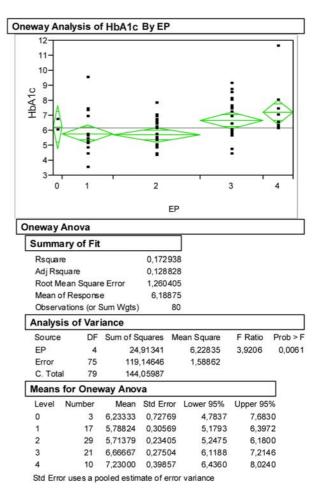


Fig. 1. Association of the HbA<sub>1c</sub> values with the severity of periodontal disease in a group of type 2 pre-gestational diabetics.

(0=Healthy gingival, 1=Early gingivitis, 2=Establisehed Gingivitis, 4=Periodontitis)

## Periodontal Treatment on the State of Diabetes

Periodontal treatment decreases local inflammation and as a consequence, decreases chemical mediators involved in inflammation, among them IL-6 and CRP, positively contributing to proper glycemic control. It is evident that PD exceeds the local environment affecting the systemic one (25).

D'Auito (26) points out that tissue insulin demand in type I diabetic patients decreases after periodontal treatment including scraping and radicular smoothing, curettage, local gingivectomies and selective extractions, scaling and root planning in addition to the use of antibiotics such as penicillin and streptomycin.

The most important concern for applying evidence in the early diagnosis of PD is educating the patient.

Periodontal disease is a silent condition. Diabetics need to be aware of the signs of PD (Table 1). Bleeding of the gums is the first sign of subgingival infection. This is when all the personnel involved in the care of diabetic patients should take active participation and therefore opportunely refer patients to the dentist.

### Table 1. Signs of Alarm related to Periodontal Disease

- Gum bleeding
- Gingival inflammation
- Halitosis
- · Sensitive denture
- Dental movement

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### DIJABETES I PERIODONTALNA BOLEST: UZAJAMNI ODNOS

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Kratak sadržaj: Periodontalna bolest (PB) i diabetes mellitus (DM) su u doslednoj vezi. DM ne samo da povećava rizik od pojave PB, a samim tim i njegovu učestalost, nego i povećava progresiju znakova koji su agresivniji i koji se brže određuju. Postoji dvosmerna veza između DM i PB. Tretiranjem periodontitisa kod pacijenata sa dijabetesom, smanjuju se posrednici odgovorni za razaranje periodontalnog tkiva a samim tim smanjuje se i rezistentnost na insulin. PB karakteriše hronična upala niskog inteziteta koja može ostati prikrivena kod dijabetičara, uzrokujući štetu koja nije lokalno ograničena već može sistematično da se širi.

Ključne reči: Periodontalna bolest, gubitak glikemičke kontrole, upala niskog inteziteta