In Brief

Periodontitis has been identified as the sixth complication of diabetes. Advanced glycation end-products, altered lipid mechanisms, oxidative stress, and systemically elevated cytokine levels in patients with diabetes and periodontitis suggest that dental and medical care providers should coordinate therapies.

Diabetes and Periodontal Disease: An Update for Health Care Providers

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Inflammation of the Periodontium

Periodontitis is a chronic inflammatory disease of the mouth that involves the gingiva (gum tissues), teeth, and supporting bone. Periodontitis is clinically defined as the loss of connective tissue attachment to the teeth and alveolar bone loss. If periodontitis is left untreated, the involved teeth will exfoliate.

In many cases, periodontitis is the second stage of an inflammatory process that begins with gingivitis. From a clinical perspective, gingivitis presents with swollen tissues and increased redness but with no loss of connective tissue attachment between root surfaces and bone. The inflammatory cell infiltrate in gingivitis is dominated by a polymorphonuclear neutrophil infiltrate (acute inflammation), whereas the histopathology of periodontitis is dominated by a plasma cell infiltrate (chronic inflammation).[1]

The clinical signs of periodontitis include swelling, redness and bleeding from the gums, spacing between teeth, loose teeth, and exposure of root surfaces through loss of bone around the teeth. The disease can present locally, involving a few teeth, or be more generalized. Figure 1 shows the severity of gingival inflammation in a patient who had received initial periodontal non-surgical treatment 3 months before the photo was taken.

In patients with a systemic disease such as diabetes, the disease is often more generalized. Patients with poor glycemic control often present with severely inflamed gum tissues and evidence of loss of tooth support that is often seen as spreading of teeth resulting in open spaces between the teeth (diastemas). Despite similar plaque scores (bacterial deposits), patients with poorly controlled type 2 diabetes display more severe gingival bleeding compared to those with diabetes in good or moderate control.[2] Patents with poorly controlled type 2 diabetes are at greater risk for periodontal disease progression than patients with well-controlled type 2 diabetes.[3]

Treatment of chronic periodontitis usually includes oral hygiene instructions, information on the role of diet, and professional cleaning of the teeth and gum tissues using hand instruments or ultrasonic devices. In addition, antibacterial mouth rinses, local or systemic antibiotics, and sur-

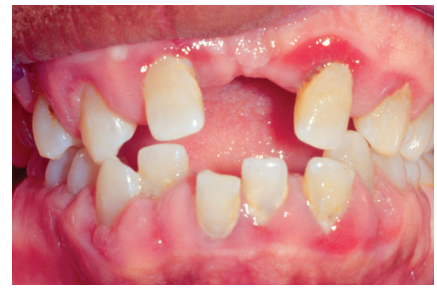

Figure 1. Example of severe periodontitis in an African-American patient with uncontrolled diabetes (A1C > 9.0%) who has not responded to initial periodontal therapy. Notice the extent of spacing between teeth and the severe inflammation (redness of gum tissues) and dental plaque (bacterial deposits).

gical intervention may be included in periodontal therapy.

Prevalence of Gingivitis and Periodontitis in Relation to Diabetes

The prevalence of periodontitis in the United States is subject to controversy. Current data suggest that the prevalence of periodontitis has decreased across ethnicity, sex, and age-groups to < 10%.[4] Different interpretations of the same data suggest, however, that up to 50% of U.S. adults may suffer from various degrees of periodontitis.[5]

The prevalence of periodontitis is significantly higher among middle-aged people with diabetes than in similar-aged people without diabetes.[6] Analysis of data from the third National Health and Nutrition Examination Survey has revealed that a self-reported family history of diabetes, hypertension, high cholesterol, and clinical evidence of periodontal disease bears a probability of 27–53% that the patient has undiagnosed diabetes.[7] Analysis of periodontal status in people with type 1 or type 2 diabetes from a population-based German study has demonstrated an association between both types of diabetes and tooth loss.[8]

Attention to oral disease in addition to medical conditions by both medical and dental care providers will improve the ability to identify individuals unaware of their diabetic status. Dentists should establish referral patterns, communicate with physicians, and use dental screening as a tool for referral of patients with severe gingival or periodontal inflammation.[9] It would be advantageous if blood glucose assessments were performed in dental offices for patients at risk for type 2 diabetes. Likewise, physicians should refer patients with type 2 diabetes to dentists for treatment of gingival or periodontal inflammation. This is especially important because the pathophysiology of periodontal inflammation is not limited to the oral cavity and can have important effects on glycemic control. Indeed, periodontitis has been identified as the sixth complication of diabetes.[10]

Pathophysiology of Periodontitis as a Complication of Diabetes

The oral cavity, as part of the gastrointestinal tract, is populated by a diverse and large microbiota and has been identified as a location with a more dense bacterial colonization than any other organ. Teeth provide a nonshedding surface with a complex biofilm containing bacteria that are in balance with the host, but bacterial species with high virulence can also be identified.

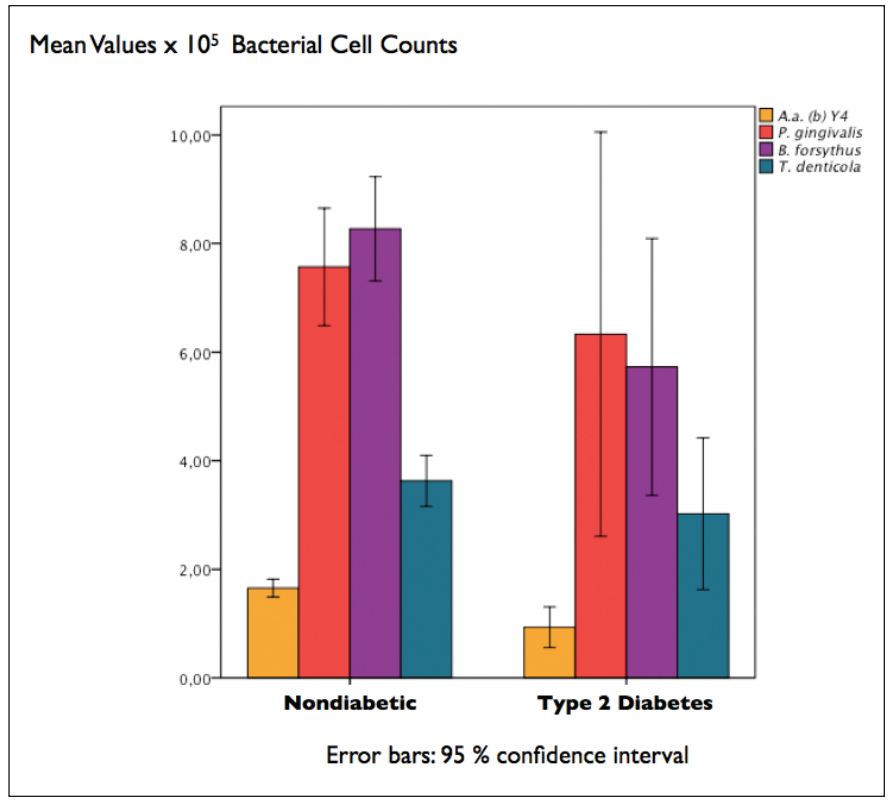

Figure 2. Levels of select bacteria associated with periodontitis in periodontal pockets of subjects without a diagnosis of diabetes and in subjects with type 2 diabetes. A similar severity of periodontitis, but with lower bacterial counts, was identified in subjects with diabetes for A. actinomycetemcomitans *serotype Y4 (A.a (b) Y4),* P. gingivalis, T. forsythia, *and* T. denticola, *all associated with periodontitis.*

Periodontitis has a complex infectious etiology, and the establishment of infection is usually slow. A bacterial biofilm of both aerobic and anaerobic bacteria, including > 500 species, may be found in periodontal pockets around teeth.[11] Bacteremia is rarely identified in periodontitis. However, endotoxins from bacteria identified in periodontal pockets and associated with periodontitis can be found in serum in > 30% of nondiabetic patients who present with early signs of periodontitis.[12]

In general, the bacterial infection in periodontitis does not differ between nondiabetic patients and those with type 2 diabetes. However, the immune response to periodontal bacterial infection does differ in that patients with type 2 diabetes do not develop antibodies to pathogens associated with periodontitis.[13] Many of the anaerobic bacteria associated with periodontitis have a lipopolysaccharide (LPS) capsule with endotoxins and heat-shock proteins. Pretreatment profiles of serum antibody titers to different heat shock proteins and LPS levels from *Porphyromonas gingivalis*, an anaerobe commonly found in periodontitis lesions, can predict the outcome of periodontal therapy in patients with diabetes such that those with elevated titers have a more favorable treatment outcome.[14]

Unpublished data based on 282 subjects, among whom 9.3% had type 2 diabetes with similar severity of periodontitis, suggest that patients with type 2 diabetes may have fewer bacteria in periodontal pockets but the same severity of disease. These data suggest that the inflammatory response to infection in people with type 2 diabetes is more severe than in nondiabetic subjects (G.R.P, unpublished observations). This may be explained by a lack of ability to produce functional antibodies against bacteria in periodontal infection. This is illustrated in the diagram in Figure 2, which includes four bacterial species associated with periodontitis.

This observation is consistent with the general perception of an increased susceptibility to infection among patients with type 2 diabetes.

Periodontal infections trigger the release of pro-inflammatory cytokines both at the site of the periodontal infection and throughout the endothelial cell system.[15] Studies of gingivitis in humans with or without type 1 diabetes have shown that both diabetic and nondiabetic subjects react to experimental plaque accumulation with gingival inflammation. However, subjects with type 1 diabetes develop an earlier and more severe local inflammatory response to a comparable bacterial challenge.[16]

Further studies have shown that two biological markers of inflammation, IL-1β and MMP-8, which are typically elevated in the fluid from inflamed periodontal pockets, are more elevated in people with diabetes.[17] People with type 2 diabetes also have higher levels of several other cytokines (i.e., interferon-γ, osteoprotegrin, tumor necrosis factor-α (TNF- α), and interleukin 17 and 23) at the site of periodontal infection but also exhibit a downregulation of interleukin 4.[18]

An increasing severity of periodontitis has been linked to the development of glucose intolerance,[19] likely because of increased inflammation leading to increase in interleukin-6 (IL-6). The liver is an important target for IL-6 action, leading to an increased inflammatory response with impaired insulin signaling and action and resultant decreased insulin production.[20] Patients with impaired insulin production are therefore unable to control for IL-6 activation and the enhanced inflammation induced by IL-6.[20] Elevated IL-6 serum levels have been identified in people with untreated chronic periodontitis.[21] These studies suggest that the presence of elevated serum levels of pro-inflammatory cytokines in patients with type 2 diabetes caused by periodontitis may aggravate inflammatory responses in other organs commonly affected in patients with diabetes.

Other pathological factors in diabetes affecting the periodontal tissue are linked to elevated glucose levels in serum with development of advanced glycation end-products (AGEs), altered lipid mechanisms, and oxidative stress. Data suggest that AGEs present in diabetic gingiva can be associated with oxidative stress.[22] Clinical data have suggested that the presence of AGEs in patients with diabetes is associated with the biofilm on teeth, indicating an increased risk for periodontal damage.[23]

Impact of Periodontal Therapies on Glycemic Control

From a Cochrane-based review,[24] the authors concluded that there is some evidence of improvement in metabolic control in people with diabetes after treatment of periodontal disease but also recognized that the evidence was weak because of statistical lack of power from available studies. Data from another meta-analysis of available literature on periodontal intervention and the effects on metabolic control in type 2 diabetic patients[25] suggest that periodontal intervention has positive effects on blood glucose levels. In patients with A1C levels > 9.0%, periodontal therapy may reduce A1C by 0.6% in the absence of changes in medication and by 1.4% if changes in diabetes medications are introduced.[26] After periodontal therapy, a tendency toward a decrease of the TNF- α, A1C, soluble E-selectin, and highly sensitive C-reactive protein levels in patients with diabetes has been demonstrated.[27,28]

Periodontal therapy with adjunctive systemic antimicrobial treatment may improve glycemic status of patients with uncontrolled type 2 diabetes by a decrease in serum A1C amounting to 0.2% from an average of 9.9% before treatment.[29]

These findings are supported by other investigators who identified that, although nonsurgical periodontal therapy eliminates local and systemic infection and inflammation via decreases in TNF-α, it is insufficient alone for significantly reducing A1C levels without strict glycemic control in poorly controlled diabetic patients.[30] Thus, clinical collaboration between physicians and dentists is an important component of holistic successful treatment of patients with diabetes.

Conclusions

Patients with diabetes are usually poorly informed about the relationship between periodontitis and diabetes.[31] Therefore, health care providers of patients with diabetes should be aware of this link and inform their patients about the need for good oral health. Referral of patients with uncontrolled diabetes for dental evaluation and periodontal treatment may result in better control of blood glucose levels.

Although a survey of the oral cavity should be included in a thorough medical examination, health care providers other than those within the dental team usually are not aware of what clinical signs of periodontitis to consider. An increased redness of the gum tissues along the teeth is a classic sign of gingivitis, a condition that indicates that there is an active inflammatory response to bacterial infection. The use of a toothbrush or a toothpick to gently touch the gums of diabetic patients with inflammation will provoke bleeding that will cease within minutes. Health care providers should suggest a thorough dental examination if such bleeding is common throughout a patient's mouth. Also, the presence of white or gray deposits on teeth suggests that dental treatment may be necessary. Spacing between upper front teeth and mobile teeth are other signs of periodontitis.

Likewise, dentists and dental hygienists should refer their patients who respond poorly to initial periodontal therapy or have advanced periodontitis without obvious signs of poor oral hygiene for diabetes screening. In fact, it might be advantageous for dental offices to monitor the blood glucose levels of patients considered to be at risk for diabetes.

In summary:

- Diabetes and periodontitis are both common chronic diseases in adults and specifically in older individuals.
- There is substantial evidence of the impact of periodontitis on systemic inflammatory markers.
- Periodontal treatment of patients with diabetes may have limited effects on slightly elevated A1C levels, but in patients with more severe diabetes, such treatment may reduce A1C levels significantly if coordinated with blood glucose control.
- Signs of periodontal inflammation, including gingivitis, can be assessed easily by all medical health care providers.
- Patients with periodontitis with severe gingival inflammation who do not respond to routine periodontal therapy should be screened for diabetes.

- By communicating and coordinating the treatment of diabetic patients, medical and dental care providers have an opportunity to provide better care of their patients.

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