DIABETES MELLITUS AND PERIODONTAL DISEASE: A BIDIRECTIONAL RELATIONSHIP AND ITS CLINICAL IMPLICATIONS

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Abstract

Diabetes mellitus and periodontitis are two highly prevalent chronic non-communicable diseases whose relationship is bidirectional. Chronic hyperglycemia promotes the accumulation of advanced glycation end products, oxidative stress, impaired neutrophil function and an exaggerated inflammatory response, which together accelerate the destruction of periodontal tissues. In turn, severe periodontitis maintains a state of low-grade systemic inflammation that may worsen insulin resistance and impair glycemic control. Current evidence indicates that non-surgical periodontal therapy can produce a modest improvement in glycated

hemoglobin (HbA1c) in people with diabetes, although the effect size varies between trials. This review summarizes the epidemiological data, pathogenic mechanisms and clinical manifestations linking diabetes and periodontal disease and outlines evidence-based preventive and therapeutic strategies, emphasizing close cooperation between dentists, endocrinologists and primary care physicians.

Keywords: diabetes mellitus, periodontitis, gingivitis, hyperglycemia, glycated hemoglobin, inflammation, advanced glycation end products, prevention

QANDLI DIABET VA PARODONT KASALLIKLARI: IKKI TOMONLAMA BOG'LIQLIK VA UNING KLINIK AHAMIYATI

Annotatsiya

Qandli diabet va parodontit keng tarqalgan surunkali noinfeksion kasalliklar bo'lib, ular o'rtasidagi bog'liqlik ikki tomonlama xarakterga ega. Surunkali giperglikemiya glikatsiyaning yakuniy mahsulotlari to'planishiga, oksidlovchi stressga, neytrofillar funksiyasining buzilishiga va yallig'lanish javobining kuchayishiga olib keladi, bu esa parodont to'qimalarining yemirilishini tezlashtiradi. O'z navbatida, og'ir parodontit organizmda sust kechuvchi tizimli yallig'lanishni saqlab turadi, insulinga chidamlilikni kuchaytirishi va glikemik nazoratni yomonlashtirishi mumkin. Mavjud dalillarga ko'ra, parodontga jarrohliksiz davo qandli diabetli bemorlarda glikatsiyalangan gemoglobin (HbA1c) ko'rsatkichini mo'tadil darajada yaxshilashi mumkin, biroq bu ta'sirning ko'lami turli tadqiqotlarda farq qiladi. Ushbu sharhda qandli diabet va parodont kasalliklarini bog'lovchi epidemiologik ma'lumotlar, patogenetik mexanizmlar va klinik belgilar jamlangan hamda stomatolog, endokrinolog va oilaviy shifokorlar hamkorligiga asoslangan profilaktik va davolash strategiyalari bayon etilgan.

Kalit so'zlar: qandli diabet, parodontit, gingivit, giperglikemiya, glikatsiyalangan gemoglobin, yallig'lanish, glikatsiyaning yakuniy mahsulotlari, profilaktika

САХАРНЫЙ ДИАБЕТ И ЗАБОЛЕВАНИЯ ПАРОДОНТА: ДВУНАПРАВЛЕННАЯ СВЯЗЬ И ЕЁ КЛИНИЧЕСКОЕ ЗНАЧЕНИЕ

Аннотация

Сахарный диабет и пародонтит являются широко распространёнными хроническими неинфекционными заболеваниями, взаимосвязь между которыми носит двунаправленный характер. Хроническая гипергликемия способствует накоплению конечных продуктов гликирования, развитию окислительного стресса, нарушению функции нейтрофилов и усилению воспалительного ответа, что в совокупности ускоряет разрушение тканей пародонта. В свою очередь, тяжёлый пародонтит поддерживает вялотекущее системное воспаление, которое может усиливать инсулинорезистентность и ухудшать гликемический контроль. По современным данным, нехирургическое лечение пародонтита способно умеренно снижать уровень гликированного гемоглобина (HbA1c) у больных диабетом, хотя величина эффекта различается в разных исследованиях. В обзоре обобщены эпидемиологические данные, патогенетические механизмы и клинические проявления, связывающие сахарный диабет и заболевания пародонта, а также изложены основанные на доказательствах профилактические и лечебные стратегии с акцентом на сотрудничество стоматологов, эндокринологов и врачей первичного звена.

Ключевые слова: сахарный диабет, пародонтит, гингивит, гипергликемия, гликированный гемоглобин, воспаление, конечные продукты гликирования, профилактика

Introduction

Diabetes mellitus is one of the most significant public health challenges of the twenty-first century. According to the International Diabetes Federation, an estimated 537 million adults aged 20–79 years were living with diabetes worldwide in 2021, and this number is projected to continue rising (International Diabetes Federation, 2021). The disease is characterized by chronic hyperglycemia and is associated with well-known microvascular and macrovascular complications,

including retinopathy, nephropathy, neuropathy and cardiovascular disease (Brownlee, 2001).

Periodontitis is a chronic multifactorial inflammatory disease associated with dysbiotic dental plaque biofilm and characterized by progressive destruction of the tooth-supporting apparatus, including the gingiva, periodontal ligament, cementum and alveolar bone (Papapanou et al., 2018). It is among the most common causes of tooth loss in adults, and its burden increases with age and in the presence of systemic risk factors such as smoking and diabetes (Genco & Borgnakke, 2013).

The link between the two conditions was recognized early. Löe (1993) described periodontal disease as the "sixth complication" of diabetes mellitus, and subsequent epidemiological studies, including work in populations with a high prevalence of type 2 diabetes, confirmed that periodontal destruction is more frequent and more severe in people with diabetes (Nelson et al., 1990; Taylor, 2001). More recent evidence has shown that the relationship runs in both directions: diabetes increases the risk and severity of periodontitis, and periodontitis adversely affects glycemic control and may contribute to the development of diabetic complications (Preshaw et al., 2012; Lalla & Papapanou, 2011; Sanz et al., 2018). Understanding this interplay is important for dentists, who are often the first clinicians to see signs of undiagnosed or poorly controlled diabetes, and for physicians, who should be aware of the oral consequences of the disease.

The aim of this review is to summarize current knowledge on the epidemiology, pathogenic mechanisms and clinical features of periodontal disease in diabetes mellitus, to analyze the effect of periodontal treatment on glycemic control, and to outline practical preventive recommendations.

Epidemiology and Classification of Periodontal Disease in Diabetes

Multiple observational studies and systematic reviews indicate that people with diabetes have a higher prevalence and greater severity of periodontitis than people without diabetes, with risk commonly estimated as two- to threefold higher (Preshaw et al., 2012; Kocher et al., 2018). The risk depends on the quality of

metabolic control: patients with poorly controlled diabetes show more extensive attachment loss and bone loss than those with well-controlled disease, while individuals whose diabetes is well controlled have a periodontal status that approaches that of non-diabetic people (Chapple & Genco, 2013; Mealey & Oates, 2006). The duration of diabetes and the presence of other complications also appear to influence periodontal outcomes (Salvi et al., 2008).

The 2017 World Workshop classification of periodontal diseases explicitly incorporates diabetes into the clinical assessment of periodontitis. In the staging and grading framework, the stage reflects severity and complexity of management, whereas the grade reflects the expected rate of progression and takes into account systemic modifiers. In patients with diabetes, the grade is influenced by glycemic status: a patient with HbA1c below 7.0% is generally assigned grade B, while an HbA1c of 7.0% or higher indicates grade C, that is, a higher risk of rapid progression (Tonetti et al., 2018). This approach underlines that glycemic control is a clinically relevant modifier in periodontal diagnosis and treatment planning.

Pathogenic Mechanisms Linking Diabetes to Periodontitis

Several interrelated mechanisms explain why hyperglycemia aggravates periodontal inflammation and tissue destruction (Graves et al., 2020; Polak & Shapira, 2018). They are summarized below.

Advanced glycation end products. Persistent hyperglycemia leads to non-enzymatic glycation of proteins and lipids and the accumulation of advanced glycation end products (AGEs) in tissues, including the gingiva. AGEs bind to their receptor (RAGE) on monocytes, macrophages, endothelial cells and other cells, triggering oxidative stress and the activation of pro-inflammatory signaling pathways (Schmidt et al., 1999). In experimental models, blockade of RAGE reduced periodontitis-associated bone loss in diabetic mice, supporting a causal role of this axis (Lalla et al., 2000).

Exaggerated inflammatory response. In people with diabetes, monocytes and macrophages exposed to AGEs and hyperglycemia secrete higher amounts of pro-

inflammatory mediators, such as interleukin-1β, tumor necrosis factor-α and prostaglandin E2, in response to the same bacterial challenge (Mealey & Ocampo, 2007; Lalla & Papapanou, 2011). This hyperinflammatory phenotype increases tissue destruction by matrix metalloproteinases and promotes osteoclast activation.

Altered bone metabolism and impaired repair. Hyperglycemia disturbs the balance between bone formation and resorption, in part through changes in the RANKL/osteoprotegerin system, favoring bone loss. In addition, diabetes limits the capacity of periodontal tissues to repair after injury by prolonging inflammation and reducing the function of fibroblasts and osteoblasts; experimental data show that diabetes aggravates periodontitis by limiting repair through enhanced inflammation (Pacios et al., 2012).

Impaired host defense and vascular changes. Neutrophil chemotaxis, adherence and phagocytosis are reduced in poorly controlled diabetes, which may allow greater bacterial persistence in the periodontal pocket (Mealey & Oates, 2006). Microangiopathy, with thickening of the capillary basement membrane, can further impair tissue oxygenation and nutrient delivery to the periodontium.

Taken together, these mechanisms mean that the periodontal tissues of a patient with diabetes respond to the same plaque burden with greater inflammation and faster destruction than those of a metabolically healthy person.

Periodontitis as a Risk Factor for Poor Glycemic Control

The reverse direction of the relationship is supported by epidemiological and mechanistic evidence. Severe periodontitis is associated with elevated systemic markers of inflammation, and the periodontal pocket epithelium, when ulcerated, represents a large surface through which bacteria and their products can enter the circulation (Lalla & Papapanou, 2011; Polak & Shapira, 2018). The resulting low-grade systemic inflammation, including raised C-reactive protein and pro-inflammatory cytokines, is thought to impair insulin signaling and contribute to insulin resistance (Grossi & Genco, 1998; Preshaw et al., 2012).

Clinically, a longitudinal study of patients with type 2 diabetes found that severe periodontitis was associated with a higher risk of worsening glycemic control over the follow-up period (Taylor et al., 1996). Data from a national health survey cohort suggested that periodontal disease may also be associated with an increased risk of incident type 2 diabetes (Demmer et al., 2008). A systematic review of observational evidence concluded that periodontal disease has an adverse effect on glycemic control and on the incidence of diabetic complications, while also noting the limitations of the available studies (Borgnakke et al., 2013). Overall, the consensus report of the joint EFP/AAP workshop considered the evidence for an effect of periodontitis on diabetes outcomes biologically plausible and supported by observational data (Sanz et al., 2018).

Clinical Manifestations in Patients with Diabetes

The oral findings in diabetes are not specific, but several features are common, particularly when glycemic control is poor. These include gingival erythema, edema and bleeding on probing that are out of proportion to the amount of plaque present, deeper periodontal pockets, rapid attachment loss, tooth mobility, and recurrent or multiple periodontal abscesses (Mealey & Ocampo, 2007; Casanova et al., 2014). Xerostomia due to reduced salivary flow, increased susceptibility to oral candidiasis, burning mouth symptoms and delayed wound healing after dental procedures are also frequently reported in people with diabetes (Casanova et al., 2014; Preshaw & Bissett, 2019).

Because periodontal destruction can be extensive and sometimes appears rapidly, a dentist confronted with severe, rapidly progressing periodontitis, recurrent abscesses or unexplained gingival inflammation in a patient of unknown diabetic status should consider the possibility of undiagnosed diabetes or prediabetes and refer the patient for appropriate medical evaluation (Casanova et al., 2014; Preshaw & Bissett, 2019).

Effect of Periodontal Treatment on Glycemic Control

Mechanical removal of subgingival biofilm and calculus (scaling and root planing) reduces the bacterial load and local inflammation and may also decrease systemic inflammatory markers (Sanz et al., 2020). Whether this translates into improved glycemic control has been tested in numerous randomized trials. A Cochrane systematic review that pooled these trials reported that periodontal treatment in people with diabetes was associated with a reduction in HbA1c of roughly 0.4 percentage points at three to four months compared with no treatment or delayed treatment, with smaller and less certain effects at longer follow-up, and rated the certainty of the evidence as low to moderate (Simpson et al., 2022). For comparison, even modest reductions in HbA1c are considered clinically meaningful in the management of diabetes.

The results of individual trials are not uniform. A large multicenter randomized clinical trial in patients with type 2 diabetes and chronic periodontitis did not find that non-surgical periodontal therapy improved HbA1c at four months compared with delayed treatment (Engebretson et al., 2013). Differences in study populations, baseline glycemic control, treatment protocols and follow-up may explain this heterogeneity. The joint EFP/AAP consensus therefore concluded that periodontal treatment is effective in improving periodontal status in people with diabetes and may contribute to better glycemic control, and recommended that patients with diabetes receive periodontal assessment and treatment as part of comprehensive diabetes care (Sanz et al., 2018).

Prevention and Management: Practical Recommendations

On the basis of current guidelines and consensus statements, the following approach can be recommended (Sanz et al., 2018; Sanz et al., 2020; Preshaw & Bissett, 2019).

First, patients with diabetes should undergo a comprehensive periodontal examination, including probing depths, clinical attachment level, bleeding on probing and, when indicated, radiographs, at diagnosis and at regular intervals thereafter. Second, patients with diabetes should be informed that periodontal

disease is a recognized complication of their condition and that good glycemic control and good oral hygiene both reduce the risk of its development and progression. Third, individual oral hygiene instruction, including effective tooth brushing, interdental cleaning and, where appropriate, the use of antiseptic mouthrinses, should be reinforced at every visit.

Fourth, periodontitis in patients with diabetes should be treated according to the stepwise approach of the EFP clinical practice guideline, beginning with behavior change, supragingival and subgingival instrumentation and control of risk factors, followed by re-evaluation and, when needed, further steps and supportive periodontal care at tailored intervals (Sanz et al., 2020). Fifth, dental appointments should be scheduled with attention to the patient's medication and meal schedule in order to reduce the risk of hypoglycemia, and invasive procedures should be avoided or deferred in patients with markedly uncontrolled diabetes unless urgent. Finally, communication between the dentist and the patient's physician is essential: dentists should refer patients with suspected undiagnosed diabetes, and physicians should refer patients with diabetes for dental assessment.

Conclusion

Diabetes mellitus and periodontitis are linked by a bidirectional relationship in which hyperglycemia and chronic inflammation reinforce each other. Poorly controlled diabetes accelerates periodontal destruction through the accumulation of advanced glycation end products, impaired host defense, an exaggerated inflammatory response and altered bone metabolism, while severe periodontitis contributes to systemic inflammation and may impair glycemic control. Periodontal therapy improves periodontal health in people with diabetes and is associated, on average, with a modest reduction in HbA1c, although further high-quality long-term trials are needed. In clinical practice, periodontal assessment should be an integral part of diabetes care, and glycemic status should be taken into account in periodontal diagnosis and treatment planning. Coordinated work between dentists,

endocrinologists and primary care physicians offers the best prospect of preventing complications and improving the quality of life of patients.

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