The relationship between periodontal disease and diabetes mellitus type ii facing the new classification of periodontal diseases: literature review

A relação entre periodontite e diabetes mellitus tipo 2 frente a nova classificação das doenças periodontais: revisão de literatura

ABSTRACT

Periodontal disease and type 2 diabetes mellitus are considered chronic diseases that at their core have a deep relationship with inflammation. It is assumed that there is a bidirectional relationship between periodontal disease and type 2 diabetes mellitus. It is estimated that approximately 10% of the world's population is affected by periodontal disease, in its most severe form, almost the same percentage estimated for people with diabetes, which is considered a 21st century emergency. The World Workshop for the Classification of Periodontal and Peri-implant Diseases and Conditions took place from September 9-11, 2017. The aim of this study is to analyze the results of this workshop with regard to the relationship between periodontal diseases/conditions and diabetes mellitus, in addition to conducting an integrative review on the topic. A literature review was conducted, using the Medline electronic databases via Pubmed, Scientific Electronic Library Online, Scientific and Technical Literature of Latin America and the Caribbean and Virtual Health Library. A new classification of periodontal disease included tools for individual assessment of the patient and recognizing risk factors that might negatively interfere in response to treatment. The occurrence of metabolic lack of control in periodontal patients with type 2 diabetes mellitus is now considered a factor of great importance for the assessment of individual susceptibility to the progression of periodontitis. Diabetes is believed to promote a hyper inflammatory response to bacterial challenge by modifying the tissue response of periodontal tissues.

Indexing terms: Classification. Diabetes mellitus. Diabetes mellitus, type 2. Periodontal diseases.

RESUMO

A doença periodontal e o diabetes mellitus tipo 2 são consideradas doenças crônicas que tem em seu cerne um profundo relacionamento com mecanismos inflamatórios, pressupõe-se que haja uma relação bidirecional entre doença periodontal e diabetes mellitus tipo 2. Estima-se que aproximadamente 10% da população do mundo seja afetada pela doença periodontal, na sua forma mais severa, quase...
INTRODUCTION

Type 2 diabetes mellitus (DM2) is a clinical syndrome with variable phenotypic expression, with no specific etiology. It is considered a disease of polygenic nature mediated by the environment and characterized by bi-hormonal dysfunction of the pancreas [1] and consequent deregulation of homeostasis mechanisms of blood glucose levels [2]. Periodontal disease (PD) is a chronic condition, associated with dysbiotic biofilm and characterized by progressive destruction of dental insertion apparati [3].

PD and DM2 are considered chronic diseases related to habits, lifestyle, socioeconomic factors and which have, at their core, a deep relationship with inflammatory mechanisms [4]. It is estimated that approximately 10% of the world’s population is affected by PD, in its most severe form [5], almost the same percentage estimated for people with diabetes, which is considered to be a 21st century emergency. In Brazil, it is believed that diabetes represents 5% of total diagnosed chronic diseases [6,7].

It is assumed that there is a bi-directional relationship between DP and DM2 [4,8]. Longitudinal studies [9,10] positively associated DM2 with increased risk in developing periodontitis, accelerating its evolution. This association can be explained by the release of hormonal and inflammatory signs related to the pathogenesis of diabetes [1] that can also contribute to tissue destruction, a characteristic of periodontitis.

PD, on the other hand, may be associated with increased risk in developing diabetes complications [4]. There is evidence that periodontal therapy can result in improved glycemic control [11] and that PD can function as a modifying factor for diabetes [4]. The establishment of a possible causal relationship between periodontal condition and DM2, however, remains uncertain [12].

Between September 9 and 11, 2017, the World Workshop for the Classification of Periodontal and Peri-implant Diseases and Conditions took place. A committee, organized by the American Academy of Periodontics and the European Federation of Periodontics, updated the 1999 Classification and developed a similar scheme for peri-implant diseases and conditions.

The aim of this study is to analyze the relationship between periodontal diseases/conditions and diabetes mellitus, as indicated by this new classification, in addition to promoting a literature review on the subject.

An integrative literature review was carried out, using Medline electronic databases via Pubmed, Scientific Electronic Library Online (Scielo), Scientific and Technical Literature of Latin America and the Caribbean (LILACS) and Virtual Health Library (VHL) between January and February 2019. The terms “Type 2 Diabetes Mellitus,” “Periodontal Diseases,” and “Periodontitis” were searched, combining Boolean AND/OR operators. Controlled clinical studies, literature reviews and consensus available in English, Portuguese or Spanish were considered as inclusion criteria.

DISCUSSION

DP and DM2 have a close relationship. This correlation has been studied for more than six decades, once it was perceived that periodontal tissues of diabetic patients are less resistant to local irritants; it was unknown at that time that high reactivity of periodontal tissues to these irritants attributes to this fact [13].

Technological evolution has opened the way for the development of methods that have broadened knowledge
and established new hypotheses about this relationship. Longitudinal studies [9, 10] positively associated DM2 with increased risk for development of periodontitis, revealing that the presence of this condition advances disease progression, leading to greater tooth loss. Systematic meta-analysis reviews [14,15] confirm diabetes as an important risk factor and modifier for the development of periodontitis, increasing its chances of incidence or progression by 86% [1.86; 95% CI; 1.3-2.8].

The coexistence of diabetes mellitus is considered an important modifying factor in the course of gingivitis and periodontitis, according to the new classification of PD [3]. It should be included as a descriptor in a clinical diagnosis of periodontitis, since this disease in diabetic patients does not have unique phenotypic characteristics, which could characterize it as a distinct condition [16]. Therefore, in this context, periodontitis is considered to be a periodontal manifestation of DM2 [17]. Most of the evidence of the effects of diabetes on periodontal tissues comes from patients with DM2, because of its prevalence [18].

DM2, in turn, is related to the accumulation of white adipose tissue that promotes the release of hormonal and inflammatory signals [1]. These can contribute to tissue destruction, characteristic of periodontitis. In sick sites of subjects with uncontrolled diabetes and periodontitis, there is a significant increase in levels of IL-6, TNF-α, known pro-inflammatory cytokines able to synergistically stimulate connective tissue degradation, and bone resorption via MMP-1, which has its production increased by fibroblasts in conditions of hyperglycemia [19,20]. Healthy sites of diabetic individuals have higher concentrations of pro-inflammatory biomarkers than healthy sites of non-diabetic subjects with the same biomarkers [19].

Hyperglycemia is accompanied by excessive production of final glycation residues (AGEs), which can activate the Nuclear Factor-Activator Receptor-Kappa B (NFκB). NFκB is involved in the differentiation of osteoclasts, which act in bone resorption, inducing insulin resistance by promoting the expression of numerous genes related to the production of inflammatory cytokines (IL1β, IL6, TNFα) [21]. Hyperglycemia can impair tissue repair mechanisms, leading to increased loss of periodontal insertion, and increased severity of the inflammatory process [18,22,23].

In a study on the influence of glycemic control on periodontal pathogens in patients with DM2, Miranda et al. [24] found an increase in the detection of F. nucleatum in sites with probing depth greater than or equal to 5 mm, in individuals with poor glycemic control. In those with critical control, they observed an increase in the frequency of T. forsythia and four other species belonging to the orange complex. According to other studies [8,25], poor glycemic control in subjects with DM2 is associated with a more pathogenic subgingival microbial profile, which can contribute to the worsening of periodontitis observed in these individuals. There is no evidence, so far, to support a causal relationship between periodontal microbiomes and the presence of diabetes [18].

On the other hand, studies suggest [26] that periodontitis increases the risk for elevated glycemic index in diabetic and non-diabetic individuals, which demonstrates that individuals with periodontitis exhibit a greater chance of developing pre-diabetes and diabetes. The coexistence of periodontitis has also been associated with an increased risk for diabetes complications [4,18], such as retinopathy, nephropathy, diabetic foot, cardiovascular diseases and mortality.

According to available evidence, periodontal therapy can result in a reduction of around 0.40% (CI 0.27-0.65) of glycated hemoglobin (Hb1AC) after 3 months [11,22]. However, there is insufficient data to demonstrate that this result is maintained for 6 months. The combined use of antibiotics did not influence the reduction of Hb1AC, beyond that which was provided only by tooth scaling and root planing among patients with DM2 [18].

The new classification of PD included tools for individual assessment of patients, recognizing risk factors that may interfere negatively in treatment response. The occurrence of metabolic lack of control in periodontal patients with DM2 is considered an important factor for evaluation in disease progression rate [17], which, as seen, tends to be more accelerated in uncontrolled diabetic individuals.

Algorithm is a tool that systematizes the patient's individual clinical data, with the purpose of grouping them into categories which indicate the severity/complexity and rate of disease progression through well-defined criteria (chart 1) [3,17].
Chart 1. Structure summarized for the stage and degree of periodontitis.

| Individual Stage and Degree Assessment | Stage I Initial Peridontitis | Stage II Moderate Peridontitis | Stage III Severe Peridontitis with potential of additional dental deterioration | Stage IV Advances Peridontitis with extensive dental deterioration and potential for tooth loss |
|---------------------------------------|-----------------------------|-------------------------------|--------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------|
| Evidence or risk of rapid progression, early response to treatment, and systemic health effects | Grade A Slow progression. Without risk modification factors | Grade B Moderate progression. Risk modification factors: smoking (up to 10 cigarettes/day); HbA1C <7% in diabetics. | Grade C Rapid progression. Risk modification factors: smoking (>10 cigarettes/day; HbA1C ≥ 7%). | |

Source: Adapted by Tonetti et al. [17].

The new classification system defines a kind of staging of periodontitis at various points in time, aiming to facilitate communication between professionals and assist in the definition of the prognosis for improving personalized care. It is understood that individuals have different severity/extension, rates of disease progression and/or associated risk factors [3,17].

According to the new classification [17], the information derived from this staging should be complemented by data about the biological level of the disease (risk or current evidence of progression) for each patient. The purpose of this gradation is to consider the patient's susceptibility to periodontitis, taking into account his clinical history, manifested by the bone loss/year ratio, and risk determinants that acted together to cause bone loss throughout his life [27].

The occurrence of recognized modifying risk factors, such as smoking and diabetes mellitus, has the power to increase the degree value, regardless of the primary criterion, represented by the rate of progression. For example, a stage II case, characterized by moderate loss of insertion, would assume a moderate rate of progression (Grade B). The detection of DM2, with poor metabolic control, could change the classification of the grade to C [17].

The 1999 Classification [28] already considered diabetes as an important modifying factor for periodontitis, capable of altering its course and expression. Periodontitis in diabetic patients was considered a manifestation of systemic disease. Under the new classification system [3], diabetes is grouped as a systemic disease that affects periodontal support tissues. Diabetes is believed to promote a hyperinflammatory response to bacterial challenge, driven by the interaction between advanced glycation end products (AGE) and their receptors (RAGE), which have increased circulation and expression in diabetic individuals [29].

CONCLUSION

The metabolic lack of control in diabetics, under the new classification, gains a more prominent position, since it is considered as an individual classification tool of the disease, in its staging and gradation. The diagnostic description will be periodontitis associated with diabetes mellitus, defining the stage and evaluating the degree of the disease, by its rate of progression over time. The degree, however, can be modified by the patient's metabolic control factors.

Collaborators

OLIVEIRA LML, bibliographical survey, article preparation, review process and writing of the final article. BARBOSA LM, bibliographical survey and review process.

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