IMPACTS OF OXIDATIVE STRESS IN DIABETIC PATIENTS TYPE 2 WITH PERIODONTAL DISEASE

IMPACTOS DEL ESTRÉS OXIDATIVO EN PACIENTES DIABÉTICOS TIPO 2 CON ENFERMEDAD PERIODONTAL

IMPACTOS DO ESTRESSE OXIDATIVO EM PACIENTES DIABÉTICOS TIPO 2 COM DOENÇA PERIODONTAL

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ABSTRACT
Objectives: to investigate the impact of oxidative stress in diabetic type 2 patients with periodontal disease; to describe the association between type 2 diabetes and periodontal disease under the influence of oxidative stress and to identify the influence of inflammation caused by type 2 diabetes and periodontal disease on oxidative stress. Materials and methods: integrative review where searches performed on the BVS and PubMed databases, in Portuguese and English, published in the period from 2014 to 2018. Theses, monographs, TCC’s, animal researches, as well as scientific papers that did not show a direct relationship with the proposed theme were excluded. Results: most of the studies reported alterations in the parameters of oxidative stress in patients with periodontal disease, diabetics and diabetics with periodontal disease. Conclusion: the presence of oxidative stress in diabetic type 2 patients with periodontal disease installed or in progression has a fundamental role in worsening the destruction of periodontal tissues. Descriptors: Diabetes Mellitus; Oxidative Stress; Periodontal Disease.

RESUMO
Objetivo: investigar os impactos do estresse oxidativo em pacientes diabéticos tipo 2 com doença periodontal; descrever a associação entre diabetes tipo 2 e a doença periodontal sob a influência do estresse oxidativo e identificar a influência das inflamações provocadas pela diabetes tipo 2 e pela doença periodontal no estresse oxidativo. Material e método: revisão integrativa com buscas nas bases de dados BVS e PubMed, nos idiomas português e inglês, publicados no período de 2014 a 2018. Excluíram-se teses, monografias, TCC’s, pesquisas em animais, bem como, artigos científicos que não mostrassem relação direta com o tema proposto. Resultado: a maioria dos trabalhos relataram alteração nos parâmetros de estresse oxidativo em pacientes com doença periodontal, diabéticos e diabéticos com doença periodontal. Conclusão: a presença do estresse oxidativo em pacientes diabéticos tipo 2 com doença periodontal instalada ou em progressão, tem um papel fundamental no agravamento da destruição dos tecidos periodontais. Descritores: Diabetes Mellitus; Oxidative Stress; Periodontal Disease.
INTRODUCTION

For Casanova et al.,(1) periodontitis and diabetes are common and complex chronic diseases, with a bidirectional relationship, that is, diabetes, in cases of lack of glycemic control, is associated with an increase in the prevalence and severity of periodontitis, and periodontitis Severe is associated with impaired glycemic control.

Chronic periodontitis is a serious public health problem that affects many people worldwide. Once associated with DM2 (Diabetes Mellitus type 2), it becomes even more severe, having systemic effects in worsening the patient's clinical condition.(2)

Patil et al.(3) state that periodontitis is significantly more prevalent among people with poorly controlled diabetes mellitus. Most tissue destruction in periodontitis is considered the result of an aberrant inflammatory / immune response to plaque and involves the prolonged release of ROS (reactive oxygen species).

According to Almerich-Silla et al.,(4) oxidative stress is related to imbalance due to the excess of reactive oxygen species or oxidants over the cell's ability to build an effective antioxidant response.

Wang et al.(5) reported that the inflammatory response in periodontitis is associated with an increase in local and systemic oxidative stress and impaired antioxidant capacity. That is, under normal physiological conditions, there is a balance between reactive oxygen species and antioxidants, while oxidative stress occurs only when the antioxidant defense system is unable to neutralize the high production of reactive oxygen species.

This study aimed to study the impacts that oxidative stress causes in type 2 diabetic patients with periodontal disease.

MATERIALS AND METHODS

The integrative review includes the analysis of relevant research that supports decision-making and the improvement of clinical practice, enabling the synthesis of the state of knowledge of a given subject, in addition to pointing out knowledge gaps that need to be filled with the realization of new studies.

Searches were carried out in the VHL (Virtual Health Library) and PubMed databases. To specify the search, the keywords were used as descriptors: oxidative stress, periodontal disease and diabetes, using the Boolean Operator "and".

As for the syntheses of the research results, these were related to oxidative stress, diabetes and periodontitis.

In the inclusion criteria, the scientific articles indexed in the selected databases with the health descriptors exposed above, in the Portuguese and English languages, from 2014 to 2018 were used for the study. Theses, monographs, TCCs, research on animals, as well as scientific articles that did not show a direct relationship with the proposed theme and articles published prior to 2014.

For the elaboration and structuring of the research, subdivisions were created classified by categories related to the exposed theme, prioritizing the essential points of the study, as well as an explanatory table of the means of inclusion and exclusion of the articles and journals found.

RESULTS
In the VHL and PubMed platform, articles with combinations of descriptors were searched as follows: “oxidative stress and periodontal disease and diabetes”; “Diabetes and periodontal disease”; and “oxidative stress and periodontal disease”.

In total, 22 articles were selected. Of these, on both platforms, 3 repeated articles were identified. Finally, 19 articles were selected for the development of the work. After a thorough reading of the selected works, six articles were found in which they fit all the objectives of the work in question. Four articles addressed the objectives related to oxidative stress, but did not interrelate with diabetes and periodontal disease. The remaining nine selected articles were used for theoretical support, reporting concepts of diabetes and periodontal disease and how these diseases influence each other.

Table 1 - Distribution of studies according to the title of the articles, authors, year of publication and research results (2014-2018)

<table>
<thead>
<tr>
<th>TITLE</th>
<th>AUTHORS</th>
<th>YEAR OF PUBLICATION</th>
<th>RESULTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxidative stress parameters in saliva and its association with periodontal disease and types of bacteria</td>
<td>Almerich-Silla et al.</td>
<td>2015</td>
<td>Periodontal disease is related to the increase in the levels of oxidative stress parameters and these levels increased according to the number and type of periodontal bacteria found in the periodontal pockets.</td>
</tr>
<tr>
<td>Global metabolomic analysis of human saliva and plasma from healthy and diabetic subjects, with and without periodontal disease</td>
<td>Barnes et al.</td>
<td>2014</td>
<td>Differences in saliva between diabetic and non-diabetic cohorts showed altered signatures of carbohydrates, lipids and oxidative stress in the diabetic samples.</td>
</tr>
<tr>
<td>Obesity, diabetes mellitus, atherosclerosis and chronic periodontitis: a shared pathology via oxidative stress and mitochondrial dysfunction?</td>
<td>Bullon; Newman; Battino</td>
<td>2014</td>
<td>Oxidative stress increases alveolar bone loss in the most rapidly progressive periodontitis that occurs as a complication of diabetes.</td>
</tr>
<tr>
<td>Systemic oxidative stress biomarkers in chronic</td>
<td>Liu et al.</td>
<td>2014</td>
<td>Levels of oxidative biomarkers TAOC1, MDA2 and NO3 were different</td>
</tr>
</tbody>
</table>
### Influence of type 2 diabetes on local production of inflammatory molecules in adults with and without chronic periodontitis: a cross-sectional study

Influence of type 2 diabetes on local production of inflammatory molecules in adults with and without chronic periodontitis: a cross-sectional study

Mohamed et al. 2015

PCB was the only clinical parameter that differed significantly between groups. It was higher in the DM + PC group than in the PC and DM groups.

### Chronic periodontitis in type 2 diabetes mellitus: oxidative stress as a common factor in periodontal tissue injury

Chronic periodontitis in type 2 diabetes mellitus: oxidative stress as a common factor in periodontal tissue injury

Patil et al. 2016

Increased levels of MDA in all patient groups compared to healthy controls. Decrease in TAC, Vitamin C and SOD levels among patients with PC and DM compared to controls.

### Influence of the periodontal disease, the most prevalent inflammatory event, in peroxisome proliferator-activated receptors linking nutrition and energy metabolism

Influence of the periodontal disease, the most prevalent inflammatory event, in peroxisome proliferator-activated receptors linking nutrition and energy metabolism

Román-Malo; Bullon 2017

- 

### Local inflammatory reactions in patients with diabetes and periodontitis

Local inflammatory reactions in patients with diabetes and periodontitis

Sonnenschein; Meyle 2015

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### Oxidative stress in chronic periodontitis patients with type II diabetes mellitus

Oxidative stress in chronic periodontitis patients with type II diabetes mellitus

Vincent et al. 2018

The clinical parameters of gingival inflammation and plaque scores were higher in participants with GCP, GCP-
DISCUSSION

Barnes et al.\(^6\) and Vincent et al.\(^7\) stated in their studies that type 2 diabetes mellitus and periodontal disease have a bidirectional relationship, in which, inadequate glycemic control increases the risk of developing periodontitis, as well how periodontitis negatively interferes with diabetes. Patil et al.,\(^3\) stated that periodontitis is more prevalent among people with poorly controlled diabetes mellitus and that the severity of tissue destruction by excess of reactive oxygen species is greater when periodontal disease is associated with type 2 diabetes mellitus, indicating that stress oxidative is a common factor involved in tissue destruction.

Sonnenschein, Meyle\(^8\) reported the increase in oxidative stress, determined by the decrease in the levels of antioxidant capacity of plasma molecules, in patients with type 2 diabetes and periodontitis. Mohamed et al.\(^9\) explain that hyperglycemia can affect periodontal tissues, leading to an increase in oxidative stress as a consequence of the imbalance between reactive oxygen species and antioxidants.

According to Almerich-Silla et al.\(^4\) the mechanisms of periodontitis development are not well understood, being probably multifactorial and characterized by the generation of reactive oxygen species by activated phagocytes in the gingival sulcus. While the meta-analysis carried out by Liu et al.\(^10\) showed that chronic periodontitis is significantly associated with circulating levels of three biomarkers of oxidative stress, indicating a role for chronic periodontitis in systemic diseases.

According to Román-Malo, Bullon,\(^11\) inflammation is the main common basis for periodontitis with other systemic diseases such as atherosclerosis, diabetes and metabolic syndrome. For Wang et al.,\(^5\) when inflammation occurs, the production of reactive oxygen species increases dramatically, mainly due to the cells of the innate immune system, for example, neutrophils and macrophages during the phagocytosis process through the metabolic pathway of “respiratory explosion”. Vincent et al.\(^7\) add that unbalanced and prolonged inflammation can lead to tissue destruction through oxidative stress, where there is a discrepancy between oxidants and...
antioxidants caused by increased production and activity of free radicals or due to a defense mechanism reduced antioxidant.

Therefore, when an inflammatory reaction occurs in the body, as with type 2 diabetes mellitus and periodontitis, oxygen production results in reactive oxygen species that should be combated by the antioxidant system, which inhibit damage caused by these molecules. When there is an imbalance between the production of reactive oxygen species and the antioxidant system, oxidative stress occurs, which can cause cell damage.

Bullon et al.\(^{(12)}\) reported that free radicals and reactive oxygen species are of such importance for many physiological processes, but when an antioxidant system is not able to efficiently neutralize its action, it can cause tissue damage, increasing the periodontal destruction. However, Sonnenschein, Meyle\(^{(8)}\) demonstrated, in a treatment-related study, a significant reduction in the generation of reactive oxygen species by peripheral neutrophils, 12 weeks after non-surgical therapy in patients with diabetes mellitus and periodontitis.

Saliva is a clinical and diagnostic tool for oral and systemic health conditions. In a study done with salivary markers, by Almerich-Silla et al.\(^{(4)}\) it can be seen that oxidative stress levels were significantly higher in the group with periodontal disease than in the gingivitis and healthy groups and have a linear tendency associated with periodontal worsening, as well as bleeding on probing.

Barnes et al.\(^{(6)}\) used the method of metabolomic analysis, in which many metabolites associated with inflammation, oxidative stress, tissue degradation and bacterial metabolism were shown to be significantly elevated in periodontal disease and reduced by treatment. Differences in saliva between diabetic and non-diabetic cohorts showed altered signatures of carbohydrates, lipids and oxidative stress in the diabetic samples. The most striking finding of the study was the direction of change in the periodontitis samples in the diabetic cohort.

In addition to these methods, according to Wang et al.\(^{(5)}\) lipid peroxidation products, protein damage and DNA damage can also be used as biomarkers of oxidative stress associated with periodontitis.

**CONCLUSION**

It is concluded that type 2 diabetes mellitus and periodontal disease are inflammatory diseases that, individually, can lead to an increase in reactive oxygen species and a decrease in antioxidant activity and that, when associated, these conditions can be aggravated, leading to a higher level of oxidative stress, worsening both the local and systemic condition of the patient.

Thus, the presence of oxidative stress in type 2 diabetic patients with installed or progressing periodontal disease plays a fundamental role in worsening the destruction of periodontal tissues.

**REFERENCES**


