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PERIODONTAL DISEASES IN DIABETES MELITUS - A TWO WAY LINK? A REVIEW OF LITERATURE

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Abstract: *Numerous studies in the last decades report a frequent association of marginal periodontal disease with some systemic metabolic disorders, such as diabetes or obesity. The prevalence of these diseases is growing alarmingly both globally and in our country. Recent data from the literature confirm that advanced forms of periodontal disease can influence the evolution of type 2 diabetes. This may provide a premise for better glycemic control.*

INTRODUCTION

The link between periodontal disease and diabetes led to the World Workshop on the Classification of Periodontal and Peri- Implant Diseases and Conditions in Chicago (IL) at the last World Workshop on Updating the Classification of Periodontal Diseases in 2017 some clarifications regarding the classification according to the stage of periodontal damage and the level of control and evolution of diabetes. Another change in connection with the pathogenesis of periodontal disease has been made depending on the smoking habit, in which the risk of periodontal disease increases 2-5 times compared to people who do not smoke.(1,2)

The main cause, incriminated in the pathogenesis of periodontal diseases, is given by the accumulation of a pathogenic bacterial biofilm, in the gingival groove, made up of Gram negative bacteria, predominantly anaerobic. Under favourable local conditions, periodontal bacteria greatly increase their number and optional anaerobic and anaerobic species are selected that achieve a biocenosis specific to periodontal pockets. These bacteria, through the enzymes and toxins secreted, cause in the first phase irritation, inflammation and slight bleeding during tooth brushing. The first inflammatory stage is called gingivitis and is reversible if dental hygiene is optimized. Gingivitis affects the general population aged 20-60 years in percentages between 50-90%.(3.4)

In addition to the main infectious factor, other secondary factors can contribute to the inflammation of the marginal periodontium. These can be: immunosuppressive medication, herpes virus or HIV viral infections, hormonal changes in pregnancy, stress or metabolic diseases such as diabetes, obesity or atherosclerosis.

The multiplication of bacteria in the subgingival biofilm, in the absence of proper individual dental hygiene and under the influence of the mentioned secondary factors, causes an evolving gingival inflammation, produces deep gingival sacs and determines the activation of the individual immune system to fight infections. In this case, there are a number of local and general changes in the cascade, which release inflammatory mediators and ultimately lead to the appearance of proteolytic and osteoclastic cells. By their action, the bone and the supporting tissues of the tooth in the alveolus are gradually destroyed.

Regarding periodontal disease, in people with type 2 diabetes, recent studies consider that periodontal disease is the 6th major complication of diabetes.(5,6) At the same time, numerous observational studies note that in people with clinical forms of undetected or incorrectly treated diabetes, the prevalence and severity of periodontal disease increases 2.8 times compared to people who do not have diabetes. In these cases, gingival sacs over 3.5 mm appear, with purulent secretions and alveolar bone loss 4.8 times higher than in non-diabetic patients.(6,7,8) Also, compared to patients without diabetes, the risk of severe forms of periodontal disease is about twice as high in diabetics.(9,10)

Other studies suggest that there is a directly proportional link between blood glucose control and impaired periodontal damage. Thus, at a deficient glycemic control, the most severe forms of periodontal disease are encountered.

This two-way relationship can be expressed as follows: 75.6% of people with severe periodontal disease are also diabetic, compared to only 22.4% of diabetics who do not have periodontal disease.(11,12)

On the other hand, data from the literature confirm that the risk of people with moderate or severe periodontal disease is about 3 times higher than those with periodontal disease or mild forms of gingivitis.(12)

In contrast, other studies do not find a significant association between glycemic control and the severity of periodontal disease.(13,14)

The mechanisms involved in the interaction of periodontal disease type 2 diabetes but also in the mutual relationship of influencing periodontal health in people with type 2 diabetes, are based on the following arguments.

Hyperglycemia present in people with type 2 diabetes also causes an increase in the percentage of carbohydrates in saliva and gingival fluid. This fact provides optimal conditions for bacterial plaque proliferation with consequences in lowering the pH of the mouth.

Another consequence of hyperglycemia is the binding through a reversible reaction of protein glucose and the

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formation of increased amounts of Advanced Glycation End-product (AGE).(15,16)

The accumulation of these products causes macrophage cells in periodontal tissue, but also other cells in adipose tissue, to secrete in the bloodstream substances with inflammatory role such as IL-6, IL-B, TNF-A or Vascular Endothelial Growth Factor (VEGF).

AGE products are attached to small blood vessels, endothelial cells, smooth muscle fibers or neurons. They produce vascular changes that are manifested by increasing the hardness of the vascular walls and decreasing permeability. The consequence of these accumulations is the migration of mono and polynuclear phagocytic cells.

At the same time, soft and hard periodontal tissues are affected by microangiopathy and changes in the structure of collagen that will accentuate tissue destruction.(17)

For this reason, type 2 diabetes is considered a risk factor for periodontal disease. On the other hand, periodontitis could influence the ability of macrophages to respond to AGE by inducing an increase in inflammatory cytokines.

In people with periodontal disease is installed simultaneously with these changes insulin resistance. This causes an increase in blood sugar, an increase in glycosylation processes and the accumulation of AGE, which accentuates tissue destruction. So, periodontal infection is able to increase the level of cytokines and AGE but vice versa.

Excessive cytokine production could influence insulin resistance by altering insulin receptors in adipocytes and altering B cells in the pancreas.

As clinical signs, in patients with type 2 diabetes, we can see a series of manifestations ranging from candidiasis, periodontitis, policing to dry mouth. Other manifestations may be delayed wound healing, gingival ulcers resistant to regular treatment, halena either from the ketotic component or from the exudate of periodontal pockets, frequent deposits of tartar, reduced mobility of the tongue and viscous saliva.(18)

Regarding the involvement of antibiotics in the treatment of periodontal disease, there are a number of important studies that claim that they could also act to reduce oxidative stress in the cell.

Thus, in a recent study on the use of tetracycline in periodontal treatments, it is claimed that in addition to the antimicrobial effect, the amtibiotic molecule has the effect of reducing oxidative stress, promo-bolic anti-inflammatory effect, immunomodulatory, angiogenetic and anti-fat effect.(19)

Other antibiotic molecules such as minocylin have also been shown to have effects in reducing oxidative stress.(19)

In other studies, it has been shown that some natural substances such as Schisandra chinesis extract and cranberry extract have antihistamine, hypoglycemic, anti-inflammatory and antioxidant pharmacological properties.(20,21)

CONCLUSIONS

Observational studies in recent decades claim that this two-way link is based on the following arguments:

- although the periodontal bacteria are the same (in the main *porfiromonas gingivalis, actinomices, tannerela fortisia, treponema denticola)* it seems that, in people with diabetes, the immune-inflammatory reactions, caused by them have wider destructive effects due to the response different from those without diabetes.(15,16)
- to diabetics, the phagocytosis destruction capacity of the bacteria is lower, which allows the formation of periodontal pouches whose contact surface is greatly increased.(17)
- the inflammatory response to people with diabetes is exaggerated. This fact determines at a deficient glycemic control, represented by HbA1c> 8%, we find a 2-fold increased value of inflammatory markers (IL, TNF-α, C-reactive protein and fibrinogen) in the gingival fluid, compared to patients who have only periodontal disease.(16,18,19)
- due to hyperglycemia, people with diabetes accumulate AGE products in the gingival tissues. They increase oxidative stress both locally and at the level of other organs, which results in microvascular manifestations manifested by exaggerated growth and abnormal capillary regeneration.(20,21)
- in diabetics, an increased concentration of matrix metalloproteinases is found in the blood. These enzymes, which play a role in local tissue healing, have a negative impact on tissue collagen causing delayed scarring of the periodontal.(19,21)

All these changes, of the biological parameters, cause a low level inflammatory reaction in the diabetic patient. In response to inflammation, at the periodontal level, ligament damage and major alveolar bone loss occur.(22)

Regarding the influence of periodontal disease on glycemic control, the following opinions are outlined in the literature:

- periodontal disease can influence the blood glucose control in the diabetic patient. This opinion is based on extensive studies conducted for 2 years in people with diabetes and severe periodontal disease, who were followed by HbA1c values. This parameter had significantly higher values than those with diabetes and without severe forms of periodontal disease.(22)
- periodontal disease can hasten the onset of diabetes. The results of studies carried out for 5 years have shown that periodontal disease aggravates the installation of tissue resistance to insulin, thus increasing the risk of diabetes. The risk increases as the periodontal disease is mild, including the risk of gestational diabetes in pregnant women.(20)
- advanced periodontal disease also increases the risk of diabetes complications. The results of studies performed on representative groups, of people with diabetes and advanced periodontal disease, confirm that the relative risk of cardiac, renal and cardio-renal complications is increased by increased values for albumin level in the urine, signs of renal insufficiency, calcium plaque of atheroma or changes in the walls of large vessels.(22,23)

In the claims of the last decades, the effects of periodontal disease treatments in type 2 diabetes patients are mentioned as follows:

- after the treatment of periodontal disease there is a reduction of the inflammatory state in the body. This can be quantified by reducing the value of inflammatory markers IL, TNF-α, C-reactive protein and fibrinogen level.(22,23)
- a better control of the blood sugar quantified by the significant decrease of the HbA1c value with percentages between 0,29-1,18% was observed that remained between 3-6 months.(22,23)

Periodontal treatments performed in the case of people with diabetes consisted of scaling and root brushing with recommendations regarding a correct dental brushing associated with auxiliary hygiene means. By adding a spectrum antibiotic to the anaerobic flora administered 10-14 days (amoxicillin 2g/day combined with metronidazole 0.5 g/day) the effect can be prolonged up to 6 months, an effect comparable to the administration of an oral anti diabetic.(21,22)

It is necessary for the diabetic patient to undergo a global treatment that also includes a periodontal evaluation, at least every 6 months, in order to reduce the "reservoirs" of periodontal bacteria (periodontal medicine), thus contributing

more easily to control of blood glucose levels.(30)

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