The oral cavity of elderly patients in diabetes

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Abstract

Diabetes mellitus is a common and growing global health problem leading to several complications. Among these periodontal diseases are considered as the sixth complication of diabetes mellitus. This article reviews the relationship between diabetes and oral health, particularly focusing on periodontal diseases, dental caries and xerostomia. There is a bidirectional interrelationship between diabetes and periodontal diseases. Periodontitis is more prevalent and severe in patients with diabetes than in normal population. Therapy of periodontal infection contributes to a positive glycaemic control management and enables reduction of the burden of complications of diabetes mellitus. Diabetics have an increased predisposition to the manifestation of oral diseases like candidiasis which is associated with poor glycaemic control and therapeutic dentures. This predisposition also contributes to xerostomia, which may be due to increased glucose levels in oral fluids or immune dysregulation.

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Résumé

La cavité buccale du diabétique âgé.

Le diabète constitue un problème de santé générale en constante augmentation qui génère plusieurs complications dont les maladies parodontales, considérées comme la sixième complication du diabète. Cet article étudie les relations entre le diabète et la santé bucco-dentaire, et plus particulièrement les maladies parodontales, la carie dentaire et la xérostomie.

Il existe une relation bidirectionnelle entre le diabète et les maladies parodontales. Les pathologies parodontales sont plus fréquentes et plus sévères chez les patients diabétiques que chez les non-diabétiques. En outre, le traitement des infections parodontales contribue à un meilleur contrôle de la glycémie et permet de prévenir d’autres complications liées au diabète.

Les patients diabétiques présentent une prédisposition à des pathologies buccales comme les candidoses qui sont associées à un mauvais contrôle de la glycémie et au port de prothèses dentaires. Cette prédisposition favorise également la xérostomie, qui semble être liée soit à des niveaux élevés de glucose dans les fluides oraux, soit à un dérèglement immunitaire.

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Key words: Diabetes mellitus; Oral health; TNF-α; Periodontal disease; Dental caries; Xerostomia; Elderly people
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Diabetes mellitus (DM) is a chronic metabolic disorder affecting children as well as adults worldwide. Only in the United States there are more than 20 million people with diabetes mellitus [1]. This disease is widely suggested to increase the risk of several diseases including periodontitis. The incidence of periodontitis has been shown to increase among diabetic subjects after puberty and as the patients’ population ages. Periodontal disease may be more frequent and severe in diabetic individuals with more advanced system complications. Therefore, there is a relationship between periodontal disease and diabetes mellitus, especially in patients with poorly controlled diabetes and hyperglycaemia.

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Periodontitis is a chronic inflammatory disease that is characterized by bleeding and inflamed gingiva, loss of attachment between the tooth and its supporting tissues and resorption of alveolar bone. This disease has a significant impact on quality of life as the teeth become progressively mobile and may fall out spontaneously if no treatment is provided. During the last years, the link between periodontal disease and systemic conditions has been evoked. The most of evidence suggests that diabetes increases the risk for gingivitis and periodontitis [2-3]. In previous study, type 1 diabetes was reported to be the main reason for the increased prevalence of periodontitis in teenagers. A recent case-control study confirmed that attachment loss is more prevalent and extensive in children with diabetes than in children without diabetes [4]. In addition, epidemiologic research supports an increased prevalence and severity of attachment loss and bone loss in adults with diabetes [5]. Furthermore, an increased incidence of dental caries in association with poorly controlled diabetes has also been reported [6-7], particularly in the elderly diabetic population.

In this review, we provide evidences for the relationship between diabetes and the development of dental- and periodontal diseases in the elderly diabetic population.

1. Periodontal disease

In the elderly patient the periodontal tissue shows morphological modifications. The basement of the junctional epithelium is moving towards the apex of the tooth creating a physiological « pocket » with anaerobic environmental conditions. The density of the connective tissue decreases with the number of ligament fibres. Through the complex aging processes the fibroblasts which produce the matrix and collagens for the connective tissue also decrease in number and become more and more pyknotic. The clinical attachment level (CAL) decreases in the course of time. CAL is defined as the distance (mm) from the cemento-enamel junction to the bottom of the periodontal pocket. In hard tissues the balance between anabolic and catabolic processes is disrupted resulting in bone loss that can be based on the increased secretion of inflammatory cytokines, like tumor necrosis factor alpha (TNF-α) and interleukin-1β (IL-1β). This clinical feature is described as periodontitis.

Gingivitis is characterized by a reversible inflammation of the gingiva caused by the presence of bacterial plaque [8]. Improved oral hygiene resolves the inflammation, but in elderly individuals, inflammation cascade develops much faster after plaque accumulation and resolves more slowly after plaque removal [9]. Whereas, periodontitis is characterized by an irreversible proinflammatory disease that extends deep in the tissues adjacent to the teeth and causes loss of supporting connective tissue and alveolar bone. Periodontitis results in the formation of soft tissue pocket or deepened crevices between the gingiva and tooth root. Severe periodontitis can result in loss of all teeth, occasional pain, discomfort and impaired mastication. The most common periodontal disease is chronic periodontitis in the adult, which is ubiquitous throughout all populations and socioeconomic classes [10-11].

Gingivitis and periodontitis are infectious diseases and their associated microflora includes Gram negative bacteria like Porphyromonas gingivalis, Prevotella intermedia, Tannerella forsythensis, Treponema denticola [12-13]. Recent studies implicate Herpes viruses in the pathogenesis of periodontitis [14-15]. In response to the invasion of the junctional epithelium, an antibody reaction is initiated to limit the progression. But, if the antibody response is inefficient, deeper bacterial penetration results in monocytic activation with secretion of cytokines and other proinflammatory mediators resulting in soft and hard tissue destruction. Fibroblasts and macrophages secrete matrix metalloproteinases that disaggregate collagens, glycosaminoglycans and bone. This process is painless, but the patient can note a disagreeable taste or fetid odour [16].

2. Diabetes and periodontal disease

The relationship between diabetes and periodontal disease is widely reported in several studies. Available data obtained from several studies strongly suggest diabetes as a risk for gingivitis and periodontitis [17]. In previous studies, the prevalence of gingival inflammation was reported to be greater in patients with type 1 diabetes than in patients without diabetes who had similar plaque level [18]. However, a greater gingival bleeding was observed in patients with poorly controlled diabetes when compared with either control subjects or with subjects with well-controlled diabetes [19]. Also subjects with type 2 diabetes demonstrated a greater gingival inflammation than did control subjects without diabetes; interestingly, the highest level of gingivitis was observed in subjects with poor glycaemic control [20]. Using an experimental gingivitis protocol, a recent longitudinal study showed more rapid and severe gingival inflammation in adult subjects with type 1 diabetes than in control subjects without diabetes, despite similar qualitative and quantitative bacterial plaque characteristics, suggesting a hyperinflammatory gingival response in people without diabetes [21]. In addition, epidemiologic research supports an increased prevalence and severity of attachment loss and bone loss in adults with diabetes [22].

2.1. TNF-α and insulin resistance

Data from the large Women’s Health study showed that elevated serum C-reactive protein (CRP) levels were associated with a four-fold increase in risk for future diabetes [23].
Moreover, in cross-sectional studies, levels of inflammatory biomarkers such as CRP and the pro-inflammatory cytokines interleukin-6 (IL-6) and TNF-α, correlated with insulin sensitivity and with features of the insulin resistance syndrome [24].

TNF-α has been shown by several studies to link obesity, a known major risk factor for type 2 DM, and insulin resistance [25]. Expression of TNF-α mRNA was increased, and was strongly correlated to the degree of obesity and the level of insulin resistance in obese animal models and humans [26]. Long-term exposure of animals to TNF-α induced insulin resistance, whereas neutralization of TNF-α increased insulin sensitivity [27]. TNF-α can induce insulin resistance by diverse mechanisms, both direct and indirect [28]. Recent data suggest that TNF-α also regulates expression of several adipocyte genes known to modulate insulin sensitivity/resistance [29].

2.2. Chronic periodontal inflammation and insulin resistance

Antimicrobial chemical treatment targeted at periodontal bacteria in patients with chronic periodontitis and type 2 diabetes was reported to improve the metabolic control of diabetes in Pima Indian population, which is known as the population with highest incidence of type 2 diabetes worldwide [30-31]. Therefore, it is possible that the improvement in insulin resistance was mediated by the reduction of circulating TNF-α since the upregulation of TNF-α was observed in diabetes-susceptible male mice. Interleukin-11 inhibits NF-kappaB and AP-1 (nuclear activator protein-1) activation in islets and prevents diabetes induced with streptozotocin in mice [32].

In fact, it is not clear if successful periodontal treatment reduces circulating inflammatory marker levels, like IL-6 or TNF-α, significantly in systemically healthy periodontitis patients [33]. In addition, CRP and IL-6 have been reported to be elevated in severe periodontitis patients and decrease after periodontal therapy [31], suggesting that periodontal infection stimulates hepatocytes to secrete such acute phase proteins. Thus, in cases of severe periodontitis, TNF-α might be secreted from both local periodontal tissue and liver, since liver cells are known to produce TNF-α in response to lipopolysaccharide [34] and hepatitis C viral infection [35]. Since the liver is one of the most important organs taking up glucose in response to insulin, periodontal infection might directly influence glucose sensitivity in the liver [35].

Figure 1 presents the current concepts for the pathogenesis of periodontal disease in diabetes.

In conclusion, further studies are needed to prove TNF-α as a link between type 2 diabetes and the development of periodontal diseases.

Fig. 1. Pathogenesis of periodontal disease in diabetes

Abbreviations:
3. Relationship between diabetes and periodontal disease

The effects of hyperglycaemia on the oral health implicate two different pathological mechanisms [36]:

- Hyperglycaemia leads to increased blood glucose levels. Oral fluids reflect elevated blood glucose levels like saliva and gingival crevicular fluid. This correlation may contribute to influence the microbial flora in the oral cavity, the bacterial populations, both in plaque and free floating. Especially anaerobic bacterial strains at the bottom of periodontal pockets may be favoured in their growth at the expense of other bacterial species. In this context, hyperglycaemia may induce and accelerate the inflammation processes in the mouth.

- Hyperglycaemia also increases the concentration of advanced glycation end-products (AGE). The elevated levels of glucose lead to pathological biochemical processes of glycation of proteins-like collagen or lipids and non-enzymatic oxidative destruction. These glycated products have the potential to create molecular complexes which reduce the solubility of the target proteins-like collagens. Thus, AGE’s induce inflammatory responses that contribute to systemic degradation of connective tissues in diabetic patients and consequently in periodontal tissue. These generalized pathologic changes in the metabolism of collagen have a great impact on both, mineralized and not mineralized tissue. Several studies indicate that in diabetic patients the cytokine level in crevicular fluid is elevated which contributes to bone loss and soft tissue decay more than in the controls although the number and composition of bacteria were the same [36-38].

It seems to be a bidirectional interrelationship between diabetes and periodontal health. Periodontitis is more prevalent and more severe in patients with diabetes than in normal populations [39]. Several studies demonstrated that treating periodontal infection contributes to a positive glycaemic control management and enables the reduction of the burden of complications of diabetes mellitus [39].

The systemic parameters mostly used in the studies are blood glucose or glycated haemoglobin (HbA₁c) levels. Blood cells have an actuarial survival rate of mostly three months; the best stable long duration control marker for diabetic patients is the HbA₁c level that should range between 6.5% and 7% [40].

4. Effect of diabetes on periodontal health

Today, it is accepted that diabetes affects the severity of periodontal disease and increases the risk of developing periodontitis showing that patients with type 2 diabetes had approximately threefold increased odds of suffering from periodontitis compared with subjects without diabetes [41-42]. A meta-analysis of different studies conducted until 1996 including more than 3,500 patients with diabetes, showed a significant association between diabetes and periodontitis [43]. Diabetes seems also to increase the risk of long lasting periodontal destruction over time. A fourfold increased risk of progressive alveolar bone loss in patients with type 2 diabetes was shown [44].

The role of glycaemic control in diabetes patients is of utmost importance for the pathogenesis of periodontitis suffering patients. It’s important to note that well-controlled diabetic individuals had better periodontal health than the controls [45].

The risk of developing periodontitis is greater (threefold increased) in diabetic patients who have a poor glycaemic control than in patients with a good glycaemic control [46].

Epidemiologic research showed an increased prevalence, severity of attachment loss and bone destruction in patients with diabetes [41-42].

The duration of diabetes mellitus appears to affect the severity of periodontal disease. The longer the diabetes mellitus duration, the more extensive and severe the pathogenesis of periodontitis is observed. The duration of diabetes disease correlates directly to the severity of periodontitis development [47].

Other studies demonstrate that the diabetic patients with periodontitis had a higher prevalence of ketoacidosis, retinopathy and neuropathy [48] and that periodontitis is a strong predictor of mortality from ischaemic heart disease and diabetic nephropathy in Pima Indians with type 2 diabetes [49].

Several mechanisms are involved in the increased periodontal tissue destruction:

- impaired wound healing: rapid degradation of collagen, by matrix metalloproteinase enzymes that are elevated in diabetes patients. Acceleration of the inflammation cascade in diabetic individuals, impeding the mechanism of wound healing and, hereby, augmenting the destruction processes [36];

- exaggerated monocyte response (elevated cytokines and mediators production) to dental plaque antigens [11];

- diabetic patients, especially with poor glycaemic control accumulate high levels of irreversibly glycosylated proteins called AGEs in tissues and in the periodontium [50-51];

- impaired neutrophil chemotactic response caused by the elevated and generalized glycosylation processes [52].

However, some studies did not find a significant relationship between glycaemic control and periodontal status [53-54]. The degree in which glycaemic control takes influence and the multifactorial nature of periodontal disease seems to depend on the individual patient’s variability.

The multifactorial aetiology of periodontitis also limits the prognosis of how glycaemic control of the diabetic patient influences the progress of disease [55].
5. Effect of the periodontal infection on glycaemic control

Inflammation processes as they occur in chronic diseases like periodontitis can potentiate insulin resistance throughout cytokine production. The effect of periodontal disease on diabetes is highly interesting because of the finding that acute infections alter the endocrinologic-metabolic status, leading to difficulties in controlling glycaemia by increasing insulin resistance. Chronic gram-negative infections and chronic endotoxemia, like those associated with periodontal disease, result in elevated IL-1β, TNF-α, IL-6 and prostaglandin E2 levels [56]. All these cytokines can induce insulin resistance and a worsening of metabolic control in diabetic patients. TNF-α, for example, inhibits the phosphorylation of insulin receptor substrate-1 (IRS-1), resulting in insulin resistance [57].

6. Effects of periodontal therapy in patients with diabetes

The literature reviewed report a similar clinical healing rate in diabetic and non-diabetic patients. No significant difference was measurable in controlled diabetic individuals concerning wound healing parameters or time duration. But in poorly controlled diabetics, periodontal health appears to deteriorate more rapidly than in healthy persons. Therefore, a stable metabolic status is the most important parameter to determine the prognosis and the interval for periodontal therapy. In this context, the compliance of diabetic patients has a much higher impact on the outcome of the therapy than in non-diabetic individuals [40].

7. Effect of periodontal therapy on glycaemic control

There are relatively few studies about the effect of periodontal therapy on the metabolic status of diabetes. A study by Stewart and coll. found that following conservative periodontal therapy (without using antimicrobials, excluding influencing metabolic control), there was a marked improvement in glycaemic control measured through HbA1c in patients with type 2 diabetes compared to the non-treatment control group. What makes this study interesting is that the follow-up period was about 18 months [58]. Another study showed a significant improvement in HbA1c following periodontal treatment even in patients with good glycaemic control [59].

As chronic periodontal disease is characterized by inflammation processes that imply the potential to exacerbate, and in this context, also may induce insulin resistance by worsening glycaemic control, periodontal treatment procedure should be carefully conducted. While the aim of periodontal treatment is to stop the inflammation cascade, this may also help to diminish insulin resistance [60]. In a recent study of patients with type 2 diabetes and periodontitis, periodontal treatment resulted in significant reduction of TNF-α in the serum correlated with significant diminution of total HbA1c level. This result leads us to the following conclusion: a reduction in periodontal inflammation may help to decrease the inflammatory mediators in the serum that are associated with insulin resistance and glycaemic control [61].

Some authors, however, did not confirm that periodontal therapy improves the metabolic status and the HbA1c level of diabetic subjects [62-64].

A recent study affiliated the association between the degree of periodontal infection and lipid profiles in diabetic patients. The authors concluded that in diabetic subjects, Porphyromonas gingivalis infection is associated with increased LDL cholesterol which may be accompanied with increased cholesterol synthesis by inflammatory cytokines. This may lead in connection to some other parameters to a higher risk for vascular diseases, as for example, atherosclerosis [65].

Table I presents an overview of studies examining the influence of periodontal therapy on HbA1c level.

8. Diabetes, periodontitis and pulmonary diseases

Aspiration pneumonia is an important cause of morbidity and mortality in persons older than 60 years. This disease represents one of the highest rates of mortality in elderly individuals [66]. The relation between oral diseases and pulmonary diseases has been previously reported and oral health status is an important etiologic factor [67-69]. A study provides evidence supporting the thesis that dental decay, presence of cariogenic bacteria and periodontal pathogens are potentially risk factors for aspiration pneumonia. The presence of Porphyromonas gingivalis, Streptococcus sobrinus, Staphylococcus aureus was significantly higher in dental plaque or saliva in patients with aspiration pneumonia. It is interesting to note that the risk to come down with pneumonia is greater for patients with diabetes mellitus [70].

The use of antibiotics, local oral antiseptics and regular tooth brushing that causes mechanical disaggregation of the dental plaque, reduces the risk for pneumonia [71].

Four different aspects in the pathogenic mechanisms of lung inflammation may explain the possible invasion of bacterial strains of the oral cavity into the respiratory tract [72]:
- periodontal pathogens and bacteria that cause caries like Streptococcus mutans may be aspirated and transported into the bronchia where they only may colonize if the patient’s immune system is suppressed like in elderly patients or diabetic individuals;
- the bacterial species of the mouth are capable of producing enzymes starting to degrade the surface proteins of epithelial cells that protect healthy individuals from bacterial adherence. Insufficient oral hygiene increases the risk of bacterial invasion into the lung.
Microbial plaque, particularly in diabetics were about double that value, being diabetics were found to range between 0.2 and 3.3 mg/dL loss are warranted.

Between diabetes and risk for coronal or root caries exists. There is insufficient evidence to determine whether a relationship between type 2 diabetes and an increased prevalence of past coronal and root-surface caries in older adults. There is no consistent relationship in the literature does not describe a consistent relationship between type 2 diabetes and an increased prevalence of past coronal and root-surface caries in older adults. There is insufficient evidence to determine whether a relationship between diabetes and risk for coronal or root caries exists.

Further investigation of diabetes with dental caries and tooth loss are warranted [73-74].

While glucose levels in parotid and pooled saliva of non diabetics were found to range between 0.2 and 3.3 mg/dL [75], those in diabetics were about double that value, being 0.45-6.3 mg/dL [76]. Microbial plaque, particularly Streptococcus mutans, and sugar are the two etiological factors of dental caries, and when these factors are well controlled in the diabetic, the caries reduction is the same as in non diabetic. Other results were observed when endodontic treatment is involved. A multivariate analysis revealed that in cases with preoperative periradicular lesions the successful treatment outcome was significantly reduced in non surgical endodontic therapy [77]. There are also preliminary findings that the necrotic pulp of diabetic shows another bacterial spectrum where some bacterial strains may be more prevalent than in non diabetics [78].

### 9. Diabetes, caries and endodontics

The literature does not describe a consistent relationship between type 2 diabetes and an increased prevalence of past coronal and root-surface caries in older adults. There is insufficient evidence to determine whether a relationship between diabetes and risk for coronal or root caries exists.

Further investigation of diabetes with dental caries and tooth loss are warranted [73-74].

### 10. Diabetes and Xerostomia

Xerostomia is associated with difficulties in chewing, swallowing, tasting or speaking. This results in poor diet, malnutrition and poor socialisation. Xerostomia can cause oral discomfort especially for patients with therapeutic dentures. Patients who suffer from xerostomia have serious problems following, tasting or speaking. This results in poor diet, malnutrition and poor socialisation. Xerostomia can cause oral discomfort especially for patients with therapeutic dentures.

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risk for dental caries and candidiasis is markedly higher than in healthy individuals [79]. Reduction of total salivary production rate seems to have a negative impact on dental caries and oral infections. This leads to decrease in salivary clearance, reduction in buffering ability and in antimicrobial activity [80]. Llamas Cadaval et al. showed that in patients older than 68 yrs, 13 diabetic patients related symptoms of “dry mouth”, whereas only three in the control group had this complaint [81-82].

In diabetics, reduced salivary flow and alterations in composition have been previously reported [83-85], but these findings implied also always contradictory data [86-88]. In type 2 diabetic patients, the secretions from the submandibular and sublingual glands are reduced [83]. Patients with type 1 diabetes who had developed neuropathy often report symptoms of dry mouth correlating directly to a decreased saliva flow rate [90]. Mandel described asymptomatic bilateral parotid swelling in diabetic individuals [91]. The parotid gland is characterized by the presence of small acini (acinar atrophy), lipid intracytoplasmic droplets, as well as adipose stroma infiltration. The acinar cytokeratins expression is heterogeneous and numerous in the hyperplastic ducts [92]. These structural changes observed in parotid gland result in biochemical unbalance of the saliva protein composition [65]. Another study revealed high levels of urea and total proteins in the blood whereas albumin was decreased [83]. The increase of free salivary glucose was related to poor metabolic control [93], but the increase of blood glucose level does not reflect the salivary glucose concentration [94]. In this context, non-invasive monitoring of saliva glucose levels is not possible.

Several authors have reported an increased predisposition to the manifestation of oral diseases like candidiasis, including median rhomboid glossitis, denture stomatitis and angular cheilitis in diabetics. Candidiasis seems to correlate with poor glycaemic control and the use of therapeutic dentures. This predisposition contributes also to xerostomia, increased salivary glucose levels or immune dysregulations [95-97].

Taken all together the clinician should identify the possible cause and provide the patient with proper treatment, although it is usually palliative, but may offer some protection from the condition’s more significant complications [79].

11. Nutritional consequences of insufficient oral health

Patients who suffer from impaired mastication and have difficulties in swallowing, also unintentionally lose weight. Through anthropometric studies a correlation was found between malnutrition and blood level of serum albumin as well as between salivary production rate and the quality of chewing. In the elderly patient the mastication function and salivary flow rate are the most used parameters to evaluate the quality of nutrition. Loss of teeth causes changes in the choice of food and therefore increases the risk for several diseases like cardiovascular diseases or cancer.

The clinician should take following points into his account [98]:
- the wish of the patient;
- the aim should be to restore the impaired mastication by fixed prosthodontic constructions and if there is non-fixed prosthetics to reevaluate this work and if necessary to change;
- implants should be assessed only if other therapeutic regimens are not applicable to improve the oral status. Compared with the general population, a higher failure rate is seen in diabetic patients. A good control of plasma glycaemia is of utmost importance to improve the percentages of implant survival in these patients. Possible microvascular complications are discussed to be the reason for less effective osteointegration in diabetes patients. Therefore clinicians have to take specific considerations into account before placing implants in diabetics [99];
- the psychological effect of this kind of treatment should be evaluated because the quality of life for the patient will rise;
- the compliance of the patient is of utmost importance and one of the most important factors is to inform the patient how to ensure his oral status after successful treatment;
- prophylactic treatment after therapy is as important as the treatment itself;
- education of the patient in nutritional aspects in relation to his disease.

References


