

RELATIONSHIP BETWEEN DIABETES AND PERIODONTAL DISEASE: A REVIEW OF LITERATURE

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Abstract

Recently, the relationship between diabetes mellitus and periodontal disease has been studied, and several studies indicated that both types of diabetes mellitus are risk factor for gingivitis and/or periodontitis. Both of these diseases have a relatively high occurrence in the general population. Bone metabolism changing is one of the important complexities associated with diabetes mellitus. Alveolar bone loss is one of the main complexities of periodontitis, and diabetes is a primary risk factor for periodontal disease. Studies have concluded a bidirectional association between periodontal disease and glycaemic control with each disease having a potential impact on the other. In this review, we summarize the adverse effects of diabetes on the periodontium.

Key words: *Diabetes complications, Diabetes mellitus Type 1, Diabetes mellitus Type 2, Periodontal diseases, Gestational diabetes, Glycaemic control.*

Introduction

Periodontitis (PD) and diabetes mellitus (DM) are generally encountered chronic diseases. Diabetes mellitus is a disease of metabolic breakdown characterized by hyperglycemia due to impairments in insulin action, insulin secretion or both. Disruption of lipid and protein metabolism also occurs.¹

DIABETES MELLITUS

Diabetes epidemiology and classification

Diabetes occurs in over 9% of adult population.^{2,3} Approximately 90% of cases correspond to patients with type 2 diabetes, whereas type 1 diabetes constitutes 5% to 10% of patients. Other types include gestational diabetes and secondary forms associated with other conditions such as pancreatic disease, drug therapies, and endocrine disorders.⁴

Diabetes has two main types, insulin-dependent type-1 diabetes and non-insulin-dependent type-2 diabetes. Despite their designations, this classification does not depend upon the need for exogenous insulin, which can sometimes also be required by type-2 patients.⁵ Type 1 diabetes usually presents in children and adolescents, although some studies showed 15% to 30% of all cases being diagnosed after 30 years of age. In type 1 in older patients, β -cell destruction occurs more slowly than in children, with a less accidental onset of symptoms.⁶

Other specific types of diabetes mellitus include all diabetes cases in which the etiological factor is known but having a lower incidence. For example, functional genetic defects of β cells with insulin secretion impairment, genetic defects in insulin action, endocrine diseases that cause hyperglycemia (acromegaly), viral infections, diseases of exocrine pancreas (pancreatitis, trauma, infection, pancreatic cancer, hemochromatosis, cystic fibrosis), certain drugs and chemicals, genetic syndromes (i.e. Down syndrome, Turner syndrome).⁷⁻¹⁰

Etiology and pathogenesis

The following two mechanisms have been proffered to describe the classic complications of diabetes:⁴

- 1) Polyol pathway: According to this theory, glucose is converted to sorbitol by aldose reductase), which is implicated as the toxin in almost all of these complications.
- 2) Production of advanced glycosylation end products (AGEs).

PERIODONTAL DISEASE

Periodontal disease is destruction of tooth supporting tissues by accumulation and maturation of oral bacteria on teeth.¹¹

Periodontal diseases include two major subtypes, gingivitis and periodontitis. Gingivitis is characterized by reversible inflammation in periodontal tissues whereas periodontitis also presents annihilation of tooth supporting structures, and tooth loss may occur. Existing evidence showed that gingival inflammation (gingivitis) is required for periodontitis, however some cases of gingivitis never transform to periodontitis.^{11,12} This is because bacterial plaque accumulation is necessary for onset of both subtypes but individual susceptibility is required to develop periodontitis.^{12,13}

Classification

Variability in diagnosis is in part caused by the lack of an adequate classification. Several attempts accomplished for classifying periodontal disease according to its clinical manifestations and etiology,¹⁴ considering periodontal disease as an entity separate from the patient that is capable of producing signs and symptoms.^{15,16} The 1999 American Association of Periodontology (AAP) classification identifies six categories:

- a) gingival disease,
- b) chronic periodontitis,
- c) aggressive periodontitis,
- d) periodontitis as manifestation of systemic disease,
- e) necrotizing periodontal disease, and
- f) periodontal abscess.¹⁴

Drawbacks of both the 1989 and 1999 AAP proposals are that periodontal disease cannot be classified according to its etiology, and there are no apparent clinical criteria for its

diagnosis, leaving this decision to health care professional.¹⁶

Etiology and pathogenesis of periodontal disease

Microorganisms in combination with individual host susceptibility and environmental factors are the main etiologic factors for periodontal diseases.¹⁷

Plaque accumulation on tooth surfaces produces gingivitis, but the degree of inflammation and destruction of the alveolar bone that supports teeth depends on the host susceptibility.¹⁷

Oral bacteria can destroy periodontal tissues through the action of matrix-degrading enzymes and molecules that affect host cells. The transformation from gingivitis to periodontitis involves spreading of the inflammatory front to deeper areas in the connective tissue. However, the reason why this happens is not well known, one etiopathogenic mechanism could involve the presence of bacteria or their products, such as lipopolysaccharides, in periodontium. They may cause an immune response with production of interleukins and tumour necrosis factor (TNF), which plays an important role in the regulation of inflammatory processes. This inflammation provokes the production of secondary mediators, which amplify the inflammatory response. Contemporarily, the presence of these cytokines reduces the ability to repair damaged tissue by cells such as fibroblasts, and finally, bacterial products and this inflammatory cascade stimulate osteoclastogenesis, leading to alveolar bone loss.^{18,19}

Diabetes as a risk factor for periodontal disease

Many authors have clarified diabetes as a risk factor for periodontal disease. Hence, Mealey showed that diabetic patients had a three-fold higher risk of periodontal disease compared with non-diabetic patients after controlling for age, gender, and other confounding factors.⁴

For diabetes to be acknowledged as a risk factor it must meet the risk analysis criteria set out by Johnson & Hill, especially the two following conditions:²⁰

- 1) Biological plausibility that the factor can account a given disease by a known action mechanism,
- 2) Demonstration in prospective studies that the factor chronologically antedates the disease.

The effect of periodontal disease on diabetes

All chronic infections affect glycaemic control in diabetic patients. Chronic inflammation leads to deficiency in cell-mediated immunity such as neutrophil (polymorphonucleocyte) chemotaxis and macrophage function and vascular disease.^{21,22} Cytokines such as IL-10 and transforming growth factor (TGF), which control humoral immune response, and IL-2 and interferon (IFN) gamma, which control the cellular immune response are produced. These changes in cellular and humoral response affect the secretion of insulin and affect glycaemic control.²³

Periodontal disease is one of chronic infections which affects the glycaemic control. A two-year longitudinal trial indicated a six-fold increase in risk of worsening glycaemic control in diabetic patients having severe periodontitis compared with diabetics without periodontitis.²³

Studies have attempted to determine the influence of periodontal diseases on control of diabetes and reported that periodontal therapy may cultivate metabolic control of diabetes.²⁴ Studies observed that mechanical periodontal treatment alone not only improves periodontal health, it also has a positive effect on level of glycosylated haemoglobin. However, the magnitude and duration of the advancement may not be clinically significant.²⁴

There is low evidence from clinical trials that diabetic patients require more aggressive periodontal treatment than non-diabetics.²⁴

The mechanisms by which periodontal diseases may affect the diabetic state have been explained only recently. Both periodontal diseases and diabetes, especially type 2 diabetes, have major inflammatory origin. Chronic periodontal diseases also have potential to aggravate insulin resistance and worsen glycaemic control, while periodontal treatment that decreases inflammation may help diminish insulin resistance.²⁵

Patients with inflammatory periodontal diseases often have increased serum levels of pro-inflammatory cytokines. These levels are aggravated in diabetics. This has the potential to increase insulin resistance and make it more difficult for patient to control his or her diabetes.²⁶

Research has shown an amendment in glycaemic control after periodontal treatment in diabetic patients. In a recent study of patients with periodontitis and type 2 diabetes, Iwamoto and colleagues found that periodontal treatment has a significant association with reduction in serum levels of TNF- α .²⁷ This reduction in TNF- α level was accommodated by a significant alleviation in mean HbA_{1c} values (from 7.1% to 8.0%). This suggests that an alleviation in periodontal inflammation helps decrease inflammatory mediators in serum that are regarded with insulin resistance, thereby improving glycaemic control.

Effects of periodontal treatments on periodontal health and glycaemic control

Studies also indicated that patients with good metabolic control exhibited a slower rate of attachment loss than patients with poor metabolic control.

By contrast, studies also showed that after periodontal treatment, better glycaemic control could be achieved.²⁸ This relevance was confirmed by several recent meta-analyses. Those studies addressed the importance of infection control in diabetic patients, where a combination of mechanical debridement (i.e., scaling and root planing) and systemic antibiotics conducted better glycaemic control.²⁹ Doxycycline, one of tetracycline derivatives, appeared to be the most potent modifier of all antibiotics,

possibly due to the effect of prohibiting glycation of the extracellular matrix (ECM).³⁰

However, there are also studies that indicate no significant alteration in glycaemic control after periodontal therapy.²⁵ A 4-month report from Christgau and colleagues indicated that periodontal treatment reduced periopathogenic bacteria, improved clinical periodontal parameters, and reduced the oxidative burst response of inflammatory cells.²⁶ However, no significant difference existed between healthy and diabetic patients. A meta-analysis from Janket and colleagues showed a facility, but no significant improvement, in HbA_{1c} levels after weight adjustment.³⁰ A long-term, follow-up study in Japan showed no significant difference between periodontal treatment and the incidence of diabetes, but did suggest periodontitis as a risk factor for developing diabetes.²⁹ Taken together, of clinical relevance to us is that dentists should treat the periodontal disease and manage the patient's diabetic condition, in order to achieve optimal results after periodontal treatment. While good periodontal health is not necessarily associated with an alteration in glycaemic control, an improvement may potentially modify metabolic control, which is accompanied with an accession in the quality of life.

Conclusion

Periodontitis is a highly prevalent infectious disease that relates to some systemic disorders, such as diabetes mellitus.

Diabetes has been associated to many oral diseases including: tooth decay, xerostomia, neuro-sensory disorders and several oral mucosal and periodontal diseases. It is well documented in the literatures that periodontal disease is more prevalent and severe in diabetic patients than in healthy subjects. However, it has to be kept in mind that the level of metabolic control and duration of diabetes appears to influence risk of periodontal disease.

Periodontal treatment is effective in diabetic patients, but more long-term recurrence can be expected in a patient with poor diabetic control. Severe periodontitis is more frequently found in diabetic patients with high HbA_{1c} levels and systemic diabetic complications.

The advantageous effects of periodontal treatment on HbA_{1c} levels seem to be clearer in type 2 diabetic patients and when antibiotics are associated with local periodontal therapy, although other reports did not find any betterment in diabetes control after periodontal treatment. More research on type 1 and type 2 diabetic patients will be needed to know how periodontal treatment is associated with diabetes metabolic control. In those, it will be more important to control other factors that may affect HbA_{1c} levels, such as diet, diabetic medication, and physical exercise. Reduction of HbA_{1c} after periodontal treatment is usually less than 0.5%. New studies are needed to evaluate the clinical significance of this improvement.

Further analysis of inflammatory mediators, such as CRP, may help to explain the association between diabetes and

periodontal disease, and the individual variations detected in samples from different severities of diabetes and periodontal disease.

Any improvement in control of diabetes and/or periodontal disease could improve significantly the quality of life in diabetic patients.

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