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Review Article

Periodontitis and systemic disease: A challenge for interdisciplinary team

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Abstract

Oral health status is an integral component of general health and well being of an individual. The oral cavity is the site of infection and inflammatory disease. Current evidence suggests that periodontal disease may be associated with systemic diseases. This paper reviews the published data about the relationship between periodontal disease and cardiovascular disease, adverse pregnancy outcomes, diabetes and respiratory disease. Although majority of them observed an association between periodontitis and systemic conditions, the cause of relationship still needs to be demonstrated. Further studies, particularly interventional, with a larger sample size need to be designed to confirm the two way relationship.

Keywords: Cardiovascular disease; Diabetes Mellitus; Pregnancy complications; Periodontitis

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1. Introduction

Knowledge about the link between periodontal disease and systemic disease are growing rapidly. The understanding of the etiology and pathogenesis of periodontal diseases and their chronic inflammatory and infectious nature necessitates admitting the possibility that these infections may influence events elsewhere in the body. The concept that oral diseases could influence distant structures in the body is to a certain extent, a return to the theory of focal infection. The return of this concept and advances in the methods of scientific investigation were undoubtedly decisive in the content. The development of epidemiological studies and statistical analysis enhanced the understanding of biological plausibility by means of advances in molecular biology, microbiology, immunology and genetics. Nevertheless, a number of hypotheses have been postulated, including common susceptibility, systemic inflammation with increased circulatory cytokines and medications, direct infection and cross reactions or molecular mimicry between bacterial antigen and self antigen. The reactive antibiotics and T-cells between self heat-shock proteins (HSPs) and porphyromonasgingivalis have been demonstrated in the peripheral blood of patient with atherosclerosis as well as in the atherosclerotic plaque themselves. This paper discusses the relationship between periodontal disease and the most studied systemic conditions like cardiovascular disease, advanced pregnancy outcomes, diabetes mellitus and respiratory disease.

2. Discussion

2.1 Cardiovascular diseases

Cardiovascular disease (CVD) is a group of diseases that includes congestive heart failure, cardiac arrhythmias, coronary artery disease (including atherosclerosis and myocardial infarction), valvular heart disease and stroke. Among these, atherosclerosis, a major component of CVD is characterised by deposition of atherosclerotic plaque on the innermost layer of walls of large and medium sized arteries. End stage outcomes associated with atherosclerosis include coronary thrombosis, myocardial infarction and stroke.[1] The role of periodontal disease in the etiology of heart disease has recently received much attention. CVD and periodontitis are both chronic and multifactorial disease and share some of their risk factors associated with low socioeconomic status, smoking and psychosocial factors such as stress.[2]

Several mechanisms that could explain the association have been investigated:[3,4]

a. Bacteria from the periodontal infection enter the blood and invade the heart and blood vessels causing harmful effects.
b. The body responds to the periodontal infection by producing inflammatory mediators that travel through the blood and cause harmful effects on the heart and blood vessels.
c. Bacterial products like lipopolysaccharides enter the blood and cause harmful effects on the heart and blood vessels.

2.2 Diabetes Mellitus

Diabetes is a group of metabolic disease characterized by hyperglycaemia and results from either a deficiency of insulin secretion and/ or reduced insulin action. The two main types of diabetes are classified primarily on the basis of their underlying pathophysiology. Type I diabetes results from autoimmune destruction of insulin producing β cells in the pancreas, leading to total loss of insulin secretion.[5] Type 2 diabetes mellitus begins with insulin resistance, a condition in which fat, muscle and liver cells do not use insulin properly. There is peripheral vascular insufficiency causing scarring disorders and physiologic changes that reduces the immunologic capacity, thereby increasing the susceptibility to infection. There exists a positive relationship between poor glycaemic control in persons with type 2 diabetes mellitus and periodontitis. A high glucose and calcium content in the saliva favours an increase in the amount of calculus formation leading to periodontal disease, which is the most common dental manifestation in the oral cavity of a diabetic patient.[6]

Severe periodontal disease often co-exists with diabetes and is considered as sixth complication of the disease. There is growing research indicating a bidirectional relationship between periodontal disease and diabetes. A number of studies have demonstrated that poor blood sugar control may contribute to poor periodontal health and such individuals have 2-3 fold greater chance of developing destructive periodontal disease as well as 3-4 fold greater chances of having progressive alveolar bone loss. Research has also demonstrated eleavated levels of inflammatory mediators in the gingival cervicular fluid of periodontal pockets of poorly controlled patients with diabetes as compared to those without diabetes or those with diabetes who are well controlled. These patients had significant periodontal destruction with an equivalent bacterial challenge.[7,8] Proposed mechanisms to explain the relationships between periodontal disease and diabetes were:[9]

a. Both stimulate the chronic release of proinflammatory cytokines that have deleterious effects on periodontium and interfere with insulin action.
b. Bacteria and their products also may

produce insulin resistance and glucose intolerance.

c. Periodontal pathogens produce toxins like lipopolysaccharide which may amplify the magnitude of the advanced glycation end products mediate cytokine upregulation.

2.3 Preterm low birth weight

In 1996, following a landmark study report by Offenbacher et al, periodontitis may be possible risk factor for adverse pregnancy outcomes. Adverse pregnancy outcomes include preterm low birth weight, miscarriage or preeclampsia. Preeclampsia and preterm birth are major causes of maternal morbidity and mortality. Low birth weight is defined as a birth weight of < 2500 grams. It is a major health problem in both developed and developing countries.[10] The etiology of preterm birth is multifactorial, but inflammation is a common pathway that leads to uterine contractions and cervical changes with or without premature rupture of membrane. Inflammation associated to preterm birth can mainly be attributed to intrauterine infection and bacterial vaginosis and the latter accounting for 40% of the cases of spontaneous preterm labour and preterm birth. There is a causal relationship between vaginosis and preterm birth and presence of significantly higher levels of proinflammatory cytokines and prostaglandins in the amniotic fluid. At the same time, an infection remote to the genital tract can also trigger preterm birth.[11]

Biological plausibility of the link between both conditions, periodontal disease and preterm birth does exist and can be summarized in three potent pathways:[4,12]

a. Haematogenous dissemination of inflammatory products from periodontal infection.
b. The foeto-maternal immune response to oral pathogen.
c. The third pathway is proposed to explain the theoretical causal relationship between periodontal disease and preterm birth involving bacteraemia from an oral infection.

The association between both conditions whether periodontitis is a confounding factor, a marker or one cause of preterm birth remains unclear. It is important to point that, out of the high number of studies published, only a few of them are randomized clinical trials which represents the research design that generates the weighing evidence when assessing claims of causation.[13] Several criteria, such as the definition of periodontal disease, experimental design, compliance with the treatment and time of periodontal treatment delivered in clinical trials, controlling for confounding variables and outcoming definitions are pointed out in order to understand the diversity of the result present.[14] Another issue addressed in the discussion is the fact that different populations may not share same risk factors to both conditions, periodontal disease and adverse pregnancy outcomes. It is necessary to account socioeconomic, biologic and environmental determinants for each population.

2.4 Respiratory Diseases

There is emerging evidence that periodontitis and poor oral health may be associated with several respiratory conditions. Chronic obstructive pulmonary diseases (COPD) is a pathological and chronic obstruction of airflow through the airway or out of the lungs and include chronic bronchitis and emphysema. There is increasing evidence that a poor oral health can predispose to respiratory disease especially in high risk patients (nursing home resident, older subjects, intensive care unit patients).[15] The oral cavity is a portal for respiratory pathogenic colonisation. Dental plaque may act as a reservoir of respiratory pathogens, which may be aspirated from the oropharynx into the upper

airway and then reach the lower airways and adhere to bronchial or alveolar epithelium. Several mechanisms have been proposed to explain the potential role of oral bacteria in the pathogenesis of respiratory infection, which include the following:[16]

a. Aspiration of oral pathogens (such as porphyromonasgingivalis, Actinobacillusactinomycetemcomitans, etc.) into the lung to cause infection;
b. Periodontal disease-associated enzymes in saliva may modify mucosal surfaces to promote adhesion and colonization by respiratory pathogens, which are then aspirated into the lung;
c. Periodontal disease-associated enzymes may destroy salivary pellicles on pathogenic bacteria to hinder their clearance from the mucosal surface; and
d. Cytokines originating from periodontal tissues may alter respiratory epithelium to promote infection by respiratory pathogens.
e. In elderly patients living in chronic care facilities, the colonization of dental plaque by pulmonary pathogens is frequent.

Notably, the overreaction of the inflammatory process that leads to destruction of connective tissue is present in both periodontal disease and emphysema. This overreaction may explain the association between periodontal disease and chronic obstructive pulmonary disease.

3. Conclusion

Periodontal disease as a risk factor for the development of various systemic conditions, such as diabetes mellitus, CVD, adverse pregnancy outcomes is a highly researched and debated topic. Nevertheless they represent a new and exciting area of research that has far reaching clinical and a public health implication.Though links have been made between oral health and CVD, Diabetes and Respiratory disease establishing cause and effect can be a complex and confusing process confounded by a myriad of variables.The strongest evidence for the role of periodontal disease as a risk factor for systemic health, for example, if resolution of periodontal infection can be shown to lead to better glycemic control in diabetes, this would lend credence to the hypothesis that periodontitis is true risk causally linked to important systemic health outcome. The mouth is truly connected to rest of the body. Much recent work has been devoted to clarifying the directionality of specific relationship. Often the associations are bidirectional. The success of periodontal treatment shift from preventing attachment loss to more on measurable reduction in bacteremia infection, inflammatory mediators. New recall regimens may be developed that focus on the reducing risk of systemic bacteraemia or reducing levels of endotoxin or host cytokines.

As the multiple risk factors for periodontal diseases become more clearly elucidated the practitioner will be able to more accurately determine an individual risks for periodontal disease, based on a systemic assessment of then individual risk characteristics. Risk factors include age smoking status, levelof oral hygiene and systemic health level. For identification of high risk individuals, microbial sampling and genetic testing may become standard practice.

The future dental practitioner will be dramatically, altered if subsequent research confirms that periodontal disease is true risk factor for systemic disease and that the intubation or progression of these medical conditions can be reduced by periodontal treatment.

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