

Periodontal disease and heart disease

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Summary

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The role of periodontal disease in the etiology of heart disease has recently received much attention. Periodontal disease, caused mainly by bacteria, is characterized by inflammation, bacteremia, a strong immune response and loss of connective tissue attachment and bone. It is speculated that a continuous long-term exposure of oral bacteremia and bacterial toxins induce immune responses which may contribute to coronary atherogenesis, and, in conjunction with other risk factors, may lead to coronary heart disease

and myocardial infarction. Periodontal disease may initiate pathological changes in blood vessel walls and act as precursor of atherosclerosis in susceptible hosts. Many causal factors may play a role in heart disease. Periodontal disease caused by pathogen bacteria as a low grade inflammation may represent one of several possible causal factors for heart diseases to occur.

Key words: periodontal disease, stroke, myocardial infarction, risk factors, inflammation, bacteremia, atherosclerosis, heart disease

Introduction

Periodontal disease is an infection of the supporting structures of the teeth. The host response to infection is an important factor in determining the extent and severity of periodontal disease. Systemic factors modify periodontal diseases through their effects on the normal immune and inflammatory mechanisms. The effects of a relevant number of systemic diseases on periodontitis are unclear and often it is difficult to causally link such diseases to periodontal disease. Severe oral infections, especially periodontal disease, in otherwise healthy individuals appear to place these individuals at increased risk for

developing certain health problems, including stroke and myocardial infarction. These effects cannot be explained by other traditional risk factors for heart disease, such as smoking, age, cholesterol levels, blood status, exercise etc. New research findings raise the possibility that periodontal disease may increase the risk of dying from a myocardial infarction almost twofold, and the risk of having a stroke almost threefold (22). The deleterious effects of periodontal disease on cardiovascular health may be as harmful as smoking or high cholesterol.

Pathogenesis of periodontitis and how it can affect overall health

The threat of periodontitis to overall health extends across the lifetime of an individual. Bacteria cause periodontitis, yet the biochemical destruction that leads to clinical signs of disease is the result of the chronic inflammatory process in the periodontal tissues. The inflammation, if uncontrolled, leads to loss of connective tissue attachment and bone.

Three key bacteria have been identified as causative of periodontal disease, and are elevated in the subgingival plaque of patients with chronic periodontitis: *Porphyromonas gingivalis*, *treponema denticola*, and *bacteroides forsythus*. They require a lush biofilm ecosystem to support adherence, growth,

and emergence and rely on host serum proteins and blood components for sustenance. These three bacterias have special enzymes and proteins that enable them to trigger mild host inflammation (19). *Porphyromonas gingivalis* is capable of evading neutrophil phagocytosis, invading through the epithelium to the tissues, get into the bloodstream, secreting enzymes that digest host tissues to enable penetration and spreading, and triggering vasopermeability to facilitate hematogenous dissemination. The bacteria have been identified at many distant sites, such as within atheromatous plaques (4,6), fetal blood cord, pneumonia areas,

brain abscess, eye- and skin inflammatory reactions. Oral bacteria have been linked to infections of the endocardium, meninges, mediastinum, vertebrae, hepatobiliary system, and prosthetic joints. Antibodies against *Porphyromonas gingivalis* were found in fetal cord blood, indicating that fetal exposure can occur in utero in mothers with periodontal disease (10). During pregnancy, the periodontal disease in the mother appears to be associated with an increased risk (to sevenfold) for premature delivery and low birth weight for gestational age. Fetal blood cord obtained at delivery contained maternal oral bacteria, which become blood-borne and target the placenta and fetus (10). In a pregnant mother with periodontal disease, the transient bacteremia associated with periodontitis and periodontal progression appear to represent a special risk (12). On base of extrapolation periodontal disease appears to be the reason in 18% of preterm low birth weight pregnancy.

Porphyromonas gingivalis avoids activating the acquired immune response and evades immune surveillance and clearance. Other periodontal pathogens also appear to gain systemic egress and become blood-borne. The periodontal pocket epithelium surface area has been suggested to approximate a wounded area for microbial penetration (13). The periodontal pathogens also

create toxic lipopolysaccharide (LPS) that is highly inflammatory. The LPS is released within the pockets and penetrates into the tissues where the LPS interacts with macrophages to stimulate the release of inflammatory mediators (PGE₂, IL- β , TNF- α). These inflammatory markers cause vasodilation and destruction of the periodontal ligament, activate fibroblasts and osteoclasts to tissue destruction and bone resorption (11). Patients who secrete more PGE₂, IL- β , and TNF- α have more inflammation and more severe periodontal disease.

Periodontal disease do not affect everyone, but we are all exposed to similar oral pathogens. Some individuals seem to never get periodontal disease, no matter how poor their oral hygiene habits are. The key dominants appear to be genetic and behavioural differences. Certain genes associated with an excess production of IL-1 β have been associated with severe periodontal disease (5,17). Periodontitis has a genetic component, and much of the susceptibility to disease is inherited. Smoking and diabetes, not plaque accumulation, enhance the inflammatory response to bacterial LPS, while also impairing the ability to fight infection by compromising neutrophil function. This exaggerated inflammatory response results in more severe periodontitis in patients with diabetes and smokers.

Periodontal inflammation and cardiac risk

In patients with periodontal pathogen bacteremia occur and initiate a systemic antibody response and the activation of the hepatic acute-phase response. The liver can be activated by bacteria, bacterial products such as LPS, cytokines like IL-1 β , TNF- α , and IL-6. This activation results in the synthesis of acute phase proteins such as CRP. The increases in CRP seen in patients with periodontitis are modest (twofold to threefold higher) compared with the increases seen in acute infection 100-fold to 1000-fold higher). Inflammation and bacteria at a systemic low grade level when repeated acutely and aggravated chronically over many years, theoretically can provide severe cumulative damage to systemic health. Ridker (14,15,16) reports that for diagnosing cardiovascular risk, serum CRP-levels, in addition to cholesterol levels, provide the best diagnostic indicators of risk for future myocardial infarction. It is suggested that even mild increases in CRP enhance cardiac risk, the small elevations in CRP elicited by periodontal disease might be considered potential cardiac risk factor. Slade et al. (18) studied the relationship between periodontal status, blood CRP levels, and the severity of subclinical atherosclerosis using B-mode ultrasonography to measure the wall thickness of the carotid vessels. Approximately half of

the linkage between high CRP levels and increased carotid wall thickness appears to be attributable to periodontal disease.

Arbes et al. (1) who have analyzed NHANES III data reveals an association between a history of myocardial infarction and increasing periodontal disease severity in a dose-response manner. The greater the periodontal disease, the greater the risk with odds ratios greater than 5 for the most severe periodontal disease groups. This was present after adjusting for age, race, gender, levels of serum cholesterol, low-density lipoprotein, and high-density lipoprotein, smoking, body mass index, physical activity, hypertension, diabetes mellitus, socioeconomic status, and education. Beck et al. (2) showed an incremental increase in risk for death due to myocardial infarction and stroke with increasing periodontal disease. Spahr et al. (20) have found an association between periodontal disease and coronary heart disease. Joshipura et al. (9) and Holmlund et al. (8) have demonstrated a strong relation between the number of remaining teeth, tooth loss due to periodontitis and coronary heart disease. Holmlund et al. (8) showed also an association between the severity of periodontal disease and hypertension. Volzke et al. (21) have found a

correlation between aortic atherosclerosis and myocardial infarction, body mass index, tooth quantity, plasma fibrinogen, lipoprotein A. Periodontal disease has an impact on chronic atherosclerotic process that leads to atheroma formation (3),

impaired perfusion and vasospasm. Periodontal disease is associated with elevated serum total cholesterol, C-reactive protein, and plasma fibrinogen, which may be the link to increased cardiovascular disease risk (23,7).

Conclusion

Periodontal bacteria are known to invade the systemic circulation. Oral pathogens and inflammatory mediators (IL-1 β , TNF- α) from periodontal lesions intermittently reach the bloodstream inducing chronic low-level bacteremia

and systemic inflammatory reactants (C-reactive protein, systemic antibodies), all of which may represent a pathogenetic link between periodontal disease and heart disease.

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