Periodontal Infection: a risk factor for cardiovascular diseases

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Abstract-Periodontal infection has emerged as useful tools to study the hypothesis that infection is a cardiovascular disease (CVD) risk factor. Periodontal infections are a leading culprit, with studies reporting associations between periodontal disease and CVD. The recent focus on the potential link between periodontal and cardiovascular disease (PD and CVD) is part of the larger renewed interest on the role of infection and inflammation in the etiology of atherosclerosis and its clinical manifestations. Periodontal disease is considered an inflammatory disorder that damages tissue through the complex interactions between periodontopathic bacteria and host defense systems. It is likely that the role of reactive oxygen species (ROS) is common to both bacterial- and host-mediated pathways of tissue damage. In recent years, there has been a tremendous expansion in the medical and dental research concerned with free radicals (FR), ROS and antioxidant defense mechanisms. This review is intended to provide a critical up-to-date summary of the field with particular emphasis on the evidence for the risk of cardiovascular status in periodontal diseases.

Key words- Antioxidants, cardiovascular disease, periodontal disease, periodontal infection, reactive oxygen species/free radicals.

INTRODUCTION

The oral cavity is a mirror of the body and reflects the general health and well-being of an individual [1]. Periodontal disease is the result of host inflammatory reaction to bacterial infection. Most studies have reported positive associations between periodontal disease and cardiovascular disease after accounting for the effects of multiple risk factors such as age, sex, diabetes, cholesterol levels, blood pressure, obesity, smoking status, dietary patterns, race/ethnicity, education and socioeconomic status. If periodontal disease and CVD simply share common risk factors, a correlation between the two would be established even if a causal link did not exist.

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Periodontal diseases might affect heart disease through the mechanism of oral bacteria, bacterial toxins and induced inflammation mediator's entering the blood stream and contributing to chronic, systemic vascular challenge. Oral microbes and their byproducts can gain systemic access via the circulatory system, which showed that gentle mastication can induce endotoxemia, and this risk was elevated according to an increased severity of periodontal disease [2]. *Porphyromonas gingivalis,* a common bacterium found in periodontal infections ***Porphyromonas gingivalis*** belongs to the phylum *Bacteroidetes* and is a non motile, Gram-negative, nonmotile, pleomorphic, rod-shaped, obligate anaerobic pathogenic bacterium. It forms black colonies on blood agar. It is found in the oral cavity, where it is implicated in certain forms of periodontal disease [3].

Periodontitis is an inflammation and infection of bones and ligaments that act as holders of teeth. It appears when inflammation and infection of gums (gingivitis) is left without treatment or when this treatment is delayed so much time. This inflammation and infection disseminate from gums to ligaments and bones that holds teeth. Due to this loss of support, teeth finally fall out. This problem is infrequent in children, but it's the first cause of dental loss in adults and it affects between 10 % – 15 % of the world population [4]. There is increasing evidence linking periodontitis to systemic diseases, such as diabetes, rheumatoid arthritis, and, especially, CVD, hence the search for factors that may explain such relationships. A potential factor which could increase insulin resistance is the production of oxidative stress enhancing ROS in affected periodontal tissues [5]. Periodontitis appears around 6 months before the

establishment of gingivitis, but it depends on every single patient [6]. There are several factors that modify the possibility of suffering periodontitis, besides a lack of dental care, such as smoking, drugs (calcium blockers as nifedipine, phenytoin or cyclosporines) hormonal status, stress, age, socioeconomic status and race, systemic diseases, genetics or individual immune response. The focus of infection in the oral cavity can lead to systemic inflammation resulting in adverse medical outcomes. There is a need to educate both dentists as well as general healthcare practitioners about this important aspect of oral health. It is also necessary to coordinate with medical institutions where the results of emerging research are translated into practice guidelines. As the prevalence of CVD, cerebrovascular accidents, respiratory infections and diabetes is increasing globally, identifying risk factors other than the traditionally recognized ones may help in effectively preventing and managing these diseases. We have summarized the available evidence on the possible mechanisms by which periodontal infections may be responsible for the initiation and progression of cardiovascular disease. Inflammation at the periodontium begins when both bacteria and leukocytes start their fight releasing lots of pro inflammatory factors. The immune response is generated by cell wall components from the bacteria, including lipopolysaccharide (LPS) [7]. In mild and chronic periodontitis, ROS generation is enhanced and plasma antioxidant levels are depleted. ROS are chemically reactive molecules (or cell signaling molecules) derived from oxygen that can damage lipids, proteins and DNA. When balance between ROS and antioxidant molecules was broken then ROS begin their harmful activity and an oxidative stress situation is established [8]. This ROS generation at the site of periodontitis can also have systemic effects on other organs as ROS can diffuse into the blood stream and reach other places on the organism. This is specially worth investigating on it, because it is known that serious diseases as cardiovascular disease and diabetes are related with ROS generation at the organism. The most important ROS involved in periodontitis are:

- Hydroxyl radical (*OH), very active in damaging DNA proteins and lipids.
- Hydrogen peroxide (H2O2), capable of crossing the nuclear membrane and damaging the DNA.
- Superoxide anion (O2*-), involved in bone reabsorption

The role of reactive oxygen species (ROS) is common to both bacterial- and host-mediated pathways of tissue damage. ROS can harm cardiac tissue because after reperfusion injury, there is a great increase in ROS production, attributed to an overload of all the ROS sources mentioned above and to a high infiltration of neutrophils that release pro inflammatory cytokines. This will damage myocytes, impair contractile function and contribute to capillary leakage [9].

METHODS

We searched the Pub Med database from 1990 through 2012 (both years included) for English language articles using the following search terms: 'Periodontal disease and cardiovascular diseases', 'periodontal disease and atherosclerosis, '*P. gingivalis* and periodontal infection. We selected and reviewed cross-sectional, longitudinal, cohort and *in vitro* studies that provided information related to periodontal infection and cardiovascular diseases.

WHAT ARE PERIODONTAL DISEASES?

Periodontal diseases are a group of diseases that cause inflammation and destruction of the investing and supporting structures of the teeth (such as the gingiva, periodontal ligament, alveolar bone and cementum of the tooth), as well as the periodontal tissues. This leads to apical migration of the junctional epithelium, resulting in the formation of periodontal pockets [10, 11]. Periodontal diseases occur due to a complex interplay of bacterial infection and host response, often modified by behavioural factors and various systemic conditions such as metabolic disorders (diabetes mellitus, female hormonal imbalance), drug-induced disorders, haematological disorders such as leukemia, and immune system disorders. These systemic disorders have been shown to affect the periodontium and/or influence the treatment of periodontal disease [10].

Periodontal disease is caused by bacteria found in dental plaque, and about 10 species have been identified as putative pathogens in periodontal disease. Pathogens frequently associated with periodontal disease include *Aggregatibacter actinomycetemcomitans* (previously *Actinobacillus actinomycetemcomitans*), *Capnocytophaga*, *Campylobacter rectus*, *Fusobacterium nucleatum*, *Porphyromonas gingivalis*, *Prevotella intermedia*, *Tannerella forsythia* and *Treponema denticola* [11].

PERIODONTAL INFECTIONS AND CARDIOVASCULAR DISEASES

Both periodontal diseases and CVD are chronic, whose causes are multifactorial. Risk factors common to both include older age, male gender and smoking, and psychosocial factors such as stress. A number of epidemiological studies in the 1990s suggested a relationship between CVD and periodontal diseases [12, 13,14].However, these observational studies did not provide a rationale for periodontal infections leading to systemic complications. There is now epidemiological evidence to support the concept that poor oral health, especially extensive and severe periodontal disease, may put patients at risk for a variety of systemic conditions such as CVD [15]. This association highlights the importance of good oral health. Poor dental health has been associated with an increased risk of fatal coronary heart disease (CHD) [16]. Thus, maintenance of good oral hygiene is important. *Porphyromonas gingivalis* (that is considered as one of the important putative periodontal pathogens) can invade aortic and heart endothelial cells via its fimbriae. It is one of the main periodontal pathogens involved in the initiation and progression of periodontal diseases and can be detected in patients with various forms of periodontitis [17-21].

The chronicity of periodontitis and the presence of periodontal anaerobic microorganism such as Streptococcus sanguis and Porphyromonas gingivalis might be responsible for CVD. These microorganisms have been associated with dental calculi formation and also have been reported to have the capability to increase the aggregation of platelets, a factor which contributes to the development of atherosclerosis [22].

CONCLUSION

The common link between periodontitis and cardiovascular disease is also the action of ROS either acting as a second messenger or directly damaging target molecules as proteins, lipids or DNA. Periodontal treatments decreased ROS generation and the risk of developing some of these illnesses. As these illnesses are risk factors for developing cardiovascular diseases, avoiding periodontitis also lowers the probability of developing these cardiovascular risk factors.

Maintenance of good oral health should be given priority. People should be educated on the importance of good oral health and the risks associated with poor oral health. Dentists and medical practitioners should work together to provide comprehensive healthcare, thereby reducing the morbidity and mortality associated with periodontal infections. However, the emergence of periodontal infections as a potential risk factor for CVD is leading to a convergence in oral and medical care that can only benefit the patients and public health.

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