INTERRELATION BETWEEN CARDIOVASCULAR RISK FACTORS, OSTEOPOROSIS AND PERIODONTAL DISEASE

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ABSTRACT

Patients with periodontal disease share many of the same risk factors to patients with cardiovascular disease including age, sex, obesity and lower socio-economic level, stress and smoking. In addition, a large proportion of patients with periodontal disease also present the cardiovascular disease. A causal hypothesis of the association of periodontal and cardiovascular disease is the participation of the periodontitis in the pathogenesis of the atheroma formation. The proposed associated risk of periodontal disease for atherosclerosis potentially is linked to mechanisms of numerous systemic effects of lipopolysaccharide. Osteopenia together with osteoporosis is bone reduction resulting from imbalance between resorption and bone formation, with resorption tending to increase. Recent studies have documented the existence of some other potentially important periodontal risk factors such as stress, sex, age, genetic factors and also osteopenia (osteoporosis as a consequence of estrogen deficit). Osteoporotic patients and those with a cardiovascular disease should be advised to give more attention toward their oral health to prevent periodontal problems.

Keywords: periodontal disease, cardiovascular risk factors, osteoporosis

INTRODUCTION

In recent times, oral diseases have gained an importance and are considered as a major health problem worldwide. Oral cancer, dental caries, and periodontal diseases are among the most important global oral health problems. The economic costs associated with poor oral health are well documented and the association between oral health, and general health and wellbeing have been noted in numerous studies, with poor oral health impacting on quality of life across the lifespan. The importance of oral health beyond dental care is reflected in the WHO Global Oral Health Program, which is predicated on disease prevention and health promotion. Priority action areas of the WHO are directed at improving oral health literacy to drive increased knowledge and health-promoting behaviours. Income, education, type of dental service most often used, lifestyle, risk behaviors, and demographic

conditions are distal, intermediate, and proximal social determinants of health associated with functional dentition in adults [1]. Periodontal disease is inflammation and infection of the ligament and alveolar bone supporting the teeth that can have significant effects on general health and vice versa, a number of systemic diseases and conditions can be potential risk factors for periodontitis as well. There is an increasing interest over recent years in the relationship between periodontal and systemic health that has labeled periodontal–systemic interlink as a two-way road.

PERIODONTAL DISEASE

Internationally, interest in oral health literacy is driven by oral health disparities, particularly for disadvantaged groups, with conditions such as dental caries and periodontal disease contributing substantially to the global burden of disease.

The term periodontal disease comprises a variety of clinical forms, including chronic periodontitis that affects mostly adults over 35 years of age, and aggressive periodontitis observed in teenagers and young adults. Aggressive periodontitis affects a minority of periodontitis patients, but the disease is still highly significant: if left untreated it can lead to early edentulism and poor oral health-related quality of life [2]. A current strategy for adult health care in developed countries is to strengthen the surveillance systems that monitor health status of adults at the national, state, and local levels, and to evaluate public health strategies for prevention. In Europe, national representative data on the prevalence and extent of periodontal disease are rare. Epidemiological studies have found low prevalence of periodontal disease in Sweden (1973–2003), and Switzerland (1992–1999). In contrast, in Germany the prevalence of periodontal disease was 70.9% in 35–44-year-old adults and 87.4% in 75–84-yearold seniors (2005). Generally, low prevalence rates (0.1% to 0.5%) of periodontal disease have been reported among Caucasians in developed countries. On the other hand, an astonishing periodontal disease ‘‘ceiling’’ prevalence of around 3% was estimated for US and of 8% for the Australian population. However, global prevalence of periodontal disease remains elusive. Nevertheless, definitions of periodontitis in epidemiological studies lack uniformity and thus the comparisons between studies must be considered with circumspection [3].

Periodontal disease is considered as one of the etiologic factors contributing to tooth loss, it is hypothesized that the environment in the subgingiva plays a role on what type of microbial flora will flourish in that area, this elicits and inflammatory response from the host, which drives the condition from health to disease. Several factors such as bleeding, deep probing, clinical attachment level increase and bone loss, eventually lead to tooth loss [4].

Periodontitis is caused by microorganisms that grow on subgingival tooth surfaces, along with a host immune response. The bacterial role on onset and progression of periodontal diseases has been extensively documented. In 1999 the American Academy of Periodontology proposed the last revised classification system for periodontal diseases identifying different forms of periodontitis. This system has lead to more focused investigations to comprehend the specificities of each form such as the microbiological aspects [5, 6]. Many clinical studies have been conducted worldwide providing evidence of associations between bacterial species and chronic periodontitis. Comparing data from different countries/populations it has become apparent that there are substantial differences in the composition of the subgingival microbiota. Environmental, economic and genetic variables have been

advocated to explain this observation [7].

Chronic periodontitis, characterized by inflammation and destruction of periodontal supporting tissues, is one of the most common oral diseases worldwide. Over 47% of American people had chronic periodontitis, and the prevalence is even higher in developing countries. Chronic periodontitis is initially caused by various hyperresponsive and destructive products of immune response stimulated by microbial plaque around the gingival margin [8].

In the pathogenesis of periodontitis, polymorphonuclear leukocytes (PMN) act as the primary mediators of the host response against proliferating periodontal pathogenic microorganisms. Activated PMN produce a large amount of reactive oxygen species and result in destruction of periodontal tissues. There is some suggestive evidence that periodontal inflammation might be associated with systemic oxidative stress. Recently, abundant evidence has shown that periodontal diseases were highly associated with several inflammation-related systemic diseases, such as chronic respiratory diseases, cardiovascular disease, and diabetes mellitus [6, 9]. Oxidative stress plays an important role in the pathogenesis of these diseases. It has been hypothesized that oxidative stress arising from periodontal lesions may be an important cause of systemic inflammation. Some but not all epidemiological studies have shown that biomarkers levels of oxidative stress in the peripheral blood of periodontitis patients were different from periodontal healthy subjects [10].

CARDIOVASCULAR RISK FACTORS AND PERIODONTAL DISEASE

Cardiovascular diseases (CVD), namely coronary heart disease, stroke, congestive heart failure, and peripheral artery disease, became the leading cause of chronic disease morbidity and mortality in industrialized countries in the twentieth century. It is widely accepted that a major component of pathology in cardiovascular disease, particularly in atherosclerosis involves multiple components of the innate and adaptive immune systems, leading to an inflammatory response within the atheromatous lesion [11].

There are well-established risk factors for cardiovascular diseases, one of them being elevated levels of serum lipids combined with infections such as odontogenic infections, which consist of dental caries and periodontal disease. Periodontal and cardiovascular diseases share many risk factors, such as age, educational level, gender, income level, smoking and drinking habits, hypertension, stress, depression, and diabetes. Several studies have shown that patients with periodontitis and acute ischemic syndromes share various characteristics. Considerable evidence indicates that periodontopathic bacteria may directly or indirectly contribute to cardiovascular disease, such as blood platelet aggregation, enhanced low-density cholesterol and lipoprotein deposition in the arterial walls, invasion of cardiac and carotid endothelium, and the high level of circulating- or tissue-derived inflammatory mediators [12, 13].

In recent decades, oral biofilm, especially in periodontitis patients, has been associated with CVD. Individuals suffering from periodontitis on average present with 14–15% greater risk of developing CVD based on prospective trials. Links between periodontitis and atherosclerosis would be predicted based on inflammatory mechanisms initiated by bacteria associated with periodontal lesions, locally or systemically, that then influence the initiation or propagation of the atherosclerotic lesion [14]. Studies on atheroma lesions have focused mainly on the detection of well-recognized putative periodontal bacteria. Moreover, it

has not yet been confirmed if atheroma lesions present the same clonal type of bacteria as in the periodontal pocket, which would strongly suggest mouth-to-heart translocation and a relationship between the two diseases [15].

The way in which the bacteria could impact on CVD has been partially explained. Atheroma lesions may be initiated by inflammatory stimuli, including systemic and locally produced inflammatory cytokines and chemotactic agents that cause changes in the endothelium such as up-regulation of adhesion molecules. These changes promote interactions with leukocytes, such as monocytes, that promote leukocyte migration into the intimal layer of the artery. Activation of the endothelium additionally leads to the release of chemotactic cytokines, such as monocyte chemotactic protein-1 (MCP-1), that further attract monocytes or other cells that can transport bacteria into the lesion. Once inside endothelial layers, bacteria can initiate or exacerbate the host-cell response. For example, P. gingivalis induces monocyte migration and can significantly enhance the production of pro-inflammatory cytokines. P. gingivalis also induces pro-coagulant effects in human aortic endothelial cells, initiates apoptosis and increases mononuclear cell adhesion to endothelial cells. It is well-known that the disease is characterized by the accumulation of cholesterol and recruitment of macrophages into the arterial wall. It can thus be considered both a metabolic and an inflammatory disease [14, 16, 17].

Although dental plaque-associated microorganisms are the primary etiologic agents of periodontal diseases, several other factors such as local, genetic, systemic, and environmental factors play an important role in determining the susceptibility of individuals to periodontal diseases.

Tobacco smoking is one of the most important environmental risk factors for periodontal diseases. Large numbers of studies have been conducted to understand the role of smoking in the etiology of periodontal diseases and the available data show that smoking is associated with increased prevalence and severity of periodontal disease, which may be due to the adverse effects of tobacco smoke on the physiology, immunology, and microbiology of the oral environment. Unlike smoking, the role of oral smokeless tobacco (SLT) in the etiology of periodontal disease has received considerably less attention. Although traditionally, oral SLT consumption has been associated with oral malignant and potentially malignant lesions, emerging data suggest that these habits may be associated with poor periodontal health also [18].

Studies conducted in Sweden also have shown that the consumption of moist snuff, an oral SLT product, is associated with increased prevalence of gingival recession. Nicotine, the principal alkaloid in tobacco, exerts a wide range of effects on the immune system and wound healing, which may play an important role in periodontal tissue destruction. Nicotine exposure has been shown to result in vasoconstriction and impaired angiogenesis. Its effects on neutrophil function include increased shedding of adhesion molecules and alteration of f-actin kinetics, resulting in reduced migration of neutrophils into the oral tissues, and inhibition of phagocytosis and oxidative killing. Nicotine exposure also results in reduced proliferation and function of T-lymphocytes, decreased phagocytosis and production of pro-inflammatory cytokines and oxygen radicals by monocytes, increased levels of tissue-destructive cytokine such as TNF-α, reduction in levels of antibodies to periodontal pathogens, and impaired attachment of human periodontal ligament fibroblasts [19, 20].

A biologically plausible role for obesity in

the development of periodontal disease has been reported. It has been suggested that the relationship between obesity and periodontal disease may be bi directional. The adipose tissue in obesity is said to actively secrete a variety of cytokines and hormones that are involved in inflammatory processes, pointing toward similar pathways involved in the pathophysiology of obesity, periodontitis, and related inflammatory diseases [21].

Genetic factors, environment, and other acquired habits differ in stage and form from one disease to another. Proinflammatory cytokines, such as IL-1B, TNF-α, and interferon Y, increase and induce the production of PGE2 and MMPS, molecules that promote the destruction of the extracellular matrix of gingival tissue and periodontal ligament as well as the reabsorption of alveolar bone. Products originating from Gram-negative bacteria cell wall (LPS), the leading cause of periodontitis, trigger a host response, with the production and release of proinflammatory cytokines (IL-1B, IL-6, and TNF-α), which in turn induce a host response themselves, elevating the levels of C-reactive protein and fibrinogen [10].

OSTEOPOROSIS AND PERIODONTAL DISEASE

Osteoporosis is a skeletal disease characterized by reduction in bone mass and micro architectural changes in the bone, which leads to an increased bone fragility and an increased risk of fracture. Osteoporosis results from an imbalance between the rate of bone formation and resorption that leads to loss of bone mineral mass. Loss of the mineral component of the bone leads to a greater tendency of the bone to be broken. The consequences of fracture in elderly people include an increased risk of death, long-term nursing home care or permanent limitations in mobility and performance of daily living activities [22]. Many of the risk factors for osteoporosis are environmental and therefore, are preventable. Established risk factors include older age; female gender; postmenopause; Caucasian or Asian race; a low body mass index; cigarette use; alcoholism; inadequate calcium and vitamin D intakes; physical inactivity; taking medications such as glucocorticoids and anticonvulsants; and anorexia nervosa. Although osteoporosis and osteopenia can affect people of all ages, they occur most often in middle-aged and elderly people [23].

According to the World Health Organization, osteoporosis is considered to be present when bone mineral density (BMD) is 2.5 standard deviations below the young normal. Osteoporosis before fractures is termed a "silent disease". Definition of osteoporosis has now evolved beyond low BMD to recognize impaired bone qualities related to bone size, bone morphology, material properties of bone, and matrix and bone remodeling are responsible for bone density insufficiency fractures. Most common insufficiency fractures are fractures of spine, hip and wrist. Discussions about the association between these two bone-damaging diseases started in 1960. According to some studies, osteoporosis may be a very important factor of tooth loss. Kribbs compared patients with osteoporosis and without it and found out that the osteoporotic group comprised more subjects with no teeth or with a greater number of lost teeth. Positive association was found in between osteoporosis and periodontal disease in a review despite of the incipient evidence linking the two diseases [24, 25].

Besides the presence of common risk factors, a possible interplay between osteoporosis and periodontal disease is also suggested at a pathogenetic level. In fact, a bi-directional interference between the two diseases has been proposed: In particular, the

reduced BMD, characterizing osteoporosis and the related alteration of trabecular pattern may lead to a more rapid jawbones resorption caused by periodontal disease, resulting in the invasion of periodontal bacteria [23]. Invading bacteria, in turn, may alter the normal homeostasis of bone tissue, increasing osteoclastic activity and reducing local and systemic bone density by both direct effects (release of toxins) and/or indirect mechanisms (release of inflammatory mediators). A significant connection between periodontitis and osteoporosis can be confirmed by the action of pro-inflammatory cytokines and prostaglandins. Since these mediators develop in both periodontitis and osteoporosis, there is a possibility of double connection between these two diseases [25].

Individuals with osteoporosis also experience an increased risk of losing teeth. The progression of osteoporosis to the point of vertebral or femoral fracture can be devastating to quality of life. Menopause, shortage of exercise, and malnutrition are key risk factors in developing osteoporosis. Periodontitis causes tooth loss similar to osteopenia and osteoporosis that in severe cases is related to alveolar bone and tooth loss in women after menopause. A number of cross sectional studies have looked at the relationship between bone mineral density of postmenopausal women and tooth loss. However, only a few studies reported statistically significant correlation between reduced BMD at varying sites and tooth loss [26].

Morphological studies have shown that the cortical bone porosity of the upper jaw increases with age; in addition, a considerable variation of the thickness and cortical porosity exists in different areas of the mandible (area of incisors, premolars and molars) in relation to sex, with significantly higher values in males than females. The body of the mandible and the posterior alveolar processes, consisting predominantly of cortical bone, are very similar to the diaphysis of long bones, while in the anterior alveolar processes of the mandible and in the alveolar processes of the jaw, bone architecture is mostly trabecular. According to some authors the rate of bone turnover at the level of alveolar processes would be greater than in long bones, so the loss of bone mass could manifest earlier at the alveolus than at other skeletal segments, thus, representing an early indicator of osteoporosis [27, 28].

CONCLUSIONS

The association between periodontal disease and atherosclerotic cardiovascular disease is supported by a large body of evidence. It seems that periodontal disease deserves serious consideration as a risk factor for CVDs, but further confirmatory investigations are needed to study this inflammatory burden. The prevention of osteoporosis is the most rational and modern approach to defeat the disease, and early diagnosis is one of the foundations of modern medicine. Further studies relating osteoporosis and periodontitis to heredity, poor oral hygiene, tobacco usage in any form should be undertaken to establish a better relationship between the two diseases.

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