Periodontitis And Cardiovascular Disease - A Much Discussed Relationship

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Abstracts: Periodontitis and atherosclerosis have many potential pathogenic mechanisms in common. Both diseases have complex etiologies, genetic and gender predispositions, and potentially share many risk factors—the most significant of which may be smoking status. The objective of this review is to consider the mechanisms whereby diseases such as Periodontitis, which is chronic and inflammatory in nature and initiated by microbial plaque, can predispose to cardiac conditions. [Nanavati B NJIRM 2014; 5(1) : 134-138]
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Introduction: A In the last few years, a rising number of epidemiological investigations have studied the possible association between chronic oral infections and cardiovascular diseases(CVD). These studies were based on the hypothesis that oral infections, including periodontitis may confer an independent risk for cardiovascular diseases.[1]

The relationship could be mediated by inflammatory responses induced by periodontal pathogens as well as direct interaction of these organisms with cardiac tissue. Periodontitis establishes a burden of bacterial pathogens, bacterial antigens, endotoxins and inflammatory cytokines that contribute to and modify the process of atherogenesis and thromboembolic events. In response to infection and inflammation certain persons may exhibit greater expression of a profile of local gingival crevicular fluid and systemic serum mediators of the inflammatory response and may be at increased risk for atherosclerosis due to the effects of these circulating inflammatory products on the formation of atherosclerotic plaques. These plaques may result in decreased vascular patency and/or decreased compliance of the vessel wall. Ultimately plaques, precipitating a myocardial infarction or stroke. Thus Cardiovascular research has focused both on mechanisms associated with the formation of atheromatous plaques and the triggering of atherothrombotic events (heart attacks and strokes).[2]

Periodontitis: Inflammation of the supportive tissue of the teeth, usually a progressively destructive change leading to loss of bone and periodontal ligament. An extension of inflammation from gingiva into the adjacent bone and ligament. Periodontal disease is one of the most frequent chronic infections in humans.[3] It is a result of the interaction between inflammatory cells and gram negative bacteria. The response is generated by cell wall components, including lipo polysaccharide (LPS).[4] In addition, their products can invade the periodontal tissue and gain access to the systemic circulation.[5] These activates the immune system, potentially deregulating lipid metabolism and increasing the expression of cytokines inflammation. [6]

Periodontal diseases are bacterial infections in which certain bacteria play an important role in the development of inflammatory processes. Periodontal infections may cause vascular events via lipo polysaccharides and inflammatory cytokines, contributing to the pathogenesis of cardiovascular disease[7]. Periodontal pathogens themselves have been shown to increase platelet aggregation and thromboembolic events.[8]

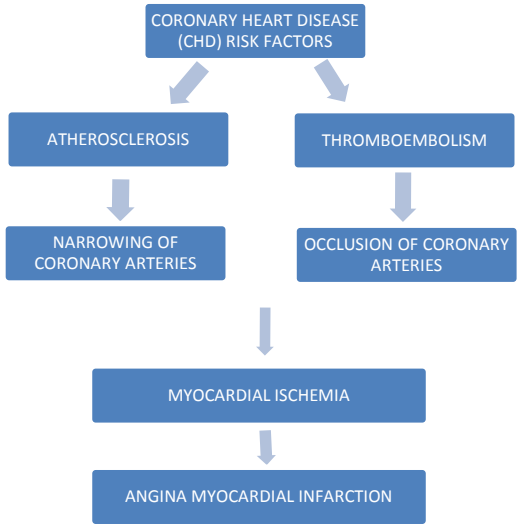
Cardiovascular Disease: Cardiovascular diseases (CVD), including acute myocardial infarction and angina pectoris are major health problems in developing countries, and are considered amongst most common medical problems in the general population.[9] Cardiovascular diseases remains the leading cause of death in industrialized countries. Although many of the risk factors associated with these diseases are well known, these do not account for all of the contributing factors.[10] Recently, it has been demonstrated that several candidate periodontal pathogens, including

porphyromonas gingivalis can be detected in atheromatous plaque .[11]In addition, preliminary evidence has suggested that infection of ApoE deficient mice with P.gingivalis increase the size of cardiac leisons.[12] These results to earlier epidemiological studies, suggest a possible contribution of periodontal pathogens to cardiovascular diseases.

The effect of periodontal infection: Periodontal infection may affect the onset or progression of atherosclerosis and coronary heart disease through certain mechanisms. Periodontitis and atherosclerosis both have complex etiologic factors, combining genetic and environmental influences. The disease share many risk factor and have distinct similarities in basic pathogenic mechanisms.

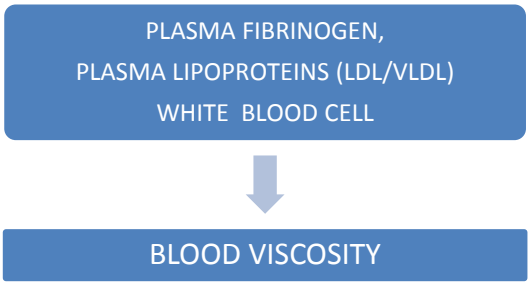
Ischemic heart disease : Ischemic heart disease is associated with the process of atherogenesis and thrombogenesis. Increased viscosity of blood may promote major ischemic heart disease and stroke by increasing the risk of thrombus formation.[13] Fibrinogen is probably the most important factor in promoting this hypercoaguable state. Fibrinogen is the precursor to fibrin, and increased fibrinogen levels increase blood viscosity.

Figure 1 : Acute and chronic pathways of to ischemic heart disease.



Coronary Heart Disease related events such as angina or myocardial infarction may be precipitated by either pathway or both pathways.

Figure 2:-Factor affecting blood viscosity in health.



Increased plasma fibrinogen is a risk factor for cardiovascular event and peripheral vascular disease[14].Elevated WBC count is also a predictor of heart disease and stroke, and circulating leukocyte may promote occlusion of blood vessels. Coagulation factor VIII/von Willebrand factor(vWF) has likewise been associated with the risk of ischemic heart disease.[15]

Thrombogenesis: Platelet aggregation plays a major role in thrombogenesis, and most cases of acute Myocardial Infarction are precipitated by thromboembolism. Oral organisms may be involved in coronary thrombogenesis. Platelets selectively bind some strains of Streptococus sanguis, a common component of supragingival plaque, and porphyromonas gingivalis, a pathogen closely associated with periodontitis.[16] Aggregation of platelets is induced by the platelet aggregation associated protein(PAAP) expressed on some strains of these bacteria.[17] In animal models, intravenous infusion of PAAP- positive bacterial strains resulted in alterations of heart rate, blood pressure, cardiac contractility, and electrocardiogram(ECG) readings consistent with Myocardial Infarction. Platelet accumulation also occurred in the lungs, leading to tachypnea. No such changes were seen with infusion of PAAP negative strains. PAAP positive bacteria caused aggregation of circulating platelets, resulting in formation of thromboemboli and the resultant cardiac and pulmonary changes. Thus periodontitis associated bacteremia with certain strains of S.sanguis and P.gingivalis may promote acute thrombolic events through interaction with circulating platelets.

Atherosclerosis: Atherosclerosis is a focal thickening of the arterial intima, the innermost layer lining the vessel lumen, and the media, the

thick layer under the intima consisting of smooth muscle, collagen and elastic fibers[18](figure 3). Early in the formation of the atherosclerosis plaques, circulating monocytes adhere to the vascular endothelium. This adherence is mediated through several adhesion molecules on the endothelial cell surface, including intercellular adhesion molecule-1(ICAM-1),endothelial leukocyte adhesion molecule-1(ELAM-1) and vascular cell adhesion molecule-1(VCAM-1).[19-20] These adhesion molecules are upregulated by a number of factors, including bacterial LPS, prostaglandins, and proinflammatory cytokines. After binding to the endothelial cell lining, monocytes penetrate the endothelium and migrate under the arterial intima. The monocytes ingest circulating low-density lipoprotein (LDL) in its oxidized state and become engorged, forming foam cells characteristic of atheromatous plaques.

Studies Establishing The Link Between Periodontal Disease And Cardiovascular Disease : In 1989, Kimmo Mattila and his co-workers [21]in Finland conducted two separate case control studies totaling 100 patients with acute myocardial infarction and they compared these patients with 102 control subjects selected from the community. A dental examination was performed on all the patients and a dental index was computed. In this original report, subjects with evidence of oral infection were 30% more likely to present with myocardial infarction as against subjects without oral infections.

In a larger six-year cohort study, Joshipura and co-workers [22]studied 44,119 men in the health professionals via mailed questionnaire with a self-reported history of periodontitis and missing teeth. This study found no significant relation between self-reported history of periodontitis and incidence of heart disease after adjusting for traditional risk factors (Risk Ratio - 1.04). The study did however demonstrate that men with tooth loss and periodontitis were 70% more likely to exhibit coronary heart disease.

Janket et al.[23] Performed a meta-analysis of nine cohort studies of periodontitis as a risk factor for future cardiovascular and cerebrovascular events Risk Ratio 1.19; (95% CI [1.08–1.32]) and found an overall 19% increased risk of such events in individuals with periodontitis. De Stefano and colleagues[24] found that periodontitis and poor oral hygiene may be an indicator or surrogate for lifestyle affecting personal hygiene and health care, and thus explains the relationship of periodontitis and heart disease. Thus cumulative index for coronary heart disease argues against lifestyle as a simple explanation for this association.

Drug Therapy: A range of different drug therapies are used in the treatment of the spectrum of conditions that come under the category of cardiovascular diseases. Only in a few areas does a patient's systemic medication affect either the periodontium or the delivery of periodontal care. Examples are as follows: drug-induced gingival overgrowth caused by calcium-channel blockers; the effect of b-adrenoceptor blocking and diuretic drugs on calculus formation.

Calcium-channel blocker-induced gingival overgrowth: This unwanted effect was first described in two case reports in 1984.[25] Virtually all the calcium-channel blockers have been cited as causing gingival overgrowth. The prevalence varies from 3% to as high as 43%.[26] More meaningful information on the prevalence of this unwanted effect comes from a community- based controlled study[27] involving 911 subjects. 6.3% of patients taking nifedipine had significant overgrowth, while the prevalence of gingival changes in patients medicated with either amlodipine or diltiazem was no greater than a non-medicated control group. Male patients were three times more likely to develop the gingival changes than females. An unusual finding with gingival overgrowth induced by calcium-channel blockers is the drug sequestration in gingival crevicular fluid (GCF). It has been shown that both nifedipine and amlodipine are significantly concentrated in gingival crevicular fluid, and such sequestration is related to the extent of gingival inflammation present in the tissues at the time of sampling.[28]

B-Adrenoceptor blockers, diuretics and calculus formation: Two studies have shown that systemic medication with either a b-blocker or a diuretic has an inhibitory effect on calculus formation or re-formation after a prophylaxis.[29] The mechanism by

which these drugs inhibit calculus formation is uncertain. It is speculated that the drug could be excreted into the saliva affecting the rate of crystallization directly by a physicochemical mechanism, or the drugs alter the composition of saliva and this affects calculus formation indirectly.[30]

Summary: Epidemiologic studies show conflicting relations between periodontitis and cardiovascular diseases. Some studies have reported that periodontitis is significantly associated with cardiovascular diseases as a risk factor,[31] while others have failed to show such correlation.[32] 1Interventional studies trying to explain this relationship generally use C-reactive protein as a major cardiac outcome with statistical methods unsuitable for its skewed distribution.[33] For this reason the interpretation and use of these results are questionable.[34]

Conclusion: A bulk of evidence has emerged in these last 10 years revealing the possible associations between periodontal infections and cardiovascular diseases. Although the reported epidemiological studies have shown a significant, albeit week associations, we still lack properly designed clinical trials demonstrating that these chronic infections are independent factors of cardiovascular risk.[35] From a public health perspective, if further studies consistently identify periodontitis as a risk factor for CHD and treatment studies show benefit, the implications are significant, since periodontitis is mostly avoidable and treatable when not prevented. In addition, good preventive dental care has multiple other benefits, particularly on quality of life. Furthermore, identifying individuals at higher risk for CHD than predicted by traditional risk factors could facilitate treatment of risk factors known to decrease CHD events in high-risk individuals and this might be significant given the high prevalence of periodontitis in the population and the common problem of CHD.

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