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Review Article

Co-relation between Periodontitis and Cardiovascular Disorders- A Review

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***ABSTRACT*:**
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 implication. Many epidemiological studies have investigated the relationship between periodontal disease (PD) and cardiovascular disease (CVD), but their results are heterogeneous. This review article is designed to update the potential association, that forms the basis of understanding for a role for PD to cardiovascular events.
Key words: Gingivitis, periodontitis, cardiovascular disorder.

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INTRODUCTION

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. Annual mortality from CVD is about 12 million cases per year and are responsible for 30% of all deaths in the United States. Cardiovascular diseases are estimated to have led to 1.59 million deaths in India in year 2000 and this figure is projected to increase to 2.03 million for the year 2010. The Framingham Heart Study revealed that for people who reach the age of 40, 49% of men and 32% for women show clinical manifestations of ischemic heart disease during their lifetime.[1]

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.[2] Periodontal Disease is an inflammatory process affecting the periodontium, the tissue that surrounds and supports the teeth. The process usually starts with an inflammatory process of the gum (gingivitis) but it may progress with an extensive involvement of the gum, as well as the periodontal ligament and the bone surrounding the teeth resulting in substantial bone loss. Periodontal disease is a common oral pathological condition in the adult age and represents the leading cause of tooth loss.[3]

International Classification of Diseases, 9th Revision defined diseases of the circulatory system as follows: (1) Ischemic heart diseases, (2) cerebrovascular diseases India (3) diseases of arteries, arterioles and capillaries (known as peripheral vascular disease), arterial septal vascular disease (ASVD) affect the heart and blood vessels; which is a major component of the cardiovascular system (CVS). It is a chronic process over many years but it can cause acute clinical events including acute coronary syndrome (ACS), myocardial infarction (MI), and strokes.[4]

Microbiology of Periodontal Disease

A newly cleaned surface of the tooth is rapidly covered with a glycoprotein deposit referred as a pellicle. The microbial composition of dental plaque differs above and below the gingival margin. Factors that influence the distinct pattern of microflora include specific local surface receptors for bacterial adherence. In the presence of gingivitis, Gram-negative anaerobic bacilli predominate in the subgingival flora.[5] Subgingival microflora in gingivitis

represents a transition between that associated with health and periodontitis. Initial (primary) supragingival colonizers have particularly affinity for constituents of pellicle. These colonizers include Streptococcus sanguis, Streptococcus oralis, Streptococcus mutans, Actinomyces naeslundii, and Actinomyces odontolyticus. The primary colonizer is followed by adherence of secondary colonizers such as Fusobacterium nucleatum, which in turn coaggregate with later colonizers. Within a short time complex communities of Gram-positive and Gram-negative bacilli and cocci become embedded in an extracellular matrix.[6]

Pathophysiology of atherosclerosis

Atherosclerosis (ATH) is an insidious process that typically takes decades to worsen to the point of causing signs and symptoms. The term is derived from the Greek words for hardening (sclerosis) and gruel or the accumulation of lipid (athere). The process is localized to the inner wall of arteries with a predisposition to form at locations of "disturbed" blood flow, such as points where arteries branch.[7]

Atherosclerosis lesions begin with deposition of lipoproteins in the intimal layer of the affected artery. The lipoprotein particles such as low-density lipoproteins (LDLs) then seem to permit the accumulation of monocytes and lymphocytes in the intimal layer. Early in the formation of atherosclerotic plaques, circulating monocytes adhere to 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).[8] Activation of monocytes (macrophage) in the blood vessels leads to release of hydrolytic enzymes, cytokines, chemokines and growth factors, which induce further damage leading to focal necrosis. The monocytes recruitment from the blood stream occurs which pass through the endothelium into the blood vessels and differentiate into macrophages, which slowly become lipid-laden "foam cells" characteristic of atheromatous plaques. Macrophages also accumulate lipids especially LDLs in both oxidized and modified form. Modified LDL can be a major cause of injury to both endothelium and underlying smooth muscles. These lipid-laden cells eventually die and leave a necrotic lipid-rich element behind, in the arterial wall. These lipid containing area calcify to varying degrees. At the same time, smooth muscle cells in the arterial wall are stimulated to migrate in the intimal layer, where they can proliferate.[9]

Pathogenic mechanism proposed as links between CVD and PD

There are several pathways which have been proposed as a potential link between CVS and PD.

Indirect Mechanisms: Systemic Inflammation

Atherosclerosis may begin during childhood with initial infiltration of the endothelium with fatty substances and progress over many decades. Plaques that contain a soft atheromatous core are unstable, and their rupture will expose highly thrombogenic contents to blood, with activation of thrombosis and ensuring ACS, MI or stroke.[10]

The link between ASVD and inflammatory mediators in blood is well-established, with consistent associations between levels of systemic inflammatory markers and increases in clinical events, such as MI and nonhemorrhagic stroke, and in surrogate markers such as increased cIMT. A well-studied inflammatory marker is CRP. Many studies of individuals with no prior history of ASVD have demonstrated that a single nonfasting measure of CRP is a predictor of future vascular events, including MI, stroke, peripheral arterial disease, and sudden cardiac death.[11] Additional inflammatory markers associated with CVD include lipoprotein-associated phospholipase A and tissue inhibitor of matrix metalloproteinase, myeloperoxidase, and fibrinogen.

Periodontal inflammation is associated with systemic markers such as CRP, tumor necrosis factor alpha, IL-1, IL-6, and IL-8.23 Systemic inflammation is similarly associated with cellular activation that involves cellular adhesion molecules, toll-like receptors, matrix metalloproteinase, and nuclear factor-k beta activation. The resulting interplay between endothelium, monocytes and platelets might be proatherogenic, contributing indirectly to atherogenesis or adverse cardiovascular outcome related to atheromatous plaque rupture in a subject with periodontitis.[12]

Indirect Mechanism: Mimicry

Molecular mimicry is thought to occur when sequence similarities between foreign and self-peptides produce cross-activation of autoreactive T or B cells that can lead to tissue pathology or autoimmunity.

Expression of host protective heat shock proteins (HSPs) such as HSP60 on endothelial cells may be induced by a variety of factors, including cytokines and shear stress and antibodies to HSP60, which have been associated with higher morbidity and mortality from atherosclerotic ASVD. Proponents of molecular mimicry as a link between PD and ASVD suggest that endothelial damage may be aggravated by an immune response to bacterial HSP, such as molecular chaperone GroEL present in *P.* gingivalis and other periodontopathic bacteria.[13]

Periodontal treatment and Inflammation markers

The studies with a randomized design and using a control group do not demonstrate consistent effects of periodontal intervention on inflammatory markers, in particular CRP. A recent report from a large multicenter pilot study to investigate the feasibility of a secondary prevention trail of PD treatment in cardiovascular disease patients confirmed the overall lack of an effect of PD treatment on CRP and suggested that the potential effect of PD treatment on CRP and other markers of inflammation could be mediated by

obesity. These findings raise doubts on the importance of CRP in mediating the observed relationship between PD and CVD.[14]

Periodontal treatment and vascular health

Few studies have been conducted to ascertain the effect of PD on a number of indicators of functional vascular health, these includes three small clinical studies (without placebo group) and a randomized controlled trial.[15] All studies show consistent findings of an improvement in endothelial function after PD treatment. The randomized controlled trial showed that the effects on vascular health was dose-dependent. In addition the study showed a possible transient worsening of the vascular health following PD treatment, possibly as a result of a sudden increase in the circulatory level of the inflammatory biomarkers secondary to the mechanical removal of the periodontal plaque. Finally a recent small non controlled intervention study showed evidence for a potential benefit of PD treatment on structural markers of vascular health (IMT).[16]

Studies establishing the link between periodontal disease and cardiovascular disease

Mattila and co-workers[17] noted association between dental infections and degree of ATH. This study examined the same subjects as the first report with diagnostic coronary angiography. Accordingly the left main coronary artery, the circumflex artery, and the left anterior descending artery were assessed diagnostically and graded for the degree of occlusion on a 5-point scale. Again the total dental index score was used as a general score for dental caries, periapical lesions, and periodontal infections.

De Stefano and co-workers[18] assessed the association between PD and CVD with National Health and Nutrition Examination survey (NHANES) I, which followed subjects for 14 years. This cohort study examined several potentially confounding variables including age, gender, race, education, marital status, systemic blood pressure, total cholesterol levels, body mass index, diabetes, physical activity, alcohol consumption, poverty and cigarette smoking. These investigators reported that among the 9760 subjects examined longitudinally, those with periodontitis has 25% increased risk of coronary heart disease related to those with minimal PD adjusted for the co-variables mentioned above. Interestingly, males younger than 50 years of age with periodontitis were 72% more likely to develop coronary heart disease compared to their periodontally healthy counterparts.

Janket et al[19]. performed a meta-analysis of nine cohort studies of PD as a risk factor for future cardiovascular and cerebrovascular events RR 1.19; (95% CI [1.08–1.32]) and found an overall 19% increased risk of such events in individuals with periodontitis. The increase in risk was greater (44%) in people under age 65.

Choe H and colleagues[20] demonstrated that C-reactive protein levels were highest in patients who were infected with periodontal pathogens where as CRP is an independent risk factor for CVD; however, detailed information is lacking about the mechanisms by which CRP participates in the pathogenesis of atheroma formation. C-reactive protein localizes the complement in human hearts during myocardial infarction, suggesting that CRP binds diseased muscle tissue, fixes complement and hence, triggers complement mediated inflammation that contributes to atheroma formation.

CONCLUSION

Author suggests that a potential link does exist between PD and CVD. Oral healthcare professionals can identify patients who are unaware of their risk of developing serious complications as a result of CVD and who are in need of medical intervention. Prospective interventional studies are required to determine the exact link between PD and CVD as well as to evaluate whether periodontal treatment may reduce the risk of developing CVD.

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