Relation between periodontal infection and cardiovascular diseases: Review of the evidence

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Introduction:

Oral cavity is the gate way of the body. Poor oral hygiene affects the system of the body health. Microbial dental plaque is the main etiological agent in chronic inflammatory periodontal disease. The progression of disease depends on the host defenses to these challenges. During normal activity such as tooth brushing, chewing and mastication, the micro organism of dental plaque and their metabolic product enter the blood stream causing bacterimia. As a result effect may be seen in remote organ causing different cardiovascular disease namely sub-acute bacterial endocarditis, atherosclerosis, atheroma, thromboembolism, myocardial infarction and even stroke (Ischemic). According to Mattila et al[1] patients with poor oral hygiene, had a two fold increase of Coronary heart disease (CHD).

More than 500 species of micro organisms have been isolated from oral flora. Micro organisms causing periodontal infection includes *Prophyromonus gingivalis*, *Prevotella intermedia*, *Tannerela forsythia*, *Actinobacillus actinomycetemcomitans actinomycetemcomitans*, *Campylobacter rectus, Ekenell a corrodens, Fusobacterium nucleatum, Peptosteptococcus micros* and *treponema denticola*.

Periodontal pocket acts as a reservoir of micro organisms and their metabolic products. The microbial & its parts and products of their metabolism e, g; toxin and enzymes causes wide spread destruction of supportive structure of tooth. According to Mattila et al 59patients with poor oral hygiene, had a two fold increase of Coronary heart disease (CHD). There may be a greater risk of CHD related events such as MI when periodontitis affects a greater number of teeth in the mouth, compare with the subject having periodontitis at fewer teeth.[2]

In this review article author will discuss the relation between periodontal infection and coronary heart disease CHD and ischemic disease.

Discussion:

Increase Blood Viscosity :

Systemic infections are known to induce thickening of blood a hypercoagulable state and to increase blood viscosity. Fibrinogen level and WBC counts are often increased in a patients with periodontal disease.[3,4] Individual with poor oral health have significant elevation in coagulation factor- viii/ vWF, antigen, increasing the risk of thrombus formation. Thus periodontal infection may also promote increased blood viscosity and thrombogenesis, leading to increased risk for central and peripheral vascular disease. Fibrinogen is probably the most important factor in promoting this hypercoagulable state. Fibrinogen is the precursor of fibrin and increased fibrinogen level increase blood viscosity.

Thrombogenesis:

Platelets binds specially some stains of *streptococcus sanguine*, a common component of supra-gingival plaque, and *Prophyromonas gingivalis*, which is closely associated with periodontitis.[5] Aggregation of platelets is induced by the platelet aggregation-associated protein (PAAP) expressed on some strains of these bacteria.[6] These causes thrombo emboli formation and the resultant cardiac and pulmonary events.

Atherosclerosis:

Atherosclerosis is focal thickening of the arterial intima , the inner most layer lying the vessel lumen, and the media. The thicker layer under the intima, consisting of smooth muscle, collagen and elastic fibers.[7] According to Beck

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JD et al, [8] early in the formation of atherosclerotic plaques, Circulatory monocytes adhere to the vascular endothelium. This adherence is mediated through several adhesion molecules on the endothelial cell surface, including intracellular adhesion molecule -1 (ICAM-1), endothelial leukocyte adhesion molecule-1(ELAM-1) and vascular cell adhesion molecule-1 (VCAM-1) . The adhesion molecules are up regulated by a number of factors, including bacterial LPS, prostaglandins and pro inflammatory cytokines. After binding to the endothelial lining, monocyte penetrates the endothelium and migrates under the arterial intima.

The moncytes also ingest circulating low density lipoprotein (LDL) in its oxidized state and become engorged, forming foam cells characteristic of atheroma plaques.

Once within the arterial media, monocytes may also transform to macrophages . According to Lowe GD,[9] a host of pro-inflammatory cytokines, such as interleukin-1 (IL-1), tumor necrosis factors alpha (TNF-á), and prostaglandin E2 (PGE2) are produced, which propagates the atheromatous lesion. Mitogenic factors such as fibroblast growth factor and platelet derived growth factor, stimulate smooth muscle and collagen proliferation within the media , thickening the arterial wall. Atheromatous plaque formation and thickening of the vessel wall narrow the lumen and dramatically decrease blood flow through the vessel. Arterial thrombosis often occur atheromatous plaque raptures exposes circulating blood to arterial collagen and tissue factor from monocytes/macrophages that activate platelets and the coagulation. Platelet and fibrin accumulation forms a thrombus that may occlude the vessel, resulting in the ischemic events such as angina or MI.[10] The thrombus may separate from the vessel wall and form an embolus, which may also occlude vessels, again leading to acute events such as MI or cerebral infarction (stroke).

Relation between Periodontal infection and Cardio vascular events:

Acute phase protein such as C-reactive protein (CRP) and fibrinogen are produced in the liver in response to inflammatory or infectious stimuli and act as inflammatory markers. CRP induces monocyte /macrophages to produce tissue factor , which stimulate the coagulation pathway and increase blood coaguability. Increase fibrinogen level may contribute to this process. CRP also stimulate the complement cascade, further exacerbating inflammation.

Recent efforts have focused on periodontitis as a trigger for systemic inflammation. Serum CRP and fibrinogen levels are often elevated in subjects with periodontitis compared with non periodontitis subjects.[11] These acute phase proteins may act as intermediary steps in the pathway

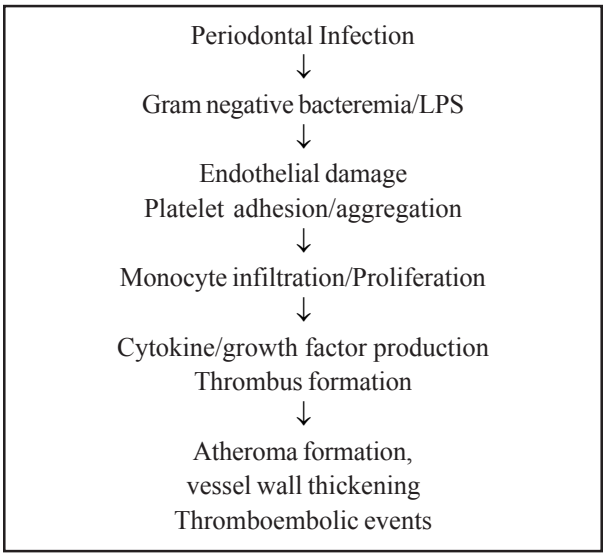

Fig.-1: *Influence of periodontal infection on atherosclerosis*

(Courtesy:Clinical periodontology *,Micheal G.Newman, DDS And Carranza's*

from periodontal infection to cardiovascular disease . Thus periodontal diseases may have both direct effects on the major blood vessel (e.g. atheroma formation) as well as indirect effects that stimulate changes in the cardiovascular system (e.g. elevation of systemic inflammatory responses).

In case-control studies , poor dental health was a significant risk factor for cerebrovascular ischemia . In one study , bleeding on probing , suppuration and sub-gingival calculus and the number of periodontal or periapical lesions were significantly greater in male stroke patients than in control.[12]Overall 25% of all strokes patients had significant dental infection 2.5% of controls. Thus study supports an association between poor oral health and stroke in men under age 50. In another study men and women age 50 and older who had a stroke had significantly more severe periodontitis and more peri-apical lesions than non stroke controls.[13] Poor dental health was an independent risk factor for stroke. In a longitudinal study over 18 years , subjects with greater than 20% mean radiographic bone loss at baseline were almost three times as likely to have a stroke than subjects with less than 20% bone loss.[14] Periodontitis was a greater risk factor for stroke than was smoking and was independent of other known risk factors. Both large epidemiological studies and systemic reviews of the evidence suggest an approximate

three fold increased risk of stroke in subjects with periodontitis.[15]

Peridontal Disease and Stroke: Ischemic crerbral infarction or stroke , is often preceded by systemic bacterial or viral infection. As shown by Grau AJ, et al [16] recent infection was a significant risk factor for cerebral ischemia and was independent of other known risk factors, such as hypertension , history of a previous stroke , diabetes, smoking, and CHD. Interestingly, the presence of systemic infection before the stroke resulted in significantly greater ischemia and a more sever post ischemic neuralgic defect than did stroke not preceded by infection.[17] According to Grau AJ et al, [17] Stroke patients with preceding infection had slightly higher level of plasma fibrinogen and significantly higher levels of CRP than those without infection.

In several studies of atheroma obtained from humans during end arterectomy , more than half of the lesions contained periodontal pathogens, and many atheromas contained multiple different periodontal species.[18,19]

Research has clearly shown a wide variation in host response to bacterial challenge . Some individuals with heavy plaque accumulation and high proportions of pathogenic organisms appear relatively resistant to bone and attachment loss. Other develop extensive periodontal destruction in the presence of small amounts of plaque and low proportions of putative pathogens. Patients with abnormally exuberant inflammatory responses often have a hyperinflammatory monocyte /Macrophage phenotype (MQ+). Monocyte /macrophages from these individual secrete significantly increased levels of proinflammatory mediators(e.g,IL-1, TNF-alpha, PGE2) in response to bacterial LPS compared with patients with a normal monocyte /macrophage phenotype. Patients with aggressive periodontitis , refractory periodontitis , and type 1 diabetes mellitus often possess the MQ+) phenotype.[20]

This monocyte / macrophage phenotype appears to be under both genetic and environmental control [20]). The monocyte /macrophage cell lines intimately involved in the pathogenesis of both periodontal disease and atherosclerosis. Diet induced elevation in serum LDL levels up regulated monocyte / macrophage responsiveness to bacterial LPS. Thus elevated LDL levels, a known risk factor for atherosclerosis and CHD, may increase secretion of destructive and inflammatory cytokines by monocytes/macrophages.[21]) This may result not only in progression of atheromatus lesions, but also in enhanced periodontal destruction in the presence of pathogenic microorganisms. This is one example of a potential shared mechanism in the pathogenesis of cardiovascular and periodontal disease.

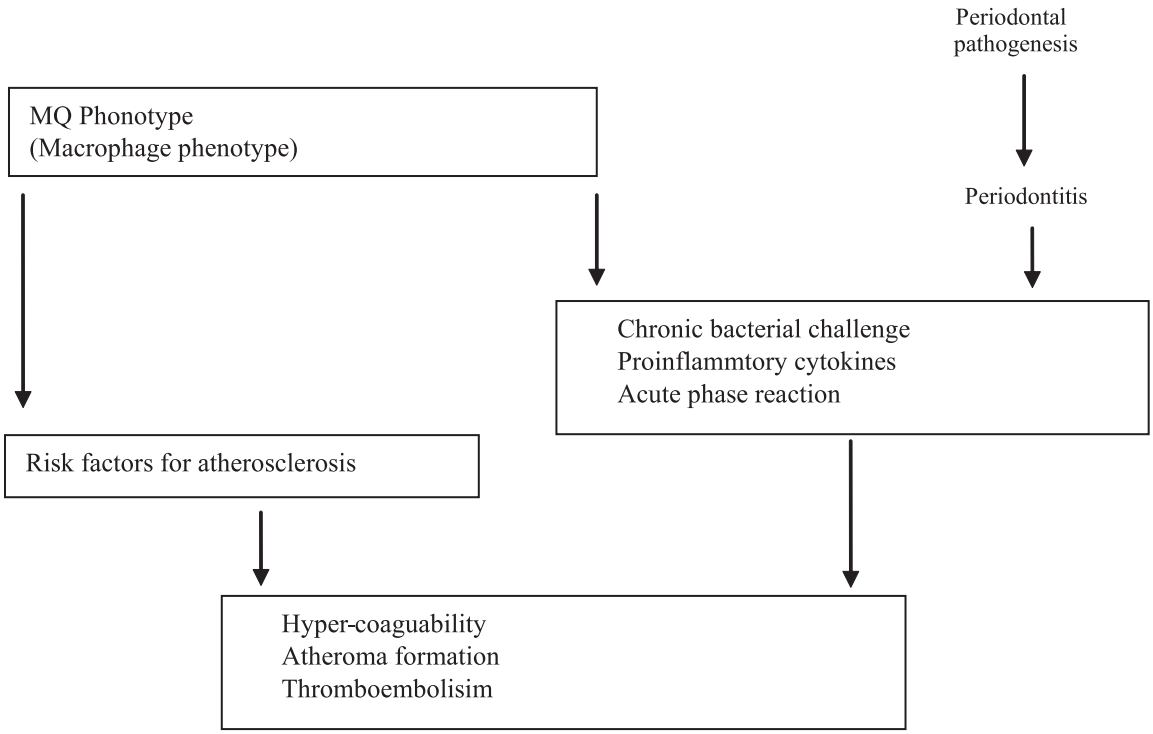

Fig.-2: *Cardiovascular and periodontal consequences of hyper responsiveness monocyte/macrophage phenotype(Courtesy: Clinical periodontology ,Micheal G.Newman, DDS And Carranza's)*

Vascular monocytes /macrophages in patients with an MQ+ phenotype meet this challenge with an abnormally elevated inflammatory response that may directly contribute to atherosclerosis and may precipitate thrombo-embolic events.

Conclusions:

Most cases of strokes are caused by thromboembolic events, where as others are related to cerebro-vascular atherosclerosis. As previously discussed , periodontal infection may contribute directly to the pathogenesis of atherosclerosis by proving a persistent bacterial challenge to arterial endothelium, contributing to the monocyte/ macrophage-driven inflammatory process that results in atheromatosis and narrowing of the vessel lumen. Furthermore, periodontal infection may stimulate a series of indirect systemic effects, such as elevated production of fibrinogen and CRP, Serve to increase the risk of stroke. Finally bacterimia with PAAP-positive bacterial strains from the supra-gingival and sub-gingival plaque can increase platelet aggregation, contributing to thrombus formation and subsequent thromboembolism, the leading cause of stroke.

Thus periodontitis initiates or exacerbates an atherosclerotic lesions. Further research is required in this field to more clarify the association or relation between periodontal infection and cardiovascular disease.

Good oral hygiene and oral health can improve our overall health, reducing the risk of serious cardiovascular diseases and most probably preserving our memory in golden years. The phrase “healthy mouth, healthy you” really is true- and this is backed by growing scientific evidence.

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