Review Article

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Association between Cardiovascular Disease and Periodontitis

Mouth is a mirror of human body and has an influence on general health of a person. Medical emergencies can and do happen in the practice of dentistry. According to World Health Organization, cardiovascular disease (CVD), including atherosclerosis and myocardial ischemia, are responsible for 20% of death worldwide. A milligram weight of dental plaque contains about 108-109 bacteria. If untreated, this large chronic wound may contribute over many years of recurrent bacteremias thus, inducing atherosclerosis. Requirements for medical emergencies is predicted on the ability to rapidly recognize a problem and to effectively institute prompt and proper management.

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Introduction

"A merry heart maketh a cheerful countenance" states the book of proverbs, "but by sorrow of the heart the spirit is broken". Several recent studies have shown a link between dental disease and CVD. Coronary heart disease (CHD) is not the only CVD that has been associated with dental disease. In a case-control study, Syrjanen, et al.[1] showed that dental infections, as measured by the level of dental morbidity detected in radiographs of the teeth and jaws, was statistically associated with cerebral vascular accidents (CVA). We must however recognize that there do appear to be statistical associations between periodontitis and CVD, but when these associations are looked at more closely, they do not appear to be as robust as we might have thought. Indeed, concepts have come to light suggesting that the apparent correlations between periodontitis and CVD may be related to the possibility that patients who are at risk for one disease may be genetically at risk for the other. This may be particularly so if such patients are exposed to the same epigenetic risk factors known to play a role in both disorder groups, e.g., smoking.

Epidemiological studies: Link between periodontitis and CVD

De Stefano, et al. conducted a prospective cohort study with 9,760 of these subjects who had a baseline dental examination from

1971 to 1974 and who had been followed through 1987. Periodontal disease had been measured by the periodontal index, a field-type index that does not rely on probing depths, so that it could not clearly distinguish between gingivitis and periodontitis. Subjects between 25 and 74 years of age with periodontitis had a significant (25%) increased risk of CHD relative to those with no periodontal disease, and those with no teeth had a significant (23%) increased risk for CHD compared to individuals with teeth. In subjects age 25-49 years, individuals with periodontitis had a 72% increased risk for CHD, and those with no teeth had a 71% increased risk compared to those with minimal periodontal disease or with teeth. Of greater concern, the younger individuals with periodontitis were found at the subsequent examination to be 2.12 times more likely and those with no teeth were found to be 2.6 times more likely to die from any cause.

De Stefano, et al. attributed these relationships to the possibility that poor oral hygiene is a manifestation of insufficient overall health practices by the individual because dental caries, periodontal disease, missing teeth and ischemic heart disease share several common etiological factors, such as low socioeconomic status, smoking, diabetes and diet. However, these dental risks were still evident after adjusting for 13 known risk factors for CVD, including many lifestyle risks.

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All these studies provide powerful evidence that dental disease, most likely periodontal disease, is a risk factor rather than a marker or indicator for CHD. Most of these studies involved convenience samples of individuals, which limits the generalizability of the findings to the entire population. But because the NHANES study was drawn from a representative US population, its conclusions can be generalized to the US population.

Risk factors: Periodontitis and CVD

The difficulty in drawing a cause and effect relationship between periodontitis and CVD stems from the fact that the two groups of diseases share many risk factors. Risk factors, such as smoking, genetics, stress and increasing age, could independently lead to periodontal disease and to CVD in a group of patients, possibly leading to the incorrect assumption that the two diseases are linked[2]. It was also suggested that statistical adjustment for confounding risk factors, such as smoking, may not be adequate and a population of non-smokers who actually never smoked should be evaluated[3]. In studies where adjustment for smoking dose (cigarettes per day) was included in the analysis, the relationship between periodontitis and CVD was shown to be insignificant. None of the studies to-date demonstrated a link between periodontitis and CVD in non-smokers[4].

Mechanisms contributing to CVD

There are several mechanisms by which dental conditions could contribute to CVD. The direct effects would be those mediated by the bacteria and/or their products or components directly on the host tissues, which would involve an inflammatory response and the generation of harmful levels of certain cytokines and activation of mononuclear cells[5]. The bacteria or their products enter into the bloodstream could elicit several host responses such as an acute phase response, a white blood cell response, or an immune response. The inflammatory response to these bacteria or bacterial products could, through activation of cell types such as monocytes/macrophages, contribute to increased levels of cytokines and inflammatory mediators that could affect the endothelial lining in ways that promote an atheroma formation on the endothelial surfaces. The inflammatory response could contribute to autoimmune events related to the similarity of bacterial heat shock protein (HSP) with host HSP in the vessel wall[6].

Periodontal disease and asymptomatic bacteremias

Under ordinary circumstances, approximately 100 billion bacterial cells, representing more than 300 different types of bacterial species, are swallowed in the saliva each day. As many as 10-100 million can exist in the dental plaques found on each tooth in the mouth. The levels of these bacteria are held in check by good oral hygiene practices, but a very small number of plaque bacteria can traverse the periodontium and enter the bloodstream[7,8].

During periodontitis, den-

tal plaque microorganism may disseminate through the blood to infect the vascular endothelium and contribute to the occurence of atherosclerosis and risk of myocardial ischemia. The bacteria most likely enter the circulation by contact with chronically inflammed and ulcerated periodontal tissues. In severe periodontitis, this complex bacterial plaques can be exposed to wounded periodontium with a planar surface area of upto 50 cm.[9] If untreated, this large chronic wound may contribute over many years to recurrent bacteremias. A milligram weight of dental plaque contains about 108-109 bacteria. Aggregation of platelets is induced by the platelet aggregation association protein (PAAP), expressed on plaque bacteria including *Streptooccus sangius*, *Proplyromonas gingivalis* and *Actinobacillus actinomycetemcomitans*. Dental surgical procedures cause detectable bacteremias in more than 80% of patients[10]. Simple oral hygiene procedures applied at home, cause bacteremia in atleast 40% of individuals.

Biological effects of lipopolysaccharides

The periodontal anaerobes contain lipopolysaccharides (LPS) on their surfaces, and because these organisms may be invasive[11], they could introduce LPS directly to the periodontal tissue. If LPS entered the systemic circulation, it could promote atherosclerosis and thrombus formation by wellknown mechanisms[12]. LPS can activate several cell types that can produce cytokines, which can affect the surface of the endothelial lining predisposing adherence of monocytes. LPS has been reported to release the von Willebrand factor antigen from endothelial cells and levels of von Willebrand factor antigen in the serum could serve as a surrogate of endothelial cell damage. Infections cause the liver to synthesize an array of proteins, known as the acute phase response, that provide protective functions to the host. In recent years, various aspects of the acute phase response, such as elevated levels of fibrinogen, C-reactive proteins and lipoproteins have been identified as risk factors for CVD. LPS will stimulate an acute phase response. One might expect that in a chronic infection, such as periodontal disease, the LPS, which could be intermittently or continuously entering the gingival tissue, would contribute to an acute phase response either directly or indirectly via cytokine production. Several studies have shown that patients with periodontal disease have elevated serum levels of fibrinogen, white blood cell counts and C-reactive proteins[13].

Other common aspects of periodontitis and CVD

One of the most intriguing notions with respect to the putative relationships between periodontitis and CVD may related to some of the similarities in their underlying pathophysiological and physiological regulatory systems. For instance, smoking is a significant risk factor for both diseases. Current data in our laboratories suggest that an important component of cigarette smoke, aryl hydrocarbons[14], have the ability to inhibit bone formation, particularly in the presence of periodontal disease causing bacterial co-factors[15,16]. Thus, a common risk factor, smoking/aryl hydrocarbons, mitigates negative effects in two disparate systems: The periodontium and vascular tissues.

Precautions to be taken by the dental practitioner[17]

Myocardial infarction

Wait a minimum of 6 months after a heart attack, before undergoing any dental treatment. The dentist should ask the patient whether he is on any anticoagulants, as these medications could result in excessive bleeding during oral surgical procedures.

Angina

Patients with angina treated with calcium channel blockers may experience gum overgrowth. While patient with stable angina can undergo any dental procedure, patients with unstable angina should not undergo elective (non-essential) dental procedures. Emergency dental care should be performed in a hospital or clinic with cardiac monitoring capabilities.

Recommended steps for a patient who had an attack of angina

- Place patient in an upright position (approximately 45 degrees).
- Put nitroglycerin under the tongue or spray twice with translingual nitroglycerin Obtain assistance from available personal.
- Administer oxygen by nasal cannula at the rate of 6 l/min.
- Take vital signs and continue to monitor.
- Give second nitroglycerin tablet

or respray if pain is not relieved in 5 minutes.

- If pain persists beyond 10 minutes, administer third nitrogylcerin tablet or respray and contact emergency system.

Atrial fibrillation[18]

To reduce the potential complications associated with dental care, dental practitioners should be familiar with atrial fibrillation.

Dental management of a patient with atrial fibrillation[18]

- Determine underlying cause of atrial fibrillation - is antibiotic prophylaxis required before dental treatment.
- If communication is difficult, consider alternative methods: Pictograms, written information, gestures, communication with other family members.
- Determine if patient is receiving anticoagulation therapy and if so what agent is being used.
- If warfarin is being used, obtain international normalized ratio or INR, values for patients with routine INR values between 2.0 and 4.0.
- Consider leaving anticoagulation protocol unchanged for simple oral surgical procedures and using tranexamic acid mouthrinses postsurgically.
- Avoid using nonsteroidal anti-inflammatory agents.
- Schedule appointments in late morning or afternoon to minimize the occurrence of ischemic events.
- To minimize the occurrence of ischemic events, treat anxious patients with anxiety reducing protocols - anxiolytic agents, nitrous oxide sedation.

If using local anesthetics with epinephrine avoid intravascular injections, periodontal ligament injections and intraosseous injections.

Dental procedures considered for antibiotic prophylaxis in suceptible patients[20]

- Dental extractions.
- Periodontal procedures including surgery, scaling, root planing and probing.
- Endodontic instrumentation or surgery beyond the tooth apex.
- Subgingival placement of antibiotic fibers or strips.
- Initial placement of orthodontic bands but not brackets.
- Intraligamentary local anesthetic injections.

Antibiotic Prophylactic Regime for Bacterial Endocarditis[19]

Situation	Antibiotic	Regimen
Standard prophylaxis	Amoxicillin	Adults: 2 g Children: 50 mg/kg: Orally 1 hour before the procedure
Cannot use oral medication	Ampicillin	Adults: 2 g: i.v./i.m. Children: 50 mg/kg: i.m./i.v.: Within 30 minutes before the procedure
Allergic to penicillin	Clindamycin	Adults: 600 mg Children: 50 mg/kg: Orally 1 hour before the procedure
	Cephalexin or cefadroxil	Adults: 2 g Children: 50 mg/kg: Orally 1 hour before the procedure
	Azithromycin or clarithromycin	Adults: 500 mg Children: 15 mg/kg: Orally 1 hour before the procedure
	Clindamycin	Adults: 600 mg Children: 15 mg/kg: i.v.: 1 hour before the procedure
Allergic to penicillin and unable to take oral medication	Cefazolin	Adults: 1.0 g Children: 25 mg/kg: i.m./i.v.: 30 minutes before the procedure

- Prophylactic cleaning of teeth or implants with anticipated bleeding.

Dental procedures not considered for antibiotic prophylaxis in suceptible patients

- Restorative dental procedures with or without retraction cords.
- Local anesthetic injections except intra-ligamentary.
- Intracanal endodontic procedures, postplacement and build-up.
- Placement of rubberdams.
- Postoperative suture removal.
- Placement of removable orthodontic or prosthetic appliances.
- Taking oral impressions.
- Fluoride treatment.
- Taking oral radiographs.
- Orthodontic appliance adjustment.
- Shedding of primary teeth.

Conclusions

Available evidence suggests a possible relationship between tooth loss, periodontal disease and CVD. It is recommended to advocate better oral care, regular professional check up, more emphasis on the retention of teeth and prevention of periodontal disease. If teeth have to be extracted, then adequate prosthetic rehabilitation should be stressed to help maintain good diet. It is very important in daily clinical practice to take proper case history, to avoid the death of the patient in dental clinic. The dental practioner should have an upto date knowledge of the current regime for bacterial endocarditis to manage a patient with CVD. Following a standard protocol for all cardiac patients and taking written informed consent is the only hope, the practioner can have, if death occurs in dental clinic. Basic preparation of the office for all emergency situations is critical to the successful management of CVD. Periodontitis needs to be prevented and treated in its own right. Yet, by studying the apparent relationships between these two diseases, it is likely that we will learn even more about both!

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