Implications of periodontitis in cardiovascular diseases: Review

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Abstract: Periodontal disease is a common condition that affects a large part of the population. Periodontitis occurs when bacteria spread deeper into the tissue and the surroundings structures leading to a chronic, destructive, irreversible inflammatory disease. Oral Gram-positive and Gram-negative bacteria have been frequently identified in blood flow and may play a role in vascular disease. The objective of the study is to examine the relationship between microbial presence in dental plaque and periodontitis, focusing on how these microorganisms may enter the bloodstream, particularly in individuals with cardiovascular diseases. Patients with severe periodontal disease showed endothelial dysfunction and signs of systemic inflammation, placing them at an increased risk level for the development of cardiovascular diseases. Dental diseases including gingivitis, periodontitis, and other odontogenic infections have a higher bacteremia regarding valvular diseases after tooth extraction. Oral bacteria can cause short-term bacteremia during dental treatment especially when is involved periodontitis. Usually, the bacteria enter the circulation and reach body organs through blood, becoming a risk factor for cardiovascular diseases.

1. Introduction

Periodontal disease (PD) is a common condition that affects a large part of the population. The periodontium is used to describe the elements that encircle the tooth

including: gingival tissue, alveolar bone, cementum, and periodontal ligament [1]. Periodontal disease should be viewed as a chronic microbial infection. The first sign of periodontal disease is gingivitis and can be found in up to 90% of the population. It represents the inflammation of the gingiva due to the multiplication of bacteria and debris between the gum line and tooth, known as dental plaque [2]. Periodontitis is when bacteria spread deeper into the tissue and the surrounding structures leading to chronic destructive, irreversible, inflammatory disease, progressive alveolar bone loss and attachment of periodontium and with a final consequence of loss of tooth [3].

The literature data showed that specific Gram-negative anaerobic bacteria and/or their toxic products are associated with inflammatory destruction in periodontal disease [4-6]; however, most of these oral bacteria have not yet been cultivated. Oral Gram-positive and Gram-negative bacteria have been frequently identified in blood flow and may play a role in vascular disease. The pathogens implicated in periodontitis include *Aggregatibacter actinomycetemcomitans, Porphyromonas gingivalis, Treponema denticola,* and *Tannerella forsythia*. In cases of dental plaque these bacteria penetrate deep into the periodontium and produce inflammation by triggering the release of inflammatory mediators, and body defense activation from the host [7]. The proportion of *Fusobacterium* and *Porphyromonas* was correlated with the development of periodontitis, while elevated proportion of *Rothia* and *Streptococcus* was found in healthy patients [8].

Furthermore, a smaller concentration of *P. gingivalis* the most studied pathogenic bacteria, can affect the homeostatic balance of oral microbiota having consequences that lead to inflammation and bone loss [9]. The incidence of bacteremia after a root canal treatment, as described by Castillo et al. study [10], revealed that *P. gingivalis* and *A. actinomycetemcomitans* were the bacteria with a higher detection in the bloodstream. There are multiple studies correlating the presence of oral bacteria within the atheromatous plaques [11-14]. Moreover, DNA implications from periodontal bacteremia were found in the atheroma plaques samples in patients with periodontitis [15].

The aim of the study is to analyze the relationship between microbial presence in dental plaque and periodontitis, focusing on how these microorganisms may enter the bloodstream, particularly in individuals with cardiovascular diseases. Therefore, by collecting data from the literature, we are trying to acknowledge the importance of periodontitis prevention because it represents an elevated risk factor inclined in the cardiovascular disease complications.

2. Materials and methods

The main electronic databases accessed for gathering information are MEDLINE/PubMed and PubMed Central (PMC), and the search was performed using the Medical Subject Headings (MeSH) keywords "periodontitis" and "cardiovascular diseases". The study includes data with reports written in English, published in the last 10 years as free full text available. This review excludes the studies conducted on animals. The purpose of the study is to acknowledge the importance of treating risk factors like periodontitis in cardiovascular diseases.

3. Results

For this review, a total of 26 studies were included in the analysis.

Table 1. MeSH terms were used to find studies.

Searches using MeSH (Medical Subject Headings) keywords- Periodontitis and aterosclerosis,	Count of records	Atherosclerosis	Cardiac valvular diseases
Total records available	861	852	9
Following the use of inclusion and exclusion criteria			
Randomized controlled trials	2	2	0
Published within the previous ten years	354	349	5
Free access to full texts	26	21	5

4. Discussion

Although the multiple studies regarding the association of periodontitis with cardiovascular disease, traditional risk factors such as smoking, diabetes mellitus, age, and socioeconomic conditions have determining roles [36]. Therefore, in a patient with a cardiovascular disease maintaining an adequate oral hygiene is crucial. A correct scaling, root planning, antibiotic therapy reduced chronic inflammatory condition caused by periodontitis.

4.1. Correlations between periodontitis and atherosclerosis

Recent epidemiological studies suggest that periodontal disease may represent an important risk factor in cardiovascular diseases. Numerous case-control studies have demonstrated a strong positive association after adjusting for conventional risk factors (smoking, hypertension, obesity, dyslipidemia) [16]. In addition, patients with severe periodontal disease showed endothelial dysfunction and signs of systemic inflammation, placing them at an increased risk level for the development of cardiovascular diseases. The relationship between periodontal disease and vascular conditions, such as peripheral vascular disease or coronary heart disease, has been studied in numerous articles [17,18]. A possible mechanism would be endothelial damage by oral microbial toxins and systemic inflammation caused by oral infections. Moreover, phagocytes from periodontal lesions can activate various bacterial cells and their antigens penetrate gingival tissue. Through circulation mechanism the bacterial toxins are transported to the heart where they adhere to the endothelium of the coronary arteries. These stored bacteria can then stimulate the release of inflammatory cytokines and initiate the formation of the characteristic foam cells associated with atherosclerosis [19]. Therefore, it is stated that patients with a history of chronic inflammatory diseases have a higher incidence of cardiovascular diseases and hypertension [20]. Moreover, an increased leukocyte count, an inflammatory marker, is linked to worse outcomes in patients with acute coronary syndromes [21] and those who have undergone coronary artery bypass grafting [22]. These correlations suggest that inflammation of any kind can induce atherosclerosis. Endothelium with normal function maintains vascular homeostasis but the dysfunctional endothelium provides a favorable environment for the initiation of bacterial plaque formation processes [23]. Finally, the mechanisms identified in the chronic inflammation process lead to the conclusion that there is a correlation between periodontal diseases to cardiovascular disease especially to atherosclerosis. Multiple pathways lead to this conclusion due to the epidemiological and clinical association.

Several meta-analyses [24-27] on coronary atherosclerosis are associated with numerous risk factors including smoking, hereditary collateral history, vascular defects, elevated LDL cholesterol and/or triglycerides, abnormal HDL cholesterol levels, hypertension, diabetes, overweight, age, sex, menopause, hyperlipidemic diet, atherosclerosis present in other organs, coronary calcifications demonstrated on CT.

In patients with newly diagnosed cardiovascular disease, treatment of periodontal disease and general management should be coordinated to achieve cardiovascular risk reduction and optimal periodontal care.

4.2. Periodontitis and valvular heart disease

Periodontitis is already known to be a multimicrobial infectious disease that have the result in loss of teeth by multiple causes one of them is regarded chronic inflammation having the effect of bone resorption [28]. Valvular heart disease is a condition that lowers the functional capacity of the heart. Patients with this condition have an elevated risk of infected endocarditis involved in surgical treatment plans [29]. Gram-positive cocci, such as *Staphylococcus aureus*, are a primary cause of infectious endocarditis. In cases of severe periodontitis, bacteremia can significantly can increase the risk of developing pyogenic valvular heart disease [30].

The mechanism within this process is that damage to vascular function is due to the chronic inflammation of the periodontitis and function may be recovered by intensive treatment of oral hygiene [31]. Unfortunately, over 1.1 billion cases of severe periodontitis were present globally in 2019, regarding infectious endocarditis over 42.5%patients were indicated with periodontitis [32,33]. *Streptococcus viridans* has a higher prevalence regarding valvular bacteremia [34]. In a worldwide study the presence of dental diseases including gingivitis, periodontitis, and other odontogenic infections had shown a higher risk of disseminating bacteremia regarding valvular diseases after tooth extraction [35, 36]. In the study by Dhotre et al. in 2017, there seem to be a positive association between periodontitis and infectious endocarditis related to *Streptococcus viridans* and other bacteria, also *Staphylococcus aureus* it has been found 6.36% from the oral cavity and 11.76% from blood stream [37]. In addition, there are similar studies where the researchers found similar associations between myocardial infarction, atherosclerosis and periodontitis [38,39].

More studies are needed to investigate the effect of periodontitis on cardiovascular diseases. Therefore, for a best outcome is necessary for physicians to take in consideration a possibility risk factor in cardiovascular diseases patients with periodontitis, symptoms such as tooth mobility, bad breath, gingival bleeding during the brushing, flossing, eating, or bad taste of mouth, can relate to an oral infection. If there are any suspected cases of oral tissue inflammation or periodontal disease, the physician must refer the patient to the periodontist for further evaluation and treatments such as scaling, root planning, oral health instruction, and other complementary treatments like local antibiotic therapy or antiseptic mouthwashes.

4. Conclusion

From the literature study most of the results lead to the conclusion that higher bacteremia is found in blood flow at patients with periodontitis. It is crucial for physicians to consider the state of oral health when dealing with heart-related diseases, oral bacteria from poor oral hygiene, calculus accumulation around teeth lead to inflammation and ulceration of the gingival tissues cause short-term bacteremia during dental treatment especially when is involved periodontitis. In today's clinical practices, the aim is to improve the patients quality of life, and this can only be achievable by handle of the entire patient's problems including oral and heart-related problems. Therefore, it is better for physicians who treat patients with cardiovascular diseases to evaluate the patient's oral health and the possible association with cardiovascular disease.

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