

Relation between periodontal disease and cardiovascular diseases a mini-review

Abstract

In recent years, literature has reported a relation between Periodontal Disease and Cardiovascular Disease. Periodontal diseases can influence the onset and/or progression of a systemic disease; therefore, to know the actors involved in it, demonstrating its presence in cardiovascular diseases, has been fundamental. This descriptive review aims to present the latest studies that evidence the importance of this epidemiological relation and how the mechanisms that act as aggravating factors in cardiovascular diseases have been enlightened. Understanding and studying this relation in the Costa Rican context could generate great benefits to the public health of the country.

Volume 4 Issue 1 - 2019

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Received: November 15, 2018 | **Published:** February 12, 2019

Introduction

In recent years, literature has reported a relation between Periodontal Diseases and Cardiovascular Diseases; however, the mechanisms by which this relation is presented are not entirely clear. So, more attention has been paid to the possibility that oral bacterial infection, particularly periodontal diseases, may influence the onset and/or the progression of systemic diseases.

Periodontal disease is a chronic multifactorial disease that is favored by the ability of the oral microbiota to form biofilms, which contribute to constant inflammation and it can lead to periods of remission or exacerbation that can extend for long.¹

Many gram-negative anaerobic bacilli have been related with this disease and, therefore, to establish the presence of these microorganisms in the circulatory system has been the subject of study by several scientific groups. Among the main bacterial groups that are presented in dental plaque, we can mention *Aggregatibacter actinomycetemcomitans*, *Porphyromonas gingivalis*, *Prevotella intermedia* and *Tannerella forsythia*.²

The aim of this descriptive review is to present the latest studies that demonstrate the importance of this epidemiological relation and how the mechanisms that act as aggravating factors in cardiovascular diseases have been enlightened.

Oral microbiota related with various cardiovascular diseases

In his study conducted in Japan during 2013, Suzuki et al.³ reported the study of 142 patients with arrhythmias and 25 aneurysms of the abdominal aortic artery, determining the presence of *Aggregatibacter*

actinomycetemcomitans, *Porphyromonas gingivalis*, *Prevotella intermedia* in samples of dental plaque analyzed by PCR and levels of antibodies against these bacteria were measured simultaneously, obtaining higher serological titles in patients who developed aneurysms compared to those who suffered arrhythmias.³

During the same period, Hanaoka et al.⁴ determined the serum levels of response against *Porphyromonas gingivalis* and he related them to the presence of hypertension and atherosclerosis in a group of 127 patients, mostly male, where high levels of antibodies were found. In turn, the serological title was correlated with the progress of both periodontal disease and hypertension and atherosclerosis.⁴

In 2014, Rath et al.² confirmed the presence of DNA from periodontal bacteria in coronary atheromatous plaques and subgingival plaque samples from the same patients. A correlation was established between the bacteria that probably contribute to the atheroma plaques and the species related with periodontal disease.²

For 2015, Oliveira et al.⁵ used real-time PCR to identify the presence of the following bacteria: *Streptococcus mutans*, *Porphyromonas gingivalis*, *Prevotella intermedia* and *Treponema denticola*. He analyzed samples of dental plaque and remains of the cardiac valves of 42 patients, obtaining that the microorganism most frequently identified is *Streptococcus mutans*, this being the only one that could be found in the analyzes of the cardiac valves.⁵

Porphyromonas gingivalis as main actor in periodontal disease and its relation with cardiovascular diseases

From these findings, the researchers took *P. gingivalis* as the pathogen to be studied and Mysak et al.⁶ presented this bacterium during 2014 as one of the main players in periodontal disease, due

to its arsenal of virulence factors ranging from its structure, its metabolism, the ability to colonize the gingival epithelial cells and the modulation of the host immune response.⁶

De Leon-Pennell et al.⁷ through an experimental model in mice, used the lipopolysaccharide of *P. gingivalis* to intensify post-infarction myocardial inflammation, demonstrating that this lipopolysaccharide generates a large recruitment of macrophages, which contribute to increase tissue damage.⁷

Recently, Lee et al.⁸ established a model by which *P. gingivalis* uses phagocytosis of gingival epithelial cells to establish and replicate within the oral mucosa, using the endocytic pathway and trafficking through the endoplasmic reticulum, thus explaining the persistence of periodontal disease and opening new lines of research.⁸

Srisuwantha and his group performed an experimental model in mice to determine the effect of the periodontal pathogen *P. gingivalis* after a myocardial infarction. Due to tissue damage and necrosis, the cardiac cells release HMGB1, which activates an inflammatory reaction. During the experiment, the level of HMGB1 protein was determined in a group of infarcted mice inoculated with the bacterium which was significantly higher than in the group of infarcted mice injected with PBS on day 5, but not on day 14. The analysis of Immunohistochemistry revealed that HMGB1 was expressed in cardiomyocytes, immune cells and vascular endothelial cells from the group of infarcted mice injected with PBS, whereas HMGB1 was widely observed in degenerated cardiomyocytes, extracellular fields, immune cells and vascular endothelial cells in the group of infarcted mice inoculated *P. gingivalis*. On the other hand, a significant increase in the number of cells positive for HMGB1 was observed in the group of mice inoculated with the bacterium, compared to the group of mice injected with PBS. Therefore, they concluded that infection with *P. gingivalis* after a myocardial infarction in mice increases the expression of HMGB1.⁹

Discussion

Studies that focused on demonstrating the presence of pathogens participating in periodontal disease by molecular and serological techniques were able to demonstrate the strong relation of cardiovascular diseases.

It is striking that ischemic heart disease has a stronger relationship than other clinical presentations according to the studies of Suzuki et al.³ and Rath et al.² and this can be explained by the virulence factors discussed by Mysak et al.⁶

On the other hand, the absence of anaerobic bacteria in the heart valves could be due to the increased capacity of *Streptococcus sp.* to colonize medical devices in addition to having the capacity to induce adhesion and platelet aggregation through a cross reaction, simulating the collagen binding sites type I and III.¹⁰

The major limitation of many of these studies has been the difficulty to take samples mainly at level of circulatory system, in addition to having very limited sample sizes, which reduces the statistical robustness of the data.

Likewise, the lines of research that focus on elucidating the molecular mechanisms that act in these diseases have shown how the ability of *P. gingivalis* to exacerbate inflammation and escape from the immune system should be the subject of studies in the future, in order to better understand the pathophysiology of periodontal disease and ischemic cardiopathies and thus understand their interconnection.

Conclusion

In carrying out this descriptive review of the relation of periodontal disease with cardiovascular diseases, there is no doubt that the interconnection of these pathologies is clear and should be widely studied, since both diseases are highly prevalent and constitute great challenges for the public health.

Additionally, the role of *P. gingivalis* in both diseases should be the object of future research, since the amplitude of the virulence factors that this bacterium possesses probably explains its role in the chronicity and severity of these pathologies. Finally, I believe that this relation should be studied in the context of the Costa Rican population with special emphasis on the adult population, which is mainly affected by cardiovascular diseases. This will significantly raise the interest of the population in oral health and reducing the risk of suffering heart attacks, strokes or cerebrovascular accidents that are the main causes of death in our country.

Acknowledgments

None.

Conflicts of interest

The authors declare no conflicts of interest.

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