Investigation of periodontal infections and its relation with cardiovascular diseases

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Abstract

The relationship between periodontitis and cardiovascular diseases has been of interest in recent years. Cardiovascular diseases in the developed countries account for 50% of the mortality rate and are the principal causes of death. Periodontitis, one of the most common diseases of humans, is an infectious condition that can result in inflammatory destruction of the peridontal ligament and alveolar bone. Periodontitis and atherosclerosis have complex etiologies such as genetics and gender, and they potentially share many risk factors, the most significant of which may be smoking. A number of studies have shown a significant relationship between periodontitis and cardiovascular diseases, but the need for further studies of new definitions of the relationship between them, especially in women, seems to be required.
Key words: Periodontal infectious diseases, Cardiovascular diseases, Periodontal diseases as a risk factor.

Please cite this article as: Nima Ghobadi. Investigation of periodontal infections and its relation with cardiovascular diseases. 2018;16(2):341-345. World Family Medicine.
DOI: 10.5742/MEWFM.2018.93282

Introduction

Cardiovascular disease is one of the most common medical problems and the main cause of death in the world. (1, 2) The relationship between periodontitis and cardiovascular diseases has recently been considered. Periodontitis is an infectious disease that results in gum inflammation, periodontal tissues, and progressive alveolar bone loss and is considered as an important focus of infection in the body. (3) Increased levels of acute inflammatory phase have been seen in patients with periodontitis as well as in cardiovascular patients. 2, 5, 4) Several studies have been done on the relationship between periodontal and cardiovascular disease. In some studies, periodontitis has been introduced as a risk factor for cardiovascular disease, while the results of some studies do not support this issue (Janket et al., 1997). In a meta-analysis, seven studies were conducted on nine cohort studies in this regard. Based on the results of these studies, the risk of such events and those with periodontitis increased by 19%. (8) In a study by Arbes et al., A direct correlation between coronary artery disease and severity of periodontitis has been emphasized. (9) Beck et al. In a broad prospective study. A total of 921 men without coronary artery disease were studied for 18 years and during the aforementioned period, they monitored the periodontal condition and the probability of developing coronary artery disease. The results showed that the probability of this disease was 2.8 times higher. (6)

Coronary artery disease is one of the most common causes of premature death in industrialized countries. (10) Various studies confirm the effect of oral cavity diseases, especially periodontal diseases on systemic diseases, such as cardiovascular diseases (29,25,26,24,23,22,30,14). Many of these studies are long-term and retrospective. Destefano, in a 14-year study reported that there is a statistically significant relationship between periodontal disease and cardiovascular disease. The present study is an overview of the mechanisms of communication between cardiovascular diseases and periodontal diseases. To better understand these mechanisms, information is provided on the pathology of cardiovascular diseases, periodontal diseases and their related risk factors.

Cardiovascular diseases
According to World Health Organization statistics, in 1995 around the world, 20% of deaths were due to cardiovascular disease, which is increasing by 50% in developed countries. (25)

Hardness of the arteries (Atherosclerosis)
The basis of pathology of cardiovascular diseases is the severity of arterial disease (26).

This condition has been known for more than a century, and clinically involves moderate-sized vessels. One of the most commonly involved vessels is coronary arteries. Early damage to the arteries can be found in children, called a fatty streak, and an advanced type of injury, called the fibrous plaque, in the adult. There are various views about the problems with arteries, but the Response-To-Injury Hypothesis approach is more likely to be confirmed (28).

Periodontal infectious diseases (periodontitis)
Infectious disease, is caused by a small group of gram-negative bacteria, anaerobic bacteria. The presence of bacteria to cause the disease is an essential factor, but host readiness is also one of the essential factors in the development of the disease. In the course of periodontal disease, connective tissue and bone destruction occurs, and inflammatory cytokines, such as (Interleukin-I) IL1 and (TNF), producing MMPS (Matrix metalloproteinases) and (Prostaglandin E2) PGE-2. The mentioned materials are mediators of intercellular matrix destruction in the gum, PDL and bone. Heritable and environmental factors vary in different stages of the disease and in different types of diseases. These conditions affect the onset of the disease, tissue degradation, the rate of progression of the disease, and response to treatment. In addition, the severity and rate of progression of the disease depends on the quantity and quality of the microbial biofilm, the pH of the environment, the amount of the oxygen and the nutrients contained in the periodontal envelope. This view can show individual differences in the susceptibility to disease. (14) Among the different species of bacteria in the oral cavity, three types of Gram-negative bacteria are found in most cases of periodontal disease, namely Porphyromonas gingivalis (P.G), Actinobacillus, Bacteroides forsythus (BF), the latter species. Actinomycetemcomitans (Aa). Most are seen in progressive periodontal disease. Of course, spirochetes are also involved in the disease process (14). Microorganisms live in a special environmental gathering called bacterial biofilm, in which the features of this biofilm are as follows: An environmental gathering, which causes the group to survive. The bacteria have a fuel cell contribution. The environment has a large number of microorganisms with varying pH, oxygen concentrations, and electrical power. Biofilm creates an environment that causes micro-organisms to resist hostile defense mechanisms. The microorganisms in the biofilm are resistant to antibiotics and anti-microbial agents (antibiotics). In patients who are prone to develop periodontitis, microbial biophilia progresses to gingivitis, causing damage to the graft (coronary part of the sticky epithelium junctional epithelium), thereby increasing the availability of bacterial products such as Lipopolysaccharides (LPS) lipoplasty saccharide to connective tissues and veins. lipopolysaccharide bacteria, by stimulating epithelial cells, secrete IL8, IL-I. These cytokines cause accumulation and activity of neutrophils, and other inflammatory cells, such as B cell, T-cell macrophages, and also play a role in the immunopathogenesis of periodontal diseases. Types of cytokines, including 1,2,3,5,6,9,10, result in the secretion of TNF and IL. Due to these cytokines, lymphocyte B cells differentiate into plasma cells and secrete immunoglobulins. The highest immunoglobulin is secreted from the IgG2 species. Macrophages, due to medium stimulation of lipopolysaccharide, secrete substances such as TNF and high levels of MMPs, PGE2, TNF, and IL-1. Due to these materials, periodontal tissues are destroyed. (14)

Mechanisms of communication between periodontal diseases and cardiovascular diseases
Dental health plays an important role in factors associated with increased cardiovascular disease. In addition to risk factors such as high cholesterol, obesity, diabetes, smoking, which are considered as classical factors, chronic infection is also a risk factor for cardiovascular disease (28). The most common chronic infections, dental caries and periodontal diseases can be mentioned. Periodontal diseases are among the risk factors for cardiovascular disease. (Cardio vascular accidents) A variety of studies show the relationship between periodontal disease and cardiovascular disease (11,27,24,25,22,14,12).

Mechanisms Effective in Infection Influence on the Hardness of the Arteries
The direct effect of infection
There are three reasons for the direct effect of periodontal bacteria on the formation of hardness of the arteries.
1. P gingivalis I=in plaques on cardiovascular and carotid arteries.
2. In the study of Deshpade and colleagues in 1993, the ability to invade of P.Gingivalis and its proliferation in endothelial cells has been identified.
3. Research by Meyer, Herzberg in 1998, P.Gingivalis

P.Gingivalis can cause platelet accumulation and an antigen such as the PAA (Platelet Aggregation Association protein) and its expression on the microorganisms. Coagulation power (thrombogenic) of this bacterium is exacerbated by high blood lipids (hyperlipidemia). Lipid elevation is one of the risk factors for stroke (MI). With this classic risk factor, is the presence of specific bacteria from species that have the ability to clot (thrombogem). They cause inflammation injuries, and active platelets play a regulating role in the release of chemokines from monocytic cells. Here, it should be noted that platelets and leukocytes are activated during bacteremia, and active platelets can regulate the release of chemokines from monocytes in inflammatory injuries. Platelets are part of the process of hemostasis, which is essential for the formation of the hardness of the arteries, and is thought to be a target cell for a number of microorganisms (29,26,20). Despite all of the above, the direct role of microorganisms in the etiology and pathogenesis of arterial stiffness is still not fully understood (27, 28). The study of Kuramitsu in 2001 showed that in the outer membrane vesicles P.Gingivalis

causes the formation of fat cells, which is an important feature of cardiovascular disease. In addition, it acts as a mediator in the oxidation of LDL and ruptures the arterial hardness plate. (32)

Indirect effect due to host intermediates

Another mechanism that supports the effects of periodontal diseases on cardiovascular disease is the creation of cytokines. The role and effect of gingival microbial plaque due to the relatively large surface area of periodontal packs (especially in the course of periodontal diseases, which is an ulcerative epithelium), high levels of endotoxin, the gram-negative bacteria are in contact with the connective tissue and enters it. Tissue defenses act to destroy bacteria and we are less likely to get bacteria in the bloodstream. But this leads to an increase in cellular debridement and lipoplasty of saccharides in the bloodstream. The effect of increasing the material on the fibrinogen is observed. Increasing fibrinogen will act as a coagulation disorder preparatory factor and will lead to coagulation changes. Studies have shown that the incidence and prevalence of cardiovascular disease are related to hemostatic and rheological changes. Rheological variables include plasma viscosity and hematocrit. The effect of plasma viscosity, is partly by fibrinogen and partly by the lipoproteins. The viscosity of the whole blood is associated with plasma viscosity and hematocrit, and the count of white blood cells. The hemostatic variables include the Von Willebrand factor, which is released by endothelium damage. One of the mechanisms of communication between cigarettes is the increase in lipid and infection, such as oral infections based on hemostatic and rheological changes. For example, in people who use cigarettes, rheological changes are high in non-smokers. In a case control study in Glasgow in 1998, the concentration of plasma fibrinogen and white blood cell count in patients with chronic gingivalis and periodontitis were significantly higher than those in other individuals. (11) A large number of studies suggest that increased white blood cell counts are an agent for ischemic heart disease. The increase in circulating leukocytes results in the closure of micro vascular arteries, especially if this increase is acute. In inflammatory periodontitis, there is the potential for making cytokines and inflammatory mediators and lipid compounds. These substances affect endothelial cells of the blood vessels in other areas. (25) Endotoxin and lipopolysaccharide gram-negative bacteria, which are microorganisms of the peri-gland in periodontal diseases, also cause damage to endothelial cells. The damage to endothelial cells causes the release of various factors, such as Von Willebrand, which can justify an increase in the size of this factor in the process of periodontal disease.

Effect of lipopolysaccharides

Infection causes the metabolism of lipids to change. IL-1 and TNF inhibit lipoprotein lipase activity, and bacterial products such as lipopolysaccharide and Muramyl dipeptide, can directly affect endothelium. Perhaps for this reason, lipid elevation is a clear indication of chronic infections. (25) In the study of peripheral blood monocyte in patients with Early-onset periodontitis and Refractory periodontitis revealed that these cells secrete 3 to 10 times the normal levels of PGE2, IL-1, and TNF. (28) Increasing the secretion and production of cytokines from gingival tissues to the general flow of blood and in distant areas. (25) Lipopolysaccharides are released from the microorganisms of the periodontal envelope, and into tissues. Periodontium is entered into the patient. lipopolysaccharide are not free in plasma, they are bound to plasma proteins. In the event of bacterial invasion and the formation of bacteremia, free lipopolysaccharides are found in plasma. Bacteremia is caused by treatment such as scar=ring and during acute and chronic abscesses, and the availability of warm bacteria causes a negative blood flow. Following is the activation of leukocytes, platelets, and endothelial cells. Circulating microorganisms liberate lipopolysaccharides, which affect fat metabolism. When lipopolysaccharide is bound to a lipopolysaccharide-binding protein, a high affinity protein, it finds the ability to transplant CD14 receptors, by binding the compound to the receptors on endothelial cells, monocytes and macrophages, and these cells are activated. By activating these cells, the appearance of adhesion molecules and release of cytokines and chemokines, and with increasing molecules, adhesion at the level of endothelial cells, leukocyte migration to (sub intima), which is explained by the effect of this event in the process of causing arterial stiffness. (28,27,26,23,15)

Hyperactive mononuclear phagocytes

We observe high activity macrophages in smokers and periodontal patients. Monocytes are highly active macrophages in high levels of inflammatory cytokines, lipopolysaccharides, and the activity of Matrix metalloproteinases (MMPs) and prostaglandin and protease. Such macrophages are involved in causing arterial stiffness in susceptible areas of the arteries, such as the placement of arches. In patients with periodontal disease, polymorphonuclears are about twice the FCR (receptor (FC) more than control group. These PMNs, in the bloodstream, contribute to the formation of the hardness of the arteries. The mechanism of this change is not known. In patients with topical periodontal disease, peripheral blood monocytes secreted high levels of PGE2 in response to lipopolysaccharide, but this reaction is not related to CD14. Laboratory studies have shown that the presence of chronic infection in periodontium causes this reaction, and this is not a characteristic of monocytes in people with progressive localized periodontal disease (15,16).

Inheritance

A recent survey of epidemiology suggests the role of hereditary factors and suggests various genes in this regard. For example, several forms of the Interleukin-1 gene are associated with periodontal disease and cardiovascular disease. The proof of this relationship requires further examination. (31)

Conclusion

Frequent studies confirm the association between oral infections and cardiovascular diseases. Longitudinal, cross-sectional and case-control studies confirm the association between periodontal diseases and other oral conditions

with cardiovascular diseases and infective endocarditis (17,21,27). In a 1998 study, Matyla et al. examined the relationship between coronary artery disease and dental infections. In this study, on 100 patients in terms of body mass index, age, lipid profile, economic status, and blood pressure, using Pantomography, they found that, Coronary atheromatosis (p = 0.003) is associated with dental infections In 1993, Mattila et al. conducted a study on 100 patients with angiography who had a degree of coronary artery bypass graft or history of stroke. They measured the patient's age, serum lipids, body mass index, economic status and blood pressure, and found that coronary arthromotosis with p = 0.001 was associated with dental infections. One of the first long-term studies was carried out by Handfano and colleagues in 1993. (27) They surveyed 9,760 people. Examination of caries and loss of teeth at the onset of cardiovascular disease were investigated over14 years. The findings showed that in subjects who at the beginning of the study had periodontal disease, the risk of cardiovascular disease was 25% higher. In this study, smoking and oral hygiene were not matched. Beck and colleagues surveyed 1,147 men in 1996 (23). Initially, bone Height was determined by radiography. In patients with a high bone fracture assay, the risk of cardiovascular disease was higher after 18 years. Joshipura. (16) A six-year study was conducted on 44,119 men. In men who reported periodontal disease and less than 10 teeth at the beginning, the risk of developing cardiovascular disease was higher than that of men who had 25 or more teeth. The periodontal disease report was studied by an individual, which is a deficiency in this study. Genco (25) and colleagues in a 10-year report from the use of the ECG in 13 patients identified age, diabetes, sex, cholesterol, weight, and blood pressure in matching patients with periodontal diseases who were below 60 years old, were 86.2 times more likely to have cardiovascular disease. In the study group, smokers were very low. In this way, cigarettes have been eliminated as a risk factor. In summary, the mechanisms of communication between cardiovascular diseases and periodontal diseases include the following: the role of lipopolysaccharides in periodontal pathogenic bacteria in the process of causing arterial hardness by transplantation to CD14 and the activation of macrophages and endothelial cells and following the release of inflammatory cytokines. These cytokines cause hemostatic and rheological changes. The effects of the changes mentioned in the pathology of heart disease have been reported. Macrophages, in areas that are lipopolysaccharides or inflammatory cytokines, have macrophages with excessive activity. The role of macrophages in causing severe arterial injury has been shown. The direct role of microorganisms in the periodontal pathogens, despite the evidence referred to, has not been completely established. Recently, studies have focused on the key role of the host's response to the microorganisms and the incidence of cardiovascular disease (30). Finally, despite the mechanisms that have been mentioned and the various studies, the abbreviations of which have been given, it has been concluded that periodontal diseases can be a risk factor for developing cardiovascular disease. Of course, it should be noted that more studies are done in men and information about the association of these two diseases in women is not enough and requires further examination (10,26,27)

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