

PERIODONTAL DISEASES AS A RISK FACTOR

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Summary

There is an increasing body of evidence in periodontology that speaks in favor of the association between human chronic inflammatory diseases and opportunistic infections. Considering their frequency and microbiological etiology, periodontal diseases, especially severe periodontitis, have become subjects of many studies. Periodontitis is a major infectious threat to the whole organism, since it can affect distant organs and tissues by releasing microbes, their products and mediators of inflammation into the bloodstream. This fact has reduced the boundaries between medicine and dentistry, but the change in thinking has developed an entirely new field of periodontology, also known as “periodontal medicine”.

Over the past decade a growing body of scientific evidence shows a strong connection between periodontal disease and systemic conditions and diseases such as atherosclerosis, cardiovascular and cerebrovascular diseases, premature birth, diabetes and respiratory diseases. Most of the research has been focused on the relationship between periodontal disease and atherosclerosis since they have many common, potential pathophysiological mechanisms, including complex etiology, and share many risk factors, especially smoking history. There is data linking periodontitis with an increased risk for atherosclerosis and thromboembolic events. Periodontitis in pregnant women may increase the risk for preterm birth and low birth-weight. The role of diabetes as a risk factor for periodontal disease has been investigated earlier, but a number of studies suggest that there may be a two-way relationship, in accordance with the concept that infection may weaken metabolic control of diabetes.

The results of numerous studies and the development of periodontal medicine have led to productive cooperation with colleagues in medicine, and discovered many new evidences that suggest that the oral cavity is an integral part of the human body, and that systemic health must include oral and periodontal health.

Key words: periodontal medicine; periodontitis; systemic disease; cardiovascular diseases; premature birth; diabetes; respiratory diseases.

INTRODUCTION

The relationship between oral infections and systemic diseases has been questioned for centuries. Even the Assyrians in the seventh century BC knew that oral health can influence health in general, or that the teeth can cause the pain in head and arms. Since the mid to late years of the 19th century there was a popular opinion that "the causes of human disease are bad blood, bad air and the evil spirit." In 1876, a new era of understanding of microbes as agents of disease in medicine and dentistry was introduced by Robert Koch. Koch's apprentice W.D. Miller and later W. Hunter were at that time the main proponents of the concept that oral sepsis is a major cause of systemic disease. The term "oral sepsis" was replaced with the "focal infections" in 1912. The consequences of these concepts were that the teeth and tonsils had been removed to prevent the most diseases caused by microorganisms.

The theory and practice were not utilized for a long time. In 1952 the prestigious American journal JADA reported that many patients with the disease that was presumably caused by focal infection have not been recovered due to removal of the focal tissues like teeth. From that year until 1989 took the era of preventive medicine and dentistry; teeth were preserved with the only exception in case of bacterial endocarditis [1]. The development of microbiology, immunology, molecular and cell biology have led to important findings about the relationship between systemic diseases and oral conditions. The theory that many systemic diseases have repercussion on the oral mucosa and periodontal tissues was not questionable. An obvious example is diabetes which has been scientifically proven as a risk factor for occurrence of periodontal diseases. The microbial ecosystem of the oral cavity is extremely sensitive to the potential adverse impacts faced by the host during his entire lifetime. The ecosystem of microorganisms of the mouth is exceedingly dynamic.

From the fetal period up to the old age, the oral cavity is constantly attacked by opportunistic infections, and oral complications of systemic disease. This dynamic interaction between host and pathogen factors was the basis for changing standpoints in oral medicine and periodontology. Every day there are more and more evidence suggesting that the bacteria found in the oral cavity contribute the development of systemic disease. Periodontal disease is a serious microbiological burden for the entire body. Furthermore, some microorganisms within the microbial ecosystem in the pathological process release toxins that cause an inflammatory response. Bacteria, bacterial toxins, cytokines as products of local tissue response and other inflammatory mediators are released in the circulation and can cause a systemic response. It is known that in patients with entire dentition and with moderate periodontitis have a remarkably large area of the pocket epithelium, which is in direct contact with periodontal pathogens. It is approximately a surface the size of a

fist or even more. A new era in medicine and dentistry began based on these theories. The reason for this was the research of Matilla et al. (1989) in which they concluded that patients with cardiac infarction had moderate to severe periodontal disease in comparison to the patients without heart failure who had mild or no periodontal disease [2]. Since then, dentistry and particularly periodontology has again started to analyze the relationship between periodontal disease and systemic conditions.

Eventually, periodontology has introduced a new term "periodontal medicine", which examines the connection between periodontal disease to systemic conditions and diseases such as atherosclerosis, cardiovascular disease, premature births and low birth weight, lung diseases and disorders, diabetes, etc. [3].

CARDIOVASCULAR DISEASES

There has been a notable opinion in cardiology that chronic infections may contribute to atherogenesis. It was confirmed by studies indicating that subjects exposed to chronic infections have up to three times higher odds of having carotid atherosclerosis [4]. Coronary heart disease and atherosclerosis are progressive diseases that represent a major cause of mortality today. On the other hand, periodontitis is a chronic disease caused by anaerobic bacteria that have very easy access to the bloodstream and are responsible for bacteremia during dental procedures. The disease progresses with age and represents the most common cause of tooth loss in adults. Periodontitis and atherosclerosis have many common potential pathological mechanisms. Both diseases have a complex etiology, genetic and gender predispositions and share many risk factors, most notably the status of smokers. Chronicity of periodontal disease provides many subgingival microorganisms and the host inflammatory products. Bacteria and soluble bacterial products can enter the bloodstream and reach distant places such as endothelium of blood vessels, and cause a local inflammatory response and consequent damage to blood vessels.

The biological likelihood of periodontal disease as a risk for atherosclerosis and consequent emergence of cardiovascular disease was a major preoccupation for the researchers in recent years. Thus the strength of an association between periodontitis and cardiovascular disease based on epidemiological, and cross-sectional studies varies widely regarding different populations of subjects. Studies such as NHANES 1 Follow-up Study, AV Normative Aging Study, Health Professions Follow-up Study and many others dealt with this issue [5]. De Stefano et al. found in their major studies that patients with periodontal disease have a 24% higher risk of coronary heart disease compared to those with minimally expressed periodontal disease [6]. Results of Beck, Morisson and Joshipura derived from national studies speak in favor that poor dental health is associated with an increased risk for coronary heart

disease [7-9]. Bone loss due to periodontitis was found to be associated with complex multiple coronary lesions that are related to multifocal destabilization of coronary plaques. Compared with patients with no significant stenosis, poor periodontal status is associated with angiographically verified coronary artery narrowing in patients with stable coronary artery disease or acute coronary syndrome [10,11].

Patients with severe periodontitis are more likely to have a thicker carotid intima-media wall than periodontally healthy subjects, and patients with a high amount of periodontal pathogens have a thicker carotid intima-media thickness than those with a low number of periodontal pathogens [12].

Several studies suggested that periodontitis may be a risk factor for hemorrhagic stroke, independent of established cardiovascular risk factors. Pradeep et al. even found that a severity of periodontal disease is the most significant factor for stroke, followed by hypertension and smoking [13,14].

Studies have usually evaluated carotid wall in relation to periodontal disease in the middle-aged to elderly population. But it was found that a severe periodontitis is also associated with subclinical atherosclerosis in young systemically healthy individuals. Therefore, some authors suggest that periodontal disease might predict a systemic atherosclerosis decades before the occurrence of clinical cardiovascular symptoms [15]. An intervention trials have shown that a nonsurgical periodontal therapy significantly decreases serum inflammatory mediators and markers of acute phase response, and thus reduces the risk for cardiovascular disease events [16].

DIABETES MELLITUS

Numerous epidemiological, clinical and experimental studies found that periodontal disease is more pronounced in patients with uncontrolled diabetes mellitus (DM), and that periodontal disease progresses more rapidly in this group of patients [17]. DM is one of the most frequently cited systemic disease that is associated with the development and progression periodontal disease, and as such is considered one of the major risk factors (in addition to smoking). Researchers have confirmed an association between both type 1 DM and type 2 DM and an increased severity of periodontal disease and tooth loss compared to non-diabetic subjects in a large homogeneous study population [18].

Although the official medicine does not agree completely, today we can surely state that periodontitis is one of the complications of DM. The relationship of periodontal disease and DM is not always unidirectional. Thus, periodontitis has a negative effect on the glycaemic control, and increases the risk for other diabetic complications [19]. A study on a large cohort of children and adolescents with DM showed an association between diabetes and an increased risk for periodontal destruction

even very early in life. Those data suggest that programmes to address periodontal needs should be the standard of care for diabetic youth [20].

Patients with DM and severe periodontal disease have nearly four times as many complications (cardiovascular, cerebrovascular or peripheral vascular events) compared to patients with DM and mild periodontitis. Also, a clinically successful non-surgical periodontal therapy tends to establish better control of blood sugar levels, reduce systemic inflammation and the concentration of some circulating inflammatory mediators [21,22]. A nonsurgical periodontal treatment can be undertaken safely along with the standard measures for the diabetic patient care. Prevention and control of periodontal disease must be considered an integral part of diabetes control [23].

ADVERSE PREGNANCY OUTCOMES

The concept of adverse pregnancy outcomes that are associated with periodontal disease commonly includes premature births and a low birth weight. Since the role of infection is receiving increasing attention, there is an indirect effect due to the production of increased levels of inflammatory mediators that may shorten the gestational age. It is also plausible that microorganisms may directly access the amniotic fluid and fetus. The implication of this concept is that periodontal disease may induce a primary host response in the chorioamnion leading to preterm birth [24].

Many risk factors such as alcoholism, drug abuse, smoking, certain medications, diseases such as diabetes are associated with preterm birth, but there is still a part of unknown etiology. Periodontitis has become the subject of numerous studies as a potential source of infection that can adversely affect pregnancy. In one of the earliest works in this field Offenbacher et al. demonstrated that women with periodontal disease have seven times higher risk for adverse pregnancy outcomes [25]. Lopez et al. have confirmed periodontal disease as an independent risk factor, and also have observed that periodontal therapy significantly reduces preterm birth with low birth weight in the population of women with periodontal disease [26]. A recent meta-analysis also confirmed a significant risk of preterm delivery for pregnant women with periodontitis (overall risk ratio: 1.70) and a significant risk for low birth weight (overall risk ratio: 2.11) [27].

Most of the evidence indicates that there is a relationship between periodontal disease and increased risk for adverse pregnancy outcomes. In addition, data suggest that periodontal nonsurgical treatment can significantly reduce the incidence of those outcomes in women with periodontitis or pregnancy-associated gingivitis [28,29].

RESPIRATORY DISEASES

Periodontal infection and respiratory pathogens in plaque are associated with increased risk for aspiration pneumonia and chronic obstructive pulmonary disease (COPD). It has been known for a long time that severe lung infections can be initiated by aspiration of anaerobes from the oral cavity, particularly in patients with periodontal diseases. Oral bacteria can also have an important role in the exacerbations of COPD [30]. Previous studies have also revealed an association between poor oral health and COPD that was independent of other confounding factors such as age, gender, and smoking [31]. Patients with COPD have more pronounced clinical attachment loss than those without COPD. In addition, the percentage of gingival bleeding sites can be significantly correlated with the severity of COPD [32].

There are several mechanisms that explain the role of oral bacteria in the oral cavity in the occurrence of respiratory infections. Concentration of bacteria in saliva is very high, and species of bacteria in oral cavity can be found in the lungs of COPD patients [33]. Poor oral hygiene especially in hospitalized patients may increase the risk of aspiration of bacteria from the mouth, and thus cause the development of serious respiratory diseases. Periodontitis and respiratory diseases also share many risk factors especially smoking, which is usually found at patients with periodontitis, emphysema, chronic bronchitis, and lung infections [34].

CONCLUSION

There is an increasing evidence that favors the association of many complex human diseases with opportunistic infections in periodontology. Uncontrolled severe periodontitis caused by periodontal pathogens represents a major infectious threat to the entire body, since released toxins and other inflammatory mediators can reach and affect distant organs. In conclusion, only the treatment and prevention of periodontal disease are becoming increasingly important factors in maintaining oral health, but also in maintaining the health of the whole organism. Development of periodontal medicine has resulted in cooperation between dentists and medical practitioners in order to more thoroughly diagnose and treat patients for better oral and general health.

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Sažetak

Parodontne bolesti kao čimbenik rizika

Sve je više dokaza koje govore u prilog povezanosti kroničnih upalnih bolesti čovjeka s oportunističkim infekcijama u parodontologiji. Parodontne bolesti, posebice uznapredovali parodontitis, postale su predmet mnogobrojnih istraživanja s obzirom na učestalost i mikrobiološku etiologiju. Parodontitis predstavlja veliku infektivnu opasnost za cijeli organizam jer otpuštajući mikroorganizme, njihove produkte te medijatore upale u krvotok može djelovati na udaljene organe i tkiva. Navedena činjenica smanjila je granice između medicine i stomatologije te je promjenom razmišljanja došlo do razvoja potpuno novog područja u parodontologiji koje je nazvano „parodontna medicina“.

Tijekom prošlog desetljeća sve veći broj znanstvenih činjenica upućuje na snažnu povezanost parodontnih bolesti i sistemnih stanja i bolesti kao što su: ateroskleroza, kardiovaskularne i cerebrovaskularne bolesti, prijevremeni porođaj, dijabetes i plućne bolesti. Najviše istraživanja bilo je usmjereno na povezanost između parodontitisa i ateroskleroze s obzirom da imaju mnogo zajedničkih, potencijalnih patofizioloških mehanizama, kompleksne su etiologije te dijele brojne rizične faktore, među kojima je najznačajniji status pušača. Pronađeni su dokazi koji povezuju parodontitis s povećanim rizikom za aterosklerozu i tromboemboličkim zbivanjima. Parodontitis trudnica može povećati rizik za prijevremeno rođenje i smanjenu porođajnu težinu djeteta. Uloga dijabetesa kao faktora rizika za parodontitis istražena je ranije, ali određen broj studija ukazuje da možda postoji i dvosmjerni odnos, u skladu s koncepcijom da infekcija može doprinijeti oslabljenoj metaboličkoj kontroli dijabetesa.

Rezultati mnogobrojnih studija i razvoj parodontne medicine doveli su do plodonosne suradnje s kolegama u medicini i otkrili mnoga nova saznanja koja potvrđuju da je usna šupljina integralni dio ljudskog tijela te da sistemsko zdravlje mora uključivati oralno i parodontno zdravlje.

Ključne riječi: parodontna medicina; parodontitis; sistemske bolesti; kardiovaskularne bolesti; prerani porod; dijabetes; respiratorne bolesti.

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