UDC 616.311.2-002+616.314.17-008.6)]-06:616.1/.4
DOI: 10.14739/2310-1210.2023.1.267456

The role of periodontal pathology and oral cavity condition in the occurrence of general somatic diseases

Z. M. Honta*[A,D,F], I. V. Shylivskyi[B,C,F], O. M. Nemesh[B,D,E], Kh. B. Burda[B,D]

Danylo Halytsky Lviv National Medical University, Ukraine

A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation; D – writing the article; E – critical revision of the article; F – final approval of the article

Key words: periodontal disease, generalized periodontitis, cardiovascular diseases, atherosclerosis, diabetes mellitus, gastrointestinal diseases.

Zaporozhye medical journal 2023; 25 (1), 50-55

***E-mail:** zoryanagonta@gmail.com

The aim of the study is a review of modern national and foreign literature on the influence of the oral cavity state and the pathology of periodontal tissues, in particular generalized periodontitis, on the occurrence and severity of the course of internal organ and body system diseases.

Inflammatory-dystrophic periodontal diseases lead to an increase in the level of chronic inflammatory agents due to the systemic spread of inflammatory mediators released during local tissue destruction, as well as the systemic spread of pathogenic microorganisms, which contributes to the development of cardiovascular diseases, atherosclerosis, pathological processes in the gastrointestinal tract, complicates the course of diabetes mellitus and respiratory diseases in patients with periodontal diseases. That is why the study on pathogenetic interrelations between periodontal diseases and comorbid conditions is an urgent problem of modern dentistry.

Conclusions. Given that certain extraoral pathologies arise as a result of damage by disseminated periodontopathogens, it is possible to provide new therapeutic opportunities to reduce the risk of developing comorbid conditions etiopathogenetically associated with generalized periodontitis.

The data of clinical and experimental studies that are presented in this literature review definitely show the need for timely treatment of periodontal diseases, which provides not only the health of the oral cavity, but also prevents the occurrence of general somatic diseases.

Ключові слова: захворювання пародонта, генералізований пародонтит, кардіоваскулярні захворювання, атеросклероз, цукровий діабет, захворювання шлунково-кишкового тракту.

Запорізький медичний журнал. 2023. Т. 25, № 1(136). С. 50-55

Роль патології пародонта та стану ротової порожнини у виникненні загальносоматичних захворювань

З. М. Гонта, І. В. Шилівський, О. М. Немеш, Х. Б. Бурда

Мета роботи – огляд сучасної вітчизняної та закордонної фахової літератури щодо впливу стану порожнини рота та патології тканин пародонта, зокрема генералізованого пародонтиту, на виникнення та тяжкість перебігу захворювань внутрішніх органів і систем організму.

Запально-дистрофічні захворювання пародонта спричиняють підвищення рівня хронічних запальних агентів через системне поширення запальних медіаторів, що вивільняються при місцевому руйнуванні тканин, а також при системному поширенні патогенних мікроорганізмів. Це зумовлює виникнення кардіоваскулярних захворювань, атеросклерозу, патологічних процесів у шлунково-кишковому тракті, ускладнює перебіг цукрового діабету та захворювань дихальної системи в пацієнтів із патологією пародонта. Саме тому дослідження патогенетичних взаємозв'язків захворювань пародонта та коморбідних станів є актуальною проблемою сучасної стоматології.

Висновки. Врахування того, що певні позаротові патології виникають внаслідок ураження дисемінованими пародонтопатогенами, може забезпечити нові терапевтичні можливості для зниження ризику виникнення коморбідних станів, етіопатогенетично пов'язаних із генералізованим пародонтитом.

Наведені в цьому огляді фахової літератури дані клінічних та експериментальних досліджень обґрунтовують необхідність своєчасного лікування захворювань пародонта, що сприяє не лише оздоровленню порожнини рота, але й запобігає виникненню загальносоматичних захворювань.

According to epidemiological studies, more than 95 % of the world population over 45 years suffer from periodontal disease, and among the people aged 31–44 years, the prevalence of periodontal pathology is more than 75 %, which indicates both a high morbidity rate and a significant reduction of patients' age [1].

In the structure of these diseases, 90 % of cases are inflammatory and dystrophic-inflammatory processes, which are usually quite often diagnosed in people aged 25–34 years.

It is worth noting a persistent tendency of dystrophic-inflammatory processes to prevail over inflammatory ones. In other words, generalized periodontitis (GP) is and continues to be dominant in the spectrum of periodontal diseases, and according to the results of epidemiological studies, it affects from 92 % to 98 % of the population in different regions of Ukraine over the age of 40 years [2,3].

At the same time, more than half of the examined patients with GP have concomitant systemic diseases. And many authors have studied the influence of concomitant pathology on the severity of a periodontal pathology course [4–6]. But it is no less important to study the impact of periodontal diseases on the development and course of general somatic pathology.

Aim

The purpose of the work: a review of modern national and foreign literature on the influence of the oral cavity state and the pathology of periodontal tissues, in particular generalized periodontitis, on the occurrence and severity of the course of internal organ and body system diseases.

A study of adverse effects of oral cavity diseases on the general condition of the human body was found by scientists in the ancient manuscripts. Researchers come across references to the fact that strong teeth are a sign of good health [7]. In a work by W. Hunter (1900), a cause of developing various pathologies of the body was called "sepsis of the oral cavity". The later-developed theory of focal infection considered that pathogenic microorganisms from infected tissues of the oral cavity spread throughout the body through the bloodstream, as a result of which various diseases develop [8]. At first sight, it seems that periodontal tissues occupy a rather insignificant place in the human body and pathological processes that develop there can not significantly affect its general condition. However, this is far from the case, and researches of recent decades have shown that any (even quite insignificant) inflammatory process in the periodontium affects the general condition of the body. Interest in the systemic effects of periodontitis was renewed in the early 1990s with clinical case-control studies and other epidemiologic studies demonstrating statistically significant associations between the oral cavity condition and systemic diseases [9].

GP is one of the most severe diseases in terms of course and occurrence of complications among diseases of the oral cavity. Inflammatory-dystrophic diseases of the periodontium have a complex, multistage character of pathological changes with gradual involvement of periodontal tissue structures, resulting in clearly defined clinical manifestations with impairment of periodontal functions. Periodontal changes are chronic, and the anti-infection protection of the oral cavity is low. At the same time, immune reactions do not provide resistance to the infected periodontium and become the pathogenetic basis of chronic processes. Among the risk factors, a violation of the oral cavity microbiocenosis and an imbalance of immunocompetent body systems, insufficient antioxidant protection, disturbances of microcirculation and transcapillary exchange in peri-dental tissues have the decisive importance. Periodontal disease contributes to an increase in chronic inflammatory agents through the systemic spread of inflammatory mediators released during local tissue destruction, the immune-inflammatory response to periodontal pathogens, and the systemic spread of pathogenic microorganisms. Frequent exacerbations of the disease and early loss of the teeth have a significant influence on the adaptation mechanisms of the entire maxillofacial system and cause a work failure of all parts of the chewing system. The formation of food chewing inefficiency, constant attacks of microbial substances from inflammatory focus of periodontal tissues create a favorable basis for the development of chronic diseases of internal organs and systems, form the background for the development of microbial and tissue sensitization, severe allergy of the body, and start the mechanisms of autoimmune disorders [8,10,11].

Periodontal diseases affect not only physical health, but also the emotional and social state of a person. People with anamnesis of GP show the signs of psycho-emotional stress as a result of aesthetic dissatisfaction with a smile and agnosia of the harmony of their appearance; the presence of discomfort manifests in the form of such symptoms as pain, bad breath, burning and gingival bleeding, lack of teeth, that generally reduce the quality of the patients' life. An aesthetic dissatisfaction with the state of periodontal tissues and dentition defects begins to dominate in the human consciousness, which worsens the quality of the life and makes impossible the normal integration in society [12,13]. Functional and organic disorders (neurasthenia, autonomic dystonia, etc.) characterized by a decrease in inhibitory processes and an increase in excitation processes were found in the majority of patients with GP [14].

Choi H. M. and co-authors (2015) studied the effect of oral hygiene on the level of blood pressure among 19,560 adults from the nationally representative KNHANES survey in 2008–2010. The analysis showed that individuals with poor oral hygiene had a higher incidence of arterial hypertension (AH) even before the development of periodontitis. The authors proposed to consider the state of oral hygiene as an independent indicator of the risk for developing AH, and hygienic care of the oral cavity – as an important preventive measure or the degree of control for the development of AH [15]. These data were confirmed by researches T. I. Vivcharenko and M. M. Rozhko (2016), who examined the oral cavity state in patients with stage II AH in combination with GP and did not find those with a good level of hygiene, while unsatisfactory hygiene was diagnosed in 40.0 %, poor – in 30.0 % of the examined [16].

The development of dental plaque (or biofilm) is one of the important mechanisms of bacterial persistence in the oral cavity in periodontal diseases. Supragingival biofilm consists mainly of gram-positive microorganisms: *Streptococcus mutans, Streptococcus sanguinis*, *Streptococcus salivarius, Streptococcus mitis, Lactobacilli*; while subgingival – from gram-negative: *Porphyromonas gingivalis, Tannerella forsythia, Aggregatibacer (Actinobacillus) actinomycetemcomitans, Campylobacter spp., Fusobacterium nucleatum, Treponema denticola.* In both cases, an accumulation of cells can generate high concentrations of metabolites (hydrogen peroxide, acids, ammonia, oxidants, etc.) that affect the species composition both within the microcolony and the organism as a whole [9,15,17].

In modern scientific studies, the role of oral microflora and GP as risk factors for cardiovascular diseases (CVD) is widely discussed [18–20]. In patients with chronic GP, the risk of CVD occurrence is significantly higher than that in patients with periodontal health. The results of studies on three proteins of the acute phase of inflammation (ceruloplasmin, α1-antitrypsin and orosomucoid) in oral fluid and blood plasma in periodontitis and myocardial infarction showed the parallelism of their changes. Authors [19] selected two main mechanisms that determined the importance of chronic GP as a risk factor for CVD: bacterial and atherosclerotic. Periodontopathogens increased the secretion of cytokines, which induced the synthesis of acute phase proteins and infected the endothelium and atherosclerotic vascular plaques, contributing to myocardial ischemia. The importance of prevention and treatment for periodontitis in reducing the prevalence of CVD was emphasized. The mechanism of the involvement of individual organs in

the systemic inflammatory response in periodontal pathology and its local manifestations require attention and further research in clinical dentistry [20].

The interest in this issue has increased in connection with the advent of the so-called "unified theory of atherogenesis" in recent years, which views atherosclerosis, having a leading role in the CVD development, as an immune-inflammatory process. The European Society of Cardiology and the European Atherosclerosis Society updated recommendations on the prevention of CVD in clinical practice, the problem of the dystrophic-inflammatory periodontal disease presence in patients with CVD and its possible relationship with the probability of the risk for adverse cardiovascular events was separately considered [21].

Chronic inflammatory-dystrophic diseases of the periodontium are viewed as a risk factor for the development of a systemic inflammatory response, which is the basis of vascular atherosclerosis. Agreement on periodontitis and atherosclerotic CVD, published in the American Journal of Cardiology and in the Journal of Periodontology, recommends informing patients with moderate and severe GP about the possible increased risk for CVD and the need to undergo a cardiac examination [22,23]. Dietrich T. and co-authors (2013) analyzed epidemiological data on the relationship between periodontal diseases and cardiovascular pathology [24]. And they proved the increased risk for CVD in patients with periodontal diseases under the age of 65 years. Madrid C. and co-authors (2009) affirm that periodontal diseases are characterized by inflammation and destructive changes and are one of the risk factors for the development of the systemic inflammatory response, that promotes to vascular damage and the development of atherosclerosis [25].

The scientists consider periodontal bacteria as factors of atherosclerosis and CVD due to the translocation of oral cavity bacteria into atherosclerotic plaque. Serra e Silva Filho W. and co-authors (2014) investigated the microbial species of periodontal pockets and atherosclerotic plaques and found 17 identical phylotypes, which were viewed by the authors as a bacterial translocation between the microflora of coronary arteries and periodontal pockets [6]. A similar possibility was also demonstrated in a study of E. Kozarov, who revealed viable *Porphyromonas gingivalis (P. gingivalis)* from an atherosclerotic plaque [26].

A number of authors emphasize that a similarity between the pathogenetic mechanisms of the periodontitis and CVD development is related to the ability of microorganisms and their endotoxins to cause inflammatory reactions, hemodynamic disturbances and metabolic tissue damage. An infected periodontium increases the risk of common pathological conditions by an involvement in the pathogenesis of the disease or by being a constant source of pathogenic microflora [27].

According to a number of authors, a damage to the internal organs and body systems is accompanied by pathological changes in the oral cavity, which become a source of chronic infection and lead to a dysfunction of the gastrointestinal tract [28,29]. On the other hand, inflammatory and destructive processes in the maxillofacial system, as a result of periodontitis, lead not only to the loss of teeth and a decrease in chewing function, but also to the secretory-motor dysfunction of the digestive system organs [30].

About 20 types of bacteria belong to periodontopathogens, which are separated into two groups according to the degree of virulence. The 1st group includes bacteria directly related to the disease progression, and the 2nd group includes bacteria that play the secondary role in the development of periodontal diseases. One of the main etiological factors of the gastrointestinal tract and oral cavity diseases is *Helicobacter pylori (H. pylori*), which colonizes very different parts of the oral cavity: periodontal pockets, mucous membrane of the tongue and cheeks, and oral and gingival fluid.

In line with epidemiological studies, more than 50 % of the adult population is infected with *H. pylori*, and the frequency of this bacterium detection in the gastrointestinal tract correlates with the socioeconomic status of the population and increases with age [31]. It has been found that the presence of *H. pylori* in the oral cavity significantly worsened the state of its hygiene. It has been proven that patients with *H. pylori* associated with gastrointestinal tract pathology were more likely to have catarrhal gingivitis and GP [32,33]. The prevalence of GP in patients with peptic ulcer disease of the stomach and duodenum in the presence of *H. pylori* is 94.6 %. Ryabokon E. N. and co-authors (2013) [34] came to the conclusion that the alterative processes occurring in the periodontium due to GP on the background of peptic ulcer disease created conditions for the contamination of periodontal pockets with *H. pylori.* And as a result, the latter turn into a permanent source of infection of the lower gastrointestinal tract. Scientists have repeatedly pointed out the ineffectiveness of eradication therapy aimed at destroying *H. pylori* in the stomach without neutralizing the pathogen persisting in the oral cavity. It has been scientifically proven that the simultaneous therapy of peptic ulcer disease and GP with the use of anti-*Helicobacter pylori* drugs in the schemes of complex treatment of GP resulted in a stabilization of periodontal status [35].

P. gingivalis found in periodontal pockets is a gram-negative obligate anaerobe that is capable of expressing specific virulence factors, gingipains, tetratricopeptide repeat sequence protein, including trichoderma, extracellular polysaccharides, lipopolysaccharides, hemoglobin uptake system, etc. A coactivation of gingipains with lipopolysaccharides leads to a disruption of the immune protection functions of periodontal tissues and causes the development of inflammation, destruction of the periodontium and the bone [34–36].

It has also been proven that *P. gingivalis* mediates a local inflammatory process in the periodontium with further adhesion and penetration into the deeper structural elements of the periodontium. At the same time, there are violations of normal physiological metabolism and a suppression of proteases involved in apoptosis, which are potential risk factors for the development of cancer. The development of neoplastic processes of the gastrointestinal tract is characterized by a high degree of comorbidity and mortality on the background of an unsatisfactory level of early diagnosis and high cost of treatment. The scientists have established a certain relationship between the tooth loss and the risk for developing gastrointestinal cancer, that was expressed by the dose-effect ratio. In particular, the overall risk for cancer was increased by 9 % for every 10 teeth lost, esophageal cancer – by 14 %, stomach cancer – by 9 %,

head and neck cancer – by 31 %, colorectal cancer – by 4 % and pancreatic cancer – by 7 % [36].

The relationship between diabetes and periodontal disease is the subject of numerous scientific studies. The frequency of periodontal diseases in diabetes is from 51 % to 98 %. At the same time, 18 % of patients with periodontitis present with diabetes. A dentist often makes a diagnosis of diabetes for the first time. Many patients are diagnosed with periodontitis at the initial stage of diabetes. It has been scientifically proven that the long course of GP led to a decompensation of diabetes, an increase in blood glucose, the need for sugar-lowering drugs and insulin resistance. Dystrophic-inflammatory processes in the periodontium complicate glucose control, increase the frequency of strokes, myocardial infarction, angina pectoris, and cardiovascular insufficiency. At the same time, the course of the pathological process in the periodontium depends not only on the decompensation of diabetes but is also largely determined by the development of vascular and infectious-inflammatory complications. Treatment of periodontal diseases at the early stages reduces the risk for severe complications of diabetes: it reduces the risk for myocardial infarction by 20 % and the risk for diabetic retinopathy with the further development of blindness or foot gangrene by 30 % [37].

Since the oral cavity is anatomically directly connected to the lower respiratory tract, pathogenic bacteria from the oral cavity can freely enter the lungs and cause inflammation. These may be exogenous bacteria, which are not characteristic of the oral cavity microflora, or endogenous bacteria, which cause opportunistic diseases. Inflammatory periodontal diseases increase the biological activity of inflammatory mediators and hydrolytic enzymes present in the oral fluid. They can also enter the respiratory tract, increasing susceptibility to infection and causing inflammation. Recent data suggest that the microorganisms that cause inflammatory periodontal disease are associated with respiratory diseases [15,38,39].

So, GP is a common inflammatory-dystrophic disease of the oral cavity, associated with other chronic disorders caused by inflammation, including, autoimmune diseases, cardiometabolic, neurodegenerative and cancer. Researches of recent years show that local treatment of periodontitis improves surrogate markers of concomitant diseases [5,30,40]. The potential causally resulting relationship between periodontitis and its comorbidities is supported by experimental animal studies. They have revealed biologically verisimilar and clinically consistent mechanisms by which periodontitis can initiate or worsen comorbidities [41].

Conclusions

1. Inflammatory-dystrophic periodontal diseases mainly have a prolonged and generalized course with low anti-infection protection of the oral cavity. Increasing the level of chronic inflammatory agents due to the systemic spread of inflammatory mediators released during local tissue destruction, immune-inflammatory response to periodontal pathogens, as well as the systemic spread of pathogens – all this can contribute to the development of atherosclerosis, cardiovascular diseases, pathological processes of the gastrointestinal tract and other body systems.

2. Given that certain extraoral pathologies arise as a result of damage by disseminated periodontopathogens, it is possible to provide new therapeutic opportunities to reduce the risk of developing comorbid conditions etiopathogenetically associated with generalized periodontitis. The data of clinical and experimental studies that are presented in this literature review definitely show the need for timely treatment of periodontal diseases, which provides not only the health of the oral cavity, but also prevents the occurrence of general somatic diseases

Funding
The study was carried out within the research work of the Danylo Halytsky Lviv National Medical University "Metabolic disorders and their influence on the development of combined dental and somatic pathology", state registration No. 0120U002131.

Conflicts of interest: authors have no conflict of interest to declare.
Конфлікт інтересів: відсутній.

Надійшла до редакції / Received: 31.10.2022
Після доопрацювання / Revised: 25.11.2022
Прийнято до друку / Accepted: 02.12.2022

Information about authors:
Honta Z. M., MD, PhD, Associate Professor of the Department of Therapeutic Stomatology, Periodontology and Stomatology of the Faculty of Postgraduate Education, Danylo Halytsky Lviv National Medical University, Ukraine.
ORCID ID: 0000-0001-9180-823X
Shylivskyi I. V., MD, PhD, Associate Professor of the Department of Therapeutic Stomatology, Periodontology and Stomatology of the Faculty of Postgraduate Education, Danylo Halytsky Lviv National Medical University, Ukraine.
ORCID ID: 0000-0001-8544-1398
Nemesh O. M., MD, PhD, Associate Professor of the Department of Therapeutic Stomatology, Periodontology and Stomatology of the Faculty of Postgraduate Education, Danylo Halytsky Lviv National Medical University, Ukraine.
ORCID ID: 0000-0002-1768-8281
Burda Kh. B., MD, PhD, Assistant of the Department of Therapeutic Stomatology, Periodontology and Stomatology of the Faculty of Postgraduate Education, Danylo Halytsky Lviv National Medical University, Ukraine.
ORCID ID: 0000-0002-1454-3079

Відомості про авторів:
Гонта З. М., канд. мед. наук, доцент каф. терапевтичної стоматології, пародонтології та стоматології ФПДО, Львівський національний медичний університет імені Данила Галицького, Україна.
Шилівський І. В., канд. мед. наук, доцент каф. терапевтичної стоматології, пародонтології та стоматології ФПДО, Львівський національний медичний університет імені Данила Галицького, Україна.
Немеш О. М., канд. мед. наук, доцент каф. терапевтичної стоматології, пародонтології та стоматології ФПДО, Львівський національний медичний університет імені Данила Галицького, Україна.
Бурда Х. Б., канд. мед. наук, асистент каф. терапевтичної стоматології, пародонтології та стоматології ФПДО, Львівський національний медичний університет імені Данила Галицького, Україна.

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