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PATHOPHYSIOLOGICAL ASPECTS OF PERIODONTAL DISORDERS IN VARIOUS SOMATIC DISEASES

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ABSTRACT

The review of scientific researches related to the study of pathophysiological basics of periodontal disorders in various somatic diseases is carried out. The study of scientific data has shown that the somatic pathology is very essential factor in the etiology of periodontal disorders. Somatic pathology includes the diseases of the digestive, respiratory, cardiovascular, urinary, endocrine and immune systems.

KEYWORDS: ***periodontal disease, oral mucosa, somatic diseases, inflammation, periodontitis, periodontal disease, microcirculation***

It is well known that there is a close morphofunctional relationship of oral diseases with the pathology of internal organs of the human body. Studies carried out by various authors have found out that severe somatic pathology (cardiovascular pathology, malignant neoplasms, diseases of the gastrointestinal tract) and alcohol or drug intoxication can be the key factor of the anamnesis leading to certain functional shift in the oral cavity.

All the data are systematized and distributed in this review based on the influence of various human body systems on the state of the periodontium and oral mucosa generally.

DIGESTIVE SYSTEM

Nowadays there are a lot of scientific researches have been carried out that are related to the corellation between diseases of the oral mucosa and the state of gastrointestinal tract. According to epidemiological studies, more than 50% of the adult population is being infected by H. pylori. The frequency of detection of this microorganism in the stomach increases with age and correlates with the socio-economic status of the patient [13,28,30]. The relationship between the presence of H. pylori in the oral cavity and its poor hygienic condition was noted [21]. It was found that chronic generalized catarrhal gingivitis and periodontitis are more common and more severe in patients with H. pylori-associated pathology of the gastrointestinal tract [6,21]. The pathological process in the mucous membrane of the stomach and duodenum is accompanied with a decrease in the content of T-lymphocytes and their functional activity, as well as local autoimmune reactions leading to damage to periodontal tissues. The persistence of H. pylori in the oral cavity can serve as a source of reinfection of the gastric mucosa providing the recurrence of peptic ulcer disease [16,17,18].

I. Lutskaya in her review study notes that diseases of the gastrointestinal tract have some specific oral symptoms which appear even before the manifestation of main pathology. Patients complain of itching and periodontal pain, especially during meals. Symptoms are aggravated by the presence of metal dentures. Hypoacid gastritis is characterized by desiccation of the oral cavity, atrophy of the filiform papillae of the tongue. Hyperacid gastritis is characterized by an abundant plaque on the tongue, hypersalivation, hyperplasia of the papillae of the tongue and increased desquamation of the epithelium [10].

Peptic ulcer is accompanied with such complaints as burning sensation, soreness and an increase in the size of the tongue due to swelling.

Enterocolitis, accompanied by water retention in the body, is characterized by swelling of the mucous membrane of the cheeks, tongue with the appearance of tooth prints. Cheek biting may be noted too. In such cases, erosions with uneven margins and scraps of epithelium are found on the surface of oral mucosa.

Liver diseases are characterized by jaundice of the sclera and oral mucosa, bleeding gums, gingivitis, periodontitis, glossitis. There is a distortion of taste, a bitter taste in the mouth. In some cases, persistent painful burning sensations, tingling in the tongue, on the palate, and lips are noted [5,10].

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RESPIRATORY SYSTEM

As the oral cavity has a direct connection with the trachea and the lower respiratory tract, pathogenic bacteria localized in the oral cavity can freely enter the lungs and cause inflammation.

N. Bulkina et al. [5] indicate that inflammatory diseases of periodintium increase the biological activity of proinflammatory mediators and hydrolytic enzymes contained in the gingival fluid, which can also reach the respiratory tract increasing sensitivity to infection and cause inflammation there. Microorganisms that cause inflammatory diseases of periodintium are associated with respiratory tract diseases.

I. Lutskaya notes that lobar pneumonia is often characterized by herpetic rashes on the oral mucosa [10].

The lips often look overdried in patients suffering from pulmonary tuberculosis. In asthma, the skin and oral mucosa are pale, the vermilion border is cyanotic. Cyanosis of the mucous membrane of the hard palate and periodontal tissues is often noted.

In case of destructive processes of the respiratory system oral mucosa loses its moisture and elasticity.

The dryness of the oral mucosa often noted in rhinosinusitis contributes to the appearance of cracks, erosions in areas prone to injury, which leads to infection and the occurrence of inflammation in the tissue.

CARDIOVASCULAR SYSTEM

According to I. Gorbacheva et al., there is a close relationship of periodontal pathology and cardiovascular diseases determined by the unity of the main pathogenetic links [8]. The scientists suppose that one of the most important common pathogenetic factors is a violation in the microcirculation. It is well known as the basis of inflammatory and destructive diseases of the periodontium and oral mucosa.

Generalized periodontitis is the most typical oral pathology in patients with cardiovascular diseases.

The study conducted by the authors at the Department of internal diseases of the St. Petersburg State Medical University once again has proved that periodontal tissues are being inevitably included in the process of tissue remodeling according to the cardiovascular continuum program, or the occurrence of atherosclerotic changes in vessels affected by endothelial dysfunction. I. Gorbacheva, A. Kirsanov et al. propose to use such termin as periodontal continuum that can be assumed in the context of assessing the interrelationships of inflammatory-degenerative modification of periodontal tissues in conditions of polymorbid pathology [7,9].

Obviously that disorders in the microcirculatory system, particularly in the head and neck region, affect the perfusion of the oral tissues, which contributes to a more active course of pathological processin the periodontium and teeth. The vessels of the dental plexuses become more vulnerable, due to their anatomical features.

It has been found that microcirculatory system of the periodontium undergoes changes with constant or frequent stress of the vascular system. Patients with chronic generalized periodontitis and comorbid cardiovascular disease such as arterial hypertension, hypoxia contributes to an increase in the excitability of the sympathoadrenal system. It provides the vasoconstriction, degradation of redox processes in periodontal tissues, a decrease in the adaptive capabilities of connective tissue and microcirculary system.

Authors point out that the thickening of the basement membrane of small vessels with a decrease in the transport of oxygen and nutrients through the blood vessel wall may be the main mechanism of the pathogenesis of periodontal diseases.

Cigarette smoking is also associated with periodontitis, and the mechanisms underlying the pathogenic effect on periodontal tissue include suppression of neutrophil function in saliva and connective tissue and the formation of defective immunoglobulin G2.

Recent researches show the relationship between periodontitis and coronary heart disease (CHD). Microcirculation disorders and increased permeability of arterioles and capillaries may be common factors in the development of a "hypertensive heart" and periodontitis in patients with arterial hypertension. Pressure overload can induce generalized narrowing of the microvessel lumen. That condition causes increase in vascular permeability that can lead to ischemia in the tissues of the heart and periodontium.

V. Tsarev et al. note that pathogenic microorganisms that have penetrated into the blood from the oral cavity can cause heart damage, leading to the development of infectious endocarditis [15].

The likelihood of development of cardiovascular and neurovascular diseases is increased by proinflammatory factors produced during the chronic infectious process –

C–reactive protein, increased white blood cell count and fibrinogen of the blood, tumor necrosis factor-alpha, pro-inflammatory cytokines, which may be an independent risk factor for atherosclerosis, angina pectoris, as well as primary or recurrent stroke [25].

Nowadays the association of IL-1ß with an increase in the risk of severe periodontitis and the development of atherosclerotic plaques inside the vessels has been proved. The level of IL-6 is also very high in chronic periodontitis. It causes the stimulation of the synthesis of fibrinogen in the liver in the acute phase response, which contributes to the formation of a blood clot in blood vessels, ending in myocardial infarction and stroke. TNF-α increases the synthesis of triglycerides in the liver, which leads to a decrease in the level of high-density lipoproteins, which is directly related to coronary heart diseases [22].

At the same time, as noted by Y. Hosokawa et al., inducers of apoptosis, similar to tumor necrosis factor by the effect, can cause programmed cell death of gingival fibroblasts and a shift in the balance of cytokines, which has a pro-inflammatory effect and probably plays a significant role in the pathogenesis of periodontitis and inflammatory diseases of the oral mucosa [26].

Abhijit N. Gurav in the study [20] concludes that , uncontrolled endothelium-dependent synthesis of NO which leads to increased vasodilation occurs in local vessels as a result of the effects on the periodontium. Long–term vasodilation leads to alteration of the vascular wall, which is accompanied by increased synthesis of proinflammatory mediators - cytokines, adhesins, IL-1, TNF-α, prostoglandins.

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Due to the weakening of local immune protection, the pathogenic effect of the microflora of plaque and the subgingival zone is activated. Monocytes actively arrive at the focus of inflammation, transforming into macrophages. Sometimes they can accumulate at damaged points of the vascular wall (as in atherosclerosis). Mediators again induce the synthesis of mediators, which further leads to the weakening of local immunity. Bacteria (anaerobic bacilli and spirochetes) actively penetrate through vessel walls and cause systemic uncomplicated bacteremia. This condition may form an autoimmune process due to the synthesis of special HSP proteins as a response to endothelial alteration.

De Stefano F. et al. noted that an increase in deaths from heart failure was related with an increased prevalence of severe forms of periodontal disease [24].

URINARY SYSTEM

Clinical observations indicate that kidney disease aggravates the pathological process in the periodontium [11,19,23], which is caused by the effect of accumulating metabolites, disorders of acid-base and water-electrolyte balance. A more significant resorption of the interalveolar septa was revealed in patients with renal pathology and periodontitis, compared with patients with periodontitis without comorbid pathology. This sign deems to be a manifestation of generalized nephropathic osteodystrophy, which is caused by such reasons as impaired formation of the active form of vitamin D in the kidneys, increased function of the parathyroid glands, the development of a negative calcium balance.

M. Medzhidov and M. Efendiev [12], summarizing the study, believe that the lower intensity of the inflammatory process in patients who had both chronic pyelonephritis and chronic generalized periodontitis is related with the use of effective anti-inflammatory drugs in the treatment of CP. At the same time, these patients, compared with patients only suffering from chronic generalized periodontitis, had a more significant resorption of the interalveolar septa which is probably a manifestation of generalized nephropathic osteodystrophy.

Moreover, conversely, the content of immunoglobulins in peripheral blood of patients suffering from chronic generalized periodontitis in combination with chronic pyelonephritis, show significant differences compared to the norm: IgG (25.65 ± 1.18) and IgM (1.32 ± 0.08) concentrations were significantly increased, and IgA (1.19 ± 0.06) levels decreased significantly, respectively.

Thus, the authors conclude that the clinical features of chronic generalized periodontitis combined with chronic pyelonephritis are a weak inflammatory reaction in periodontal tissues, the absence of deep gingival pockets, no suppuration, significant mobility of teeth, abundant deposition of sub- and supra-gingival stone, as well as a high level of gum recession. The above-mentioned clinic features may be caused by the antibacterial and anti-inflammatory therapy that patients have repeatedly received due to the exacerbation of the chronic inflammatory process in the kidneys.

Patients with chronic renal insufficiency suffer from spontaneous bleeding of the gums, they often complain of a taste of blood in the mouth.

M. Astakhova et al. note that the leading complaint from patients with chronic pyelonephritis is the exposure of the necks of the teeth, but since the process proceeds painlessly, patients get to the dentist too late. Laser Doppler flowmetry shows in such situation significant changes in the microcirculation of periodontal tissues were noted [1].

Patient with chronic pyelonephritis usually have detectable inflammatory and dystrophic changes in periodontal tissues, occurring painlessly and without bleeding gums at the time of the study; a decrease in the effectiveness of microcirculation of the gum vessels according to LDF data is found.

THE ENDOCRINE SYSTEM

The most distinct changes in periodontal disease are noted in patient with the pathology of the pancreas, manifested with a violation of carbohydrate metabolism and the development of diabetes mellitus.

N. Bulkina et al. [3,4,5] say that angiopathies are the main elements in the pathogenesis of periodontal syndrome in patients with diabetes mellitus. The starting point is a violation of carbohydrate and glycosamine metabolism, which determine the functional and structural integrity of the vascular basement membrane. Diabetic microangiopathy is based on the plasmorrhagia. It is a primary plasma damage of the basement membrane of the microcirculatory system, after which sclerosis and hyalinosis of the vessel walls begins. According to the authors, these changes have nothing to do with inflammation. Consequently, microcirculatory disorders are primary on the background of already existing transcapillary metabolism, increased permeability of connective tissue structures of the periodontium, hypoxia and decreased resistance of periodontal tissues to negative factors. The pathogenic microflora of the gingival fissure causes inflammatory and destructive processes, and the arising overload of periodontal tissues further aggravates the situation [14]. It is also believed that changes in the gum and bone are dystrophic, and inflammation joins as a secondary component due to weakening of the body's resistance [29]. The most characteristic and severe sign of periodontitis in patients suffering from diabetes mellitus is dystrophy of the alveolar process with resorption of the interdental septa, which leads to early loss of permanent teeth. Rapid progression of the dystrophic and inflammatory process in the periodontal tissues and frequent recurrence of periodontal abscesses are noted.

M. Bogomolov notes that the symptoms and causes of the peculiar development of periodontitis in diabetes are based on the mutually aggravating course of both diseases [4]. The early stage of periodontitis is gingivitis. The painlessness of gingivitis in diabetes can be provoked by peripheral diabetic polyneuropathy. However. there are signs of inflammation – swelling, redness and bleeding gums. However, if gingivitis is not treated, it leads to further progression and development of periodontitis, in which as well the soft tissues as bone supporting the tooth too are affected, which eventually leads to adentia. Diabetes also independently aggravates the course of osteoporosis. Prolonged periodontitis leads to decompensation of diabetes,

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an increase in blood sugar level, an increase in the need for hypoglycemic drugs.

The inflammatory and cytokine response observed in diabetes leads to impaired lipid metabolism, insulin resistance, and long-term microvascular complications. Chronic periodontitis can enhance the cytokine response that has already begun and provoke the development of systemic inflammation syndrome.

S. Babadjanian in his review study notes the fact that vascular disorders in diabetic patients develop not only due to spastic changes in blood vessels and capillaries, but also due to changes in the function of the blood itself (an increase in the diameter of red blood cells, the accumulation of glycated hemoglobin) [2].

THE IMMUNE SYSTEM

The inflammatory process in periodontitis has some autoimmune features. As the concentration of specific IgA antibodies to periodontopathogenic microorganisms increases it may increase the risk of autoimmune reactions towards the vascular endothelium. Thus, some patients with periodontitis have cross-immune reactions towards both bacterial antigens and arterial wall cells. At the same time, it was shown that all the studied samples of arterial tissues could cross-react with P. gingivalis antigens.

According to the study of I. Lutskaya [10], ulcerative-necrotic gingivitis develops in HIV-infected patients both during periods of clinical manifestations of AIDS, and without them in the presence of antibodies against the virus. Patients complain of pain and bleeding gums during brushing and eating, bad breath. A gray-yellow plaque (necrotic film) covering the gingival margin and interdental papillae is found during the examination. The mucous membrane of the gum area is hyperemic, edematous, tense. The symptoms disappear after treatment, but there is a huge tendency to relapse. Prolonged course can contribute to the development of deep ulcers with damage to bone structures, necrotization of the interdental septum.

The complication of this type of gingivitis is periodontitis with irregular generalized destruction of bone tissue and the supporting apparatus of the tooth. Treatment of patients does not provide a stable result.

G. Barer [3] notes that there are a lot of violations of the immune response at the cellular level detected in the inflamed periodontium caused by damage and weakening of neutrophils and monocytes. At the same time, a decrease in all cellular functions of polymorphonuclear neutrophil leukocytes, including their chemotaxis and adhesion, is found [27].

CONCLUSION

Thus, pathological processes of somatic genesis have a negative impact on the state of periodontal tissue, and this influence is manifested by the development of inflammatory and degenerative phenomena, leading to periodontal disease. It is interesting that the process is not limited. Both the complex of supporting tissues of the tooth and oral mucosa, including the tongue, gums, hard and soft palate, are being involved. This fact again proves the inseparable connection between the oral cavity and other morphological structures.

A number of questions related to the fact of the degree of reversebility of the pathological processes in the periodontium in case of elimination of the main pathological focus are not revealed. There have not been found any data on the reparative and regenerative direction of the processes in the periodontal tissues in this case.

LITERATURE

1. *Астахова М. И., Герасимова А. П., Павлов В. Н. Состояние тканей пародонта у больных хроническим пиелонефритом по данным лазерной допплеровской флоуметрии. – «Пародонтология», № 2 (47), 2008, с. 15-19*
2. *Бабаджанян С. Г., Казакова Л. Н.. Влияние эндокринной патологии на развитие и течение заболеваний в полости рта (обзор). // Саратовский научно-медицинский журнал. 2013. Т. 9, № 3. С. 366–369.*
3. *Барер Г. М., Григорян К. Р.. Пародонтит у больных сахарным диабетом I типа (обзор литературы). – «Пародонтология», № 2 (39), 2006, с. 6 – 10*
4. *Бабаджанов Ж. Б., Шарипова П. А. Патофизиологические основы нарушений состояния пародонта при различных соматических заболеваниях –*
5. *Научно-практический журнал «Stomatologiya», № 2 (75), 2019, с. 72-75*
6. *Булкина Н. В., Ведяева А. П., Савина Е. А. Коморбидность заболеваний пародонта и соматической патологии / Медицинский вестник Северного Кавказа, № 3, 2012, с. 110 – 115*
7. *Булкина, Н.В. Сочетание заболеваний полости рта и органов пищеварения / Н.В. Булкина, А.В. Лепилин, М.А. Осадчук. – Саратов, 2005. – 121 с.*
8. *Горбачева И. А., Кирсанов А. И. Патогенетическая роль системных механизмов свободнорадикального окисления при сочетанных заболеваниях внутренних органов и пародонта // Вестник Санкт-Петербургской государственной медицинской академии им. И. И. Мечникова. 2003. №3. С. 135-138.*
9. *Горбачева И. А., Орехова Л. Ю., Сычева Ю.А., Шабак-Спасский П.С., Султанова Н.Ф., Зайцева М.А.. Роль сердечно-сосудистой патологии в формировании воспалительно-дегенеративных заболеваний пародонта. «Пародонтология», № 4 (49), 2008, с. 18 – 21*
10. *Кирсанов А. И., Орехова Л. Ю., Горбачева И. А. Единство системных патогенетических механизмов при заболеваниях внутренних органов, ассоциированных с генерализованным пародонтитом // Ученые записки СПбГМУ им. акад. И. П. Павлова. Т. IX. 2002. №3. С. 71-78.*
11. *Луцкая И. К. Проявления на слизистой оболочке полости рта заболевания внутренних органов и СПИДа // Журнал "Клиническая практика и здоровье", № 6, 2013, с. 32 – 53*
12. *Мартьянова Т. С. Состояние пародонта у больных хроническим гломерулонефритом: Автореф. дис. канд. мед. наук. – СПб., 2009. – С. 19.*
13. *Меджидов М. Н., Эфендиев М. Н. Клинические особенности течения пародонтита и состояние гуморального иммунитета у больных хроническим пиелонефритом. - «Пародонтология», № 4 (69), 2013, с. 54 – 58*
14. *Орехова, Л.Ю. Клинико-иммунологические и микробиологические параллели при хроническом генерализованном пародонтите и язвенной болезни желудка / Л.Ю. Орехова, Д.М. Нейзберг, И. Ю. Стюф // Стоматология. – 2006. – № 6. – С. 22–26.*

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Volume: 8| Issue: 5| May 2022|| Journal DOI: 10.36713/epra2013 || SJIF Impact Factor 2022: 8.205 || ISI Value: 1.188

15. *Прохончуков, А.А. Патогенез экспериментальных пародонтопатий / А.А. Прохончуков, Н.А. Жижина. – М., 1971. – 175 с.*
16. *Царев, В.Н. Возможная роль микрофлоры полости рта в развитии инфекционного эндокардита / В.Н. Царев, М.А. Саркисян, Г.А. Шамсиев // Медицина критических состояний. – 2010. – № 1. – С.11–15.*
17. *Цимбалистов, А.В. Пародонтологический статус Helicobacter pylori-инфицированных больных язвенной болезнью / А.В. Цимбалистов, Н.С. Робакидзе // Труды IV съезда стоматологических ассоциаций России. – М., 2000. – С. 255–257.*
18. *Цимбалистов, А.В. Патофизиологические аспекты развития сочетанной патологии полости рта и желудочно-кишечного тракта / А.В. Цимбалистов, Н.С. Робакидзе // Стоматология для всех. – 2005. – № 1. – С. 28–34.*
19. *Циммерман, Я.С. Helicobacter pylori – инфекция: внежелудочные эффекты и заболевания (критический анализ) / Я.С. Циммерман // Клиническая медицина. – 2006. – № 4. – С. 63–67.*
20. *Ящук Е. В. Состояние полости рта у больных с терминальной стадией хронической почечной недостаточности, находящихся на диализной терапии: Автореф. дис. канд. мед. наук. – СПб., 2009. – 24 с.*
21. *Abhijit N. Gurav. The implication of periodontitis in vascular endothelial dysfunction // European Journal of Clinical Investigation, Vol. 44 (10) – 2014. – P. 1000–1009*
22. *Anand, P.S. Are dental plaque, poor oral hygiene and periodontal disease associated with Helicobacter pylori infection? / P.S. Anand, K. Nandakumar, K.T. Shenoy // J. Periodontol. – 2006. – Vol. 77,№ 4. – P. 692–698.*
23. *Armitage, G.C. Periodontal infections and cardio-vascular disease-how strong is the association? / G.C. Armitage // Oral. Dis. – 2000. – Vol. 6, № 6. – P. 335–350.*
24. *Craig R. G. Interactions between chronic renal disease and periodontal disease // Oral Dis. 2008. Jan. №14 (1). P. 8-9.*
25. *De Stefano, F. Dental disease and risk of coronary heart disease and mortality / De Stefano F. [et al.] // Brit. Med. J. – 1993. – Vol. 306. – P. 688-691.*
26. *Hajishengallis, G. Interactions of oral pathogens with toll-like receptors: possible role in atherosclerosis / G. Hajishengallis, A. Sharma, M.W. Russell, R.J. Genco // Ann. Periodontol. – 2002. – Vol. 7, № 1. – P. 72–78.*
27. *Hosokawa Y., Hosokawa I., K. Ozaki, H. Nakae and T. Matsuo. Proinflammatory effects of tumour necrosis factor-like weak inducer of apoptosis (TWEAK) on human gingival fibroblasts // British Society for Immunology, Clinical and Experimental Immunology – 2006 - 146: P. 540–549*
28. *Iacopino A. Diabetic periodontitis: possible lipid-induced defect in tissue repair through alteration of macrophage phenotype and function // Oral Diseases. – 1995. – Vol. 1. – P. 214-229.*
29. *Kim N., Lim S.H., Lee K.H. [et al.]. Helicobacter pylori in dental plaque and saliva / // Korean J. Int. Med. – 2000. – Vol. 15. – P. 187–194.*
30. *Kraemer, H.C. Statistical issues in assessing comorbidity / H.C. Kraemer // Stat Med. – 1995. – Vol.14. – P. 721–723.*
31. *Malaty, H.M. Epidemiology of Helicobacter pylori infection /H.M. Malaty // Best Pract. Res. Clin. Gastroenterol. – 2007. – Vol. 21, № 2. – P. 20 –214*