INFLUENCE OF ORAL MICROBIOTA ON THE DEVELOPMENT OF INFLAMMATORY AND SOMATIC DISEASES

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ANNOTATION

The review presents the modern concept of the oral microbioma, its species diversity, the properties of microbial associations and their effect on the immunobiological resistance of the organism, the development of chronic inflammation and the two leading infectious and inflammatory diseases, dental caries and periodontal diseases. Briefly summarized information about the presence and nature of the relationship between the composition of periodontal microorganisms and concomitant somatic diseases: in atherosclerotic plaques in cardiovascular diseases, with pathology of the gastrointestinal tract, respiratory system and other organs and systems.

Keywords: *microbiology, oral cavity, somatic diseases.*

The connection between infections of the dentition and diseases in other anatomical areas of the body has been known for more than a hundred years, which contributes to the search for common etiological and pathogenetic factors of these disorders. But only with the advent of molecular genetic methods of research did the study of the biology of microorganisms (microbiome) really begin as one of the leading triggers for the development and progression of inflammatory diseases of the dental system. This is very important to take into account in the treatment of diseases of hard tissues of the tooth, periodontium and the prevention of inflammatory complications after relatively clean operations in the oral cavity.

Various microorganisms inhabit the mucous membranes, back of the tongue, gingival sulcus, oral fluid and plaque, receiving the necessary proteins, carbohydrates, amino acids, inorganic and other substances from the oral fluid. Occupying only 0.03–0.05 m2 of the area of the oral cavity, the microbiome of this ecological niche includes representatives from 530 to 700 stable species [1, 2]. In addition to the leading bacteria Actinomyces, Campylobacter, Capnocytophaga, Corynebacterium, Fusobacterium, Neisseria, Granulicatella, Prevotella, Streptococcus, Veillonella, including anaerobic protelytic Filifactor, Fusobacterium, Parvimonas, Porphyromonas, Prevotella, Tannerella and Treponema, Candida albicans constantly exists in the oral cavity, C. tropicalis, C. pseudotropicalis, C. guilliermondi, Paramyxoviridae and Herpesviridac viruses, protozoa Entamoeba gingivalis and Trichomonas tenax, mycoplasmas M. ovale and M. salivarium, arhaea, etc. [3–6]. Accumulating in dental plaque (a combination of plaque and tartar), which, according to modern interpretation, is nothing more than a biofilm consisting of polymicrobial communities [7–9], the populations of the above microorganisms develop sequentially, are closely related to the internal environment of the body and his environment, sensitively reacting to their condition.

One of the most important functions of the oral microbiome is the maintenance of specific and non-specific, humoral and cellular mechanisms of immunity. Thus, bifidobacteria stimulate the development of the lymphoid apparatus, the synthesis of immunoglobulins, increase the level of properdin and complement, activate lysozyme, reduce the permeability of histohematic barriers, prevent the development of bacteremia, sepsis, etc. At the same time, a number of bacterial species that persist on the surface of the teeth and periodontal pockets, produce lipopolysaccharides (endotoxins), carboxylic acid, hydrolytic and proteolytic enzymes and other metabolites that trigger a cascade of immunological processes that cause inflammation and destruction of periodontal cells. Strains of Streptococcus mutans, S. mitis, S. Salivarius, S. sanguis, Lactobacillus, Actinomyces israelii, A. viscosus and A. naeslundi ferment carbohydrates, primarily sucrose to malic, pyruvic, lactic, formic and other organic acids, which destroy tooth enamel and wash out calcium and fluorine from it. As a result, permanent (resident) microorganisms of the oral cavity are more often associated with two leading infectious and inflammatory diseases - dental caries and periodontal diseases (a complex of tissues surrounding and holding the tooth in the alveolus). Their development also depends on the state and structure of the oral mucosa and gum pockets, the condition of the teeth, temperature, pH, properties, rate of secretion and chemical composition of saliva, nutrition, oral hygiene, oral breathing, etc. [10] .

According to the conclusion of the World Health Organization (WHO), in most developed countries of the world, caries affects from 60 to 90% of young people and adults, while in Asian and Latin American countries it covers them in 100%. In Russia, more than 80% of the population suffers from caries [11].

The more carious teeth in the oral cavity and the longer they are delayed with their treatment, the faster the periodontium is damaged. With a deterioration in the hygienic condition of the oral cavity or somatic pathology, a spontaneous, with minor symptoms (blood streaks when brushing teeth, bad breath), the disease begins - periodontitis, which progresses over the years, is characterized by the complete destruction of all periodontal tissues and leads to loss of teeth, impaired speech and chewing apparatus. Moreover, foci of infection in periodontal pockets adversely affect the body as a whole, even life threatening. Periodontitis affects 98% of the adult population of the planet. In Russia, an intact periodontium occurs only in 12% of the population, 53% have initial inflammatory phenomena, and 12% have moderate and severe lesions. The prevalence of periodontal disease among the adult population is 82% [7, 12]. The development of periodontitis is mainly associated with the action of mixed bacterial-yeast infections in combination with anaerobic bacteria. Among the periodontal microbial complex, anaerobic bacteria Aggregatibacter actinimycetemcomitans, Porphyromonas gingivalis, Tannerella forsythia, Treponema denticola are extremely aggressive and tend to intracellular parasitism in the gingival epithelium and periodontal tissues [4, 7]. Overcoming the epithelium of the periodontium and inducing the inflammatory process, they migrate hematogenously to other parts of the body.

In the scientific literature, there is a lot of evidence of the conjugation of inflammatory lesions of the periodontium with diseases of the internal organs. First of all, a number of researchers come to the conclusion about the pathogenetic commonality of generalized periodontitis and atherosclerosis with damage to the aorta, coronary and peripheral vessels [4, 13]. V.I. Haraszthy et al. [14], studying atherosclerotic plaques of human carotid arteries using polymerase chain reaction (PCR), found Chlamydia pneumoniae, human cytomegalovirus, and bacterial 16S rRNA in them. F. Cairo et al. [15] found T. forsynthensis in 79% of carotid artery plaques, F. Nucleatum in 63%, P. intermedia in 53%, P. gingivalis in 37%, and A. Actinomycetemcomitans in 5%. A. Pucar et al. [16] identified the same bacteria in large and small arteries with atherosclerotic lesions. Somewhat later, K. Nakano et al. [17] reported that A. Actinomycetemcomitans, Streptococcus mutans, S. sanguinis, P. gingivalis, and T. denticola were found in aortic and heart valve plaques.

There is even evidence of a direct effect of bacteria on the endothelial cells of blood vessels. In 2012

The American Heart Association (AHA) published an analysis of 537 literature sources confirming the influence of periodontitis on the development of atherosclerosis [4]. This happens in two ways: either bacteria from the bloodstream penetrate into the vascular endothelium and cause endothelial dysfunction, inflammation, and atherosclerosis, or they indirectly stimulate the production of mediators with atherogenic and pro-inflammatory systemic effects [18, 19]. The penetration and survival of the bacteria S. mutans, P. gingivalis, and P. intermedia inside aortic endothelial cells was confirmed in experiments in vitro. In his work, O.A. Gulyaeva et al. [7] cite further facts: with a severe degree of periodontitis, the risk of myocardial infarction increases by 3 times, atherosclerosis and stroke - by 2 times, osteoporosis - by 4 times, diabetes - by 2–11 times, chronic bronchitis - by 2 times. -4 times, 4-8 times increased risk of complications during pregnancy. Microbiological studies of atherosclerotic plaques in human carotid arteries revealed not only Porphyromonas gingivalis and Streptococcus sanguis. Using PCR, Actinobacillus actinomycetemcomitans, Porphyromonas gingivalis, Bacteroides forsythus, Treponema denticola, and Campylobacter rectus were verified in atherosclerotic plaques of coronary vessels. The presence of Actinobacillus actinomycetemcomitans, Porphyromonas gingivalis, Prevotella nigrescens, Fusobacterium nucleatumperiodonticum and Tannerella forsythia in coronary atheromas has been proven. The same PCR method in 19.7% of patients with acute myocardial infarction in blood clots revealed Aggregatibacter actinomy-cetemcomitans, 3.4% - Porphyromonas gingivalis and 2.3% - Treponema denticola. In chronic generalized periodontitis associated with coronary heart disease, A.F. Eliseeva found Treponema forsythensis, T. denticola, Porphyromonas gingivalis and their combination with Chlamydia trachomatis in the contents of periodontal pockets and vessels of the heart. It is assumed that Porphyromonas gingivalis, penetrating into endothelial cells, triggers the process of platelet aggregation and participates in thrombus formation of blood vessels. Many Streptococci species, predominantly S. viridans, S. sanguinis, S. gordonii, S. mutans and S. mitis, can induce platelet adhesion and aggregation even in vitro. Many studies have shown that periodontopathogenic bacteria are able to stimulate the secretion of pro-inflammatory cytokines and mediators, thereby accelerating the development of atherosclerosis. Thus, even this small amount of data provides sufficient information on the relationship between the periodontal pathogenic microbiome and the development of atherosclerosis and cardiovascular pathology.

The close proximity of the oral cavity to the respiratory tract makes it a reservoir for respiratory infections, in particular pneumonia. In 30-40% of all cases, aspiration pneumonia and lung abscess are caused by anaerobes Actinobacillus actinomycetemcomitans, Porphyromonas gingivalis, Bacteroides gracilus, B. buccae,

Eikenella corrodens, Fusobacterium nucleatum, F. necro-phorum, Peptostreptococcus, Clostridium and Actinomyces [20, 21]. It should be borne in mind that, according to molecular genetic methods, the bronchi along their entire length up to the terminal bronchioles and alveolar ducts are normally colonized by various symbiotic microorganisms [22, 23]. M. Hilty et al. [24] identified about 2,000 bacterial genomes per 1 cm2 in the bronchial tree, and bacteria of the genus Pseudomonas, Streptococcus, Prevotella, Veillonella, and Fusobacteria were identified in the lower respiratory tract, among them potentially pathogenic Haemophilus, Moraxella, and Neisseria. There are anaerobes Prevotella spp. and Bacteroides. Bacteria Haemophilus spp. were more frequently detected in the bronchi of asthmatic patients and in patients with COPD. In COPD patients with decompensated chronic pulmonary heart, changes in the oral mucosa are similar to changes in the mucous membrane in people with heart failure. Sometimes oral bacteria are the cause of emphysema or candidiasis.

It has long been noted that due to morphofunctional similarity, common innervation and humoral regulation, inflammatory periodontal diseases are involved in the pathology of the digestive system [10]. A number of authors attribute this to the expansion of Helicobacter pylori in the oral cavity [25–27], which covers more than 50% of the adult population of the world. The frequency of detection of this microbe in the stomach increases with age and correlates with the socioeconomic status of the population [28]. The presence of H. pylori in dental plaques, saliva, gum pockets ranges from 0 to 100%, and all authors note its dependence on poor oral hygiene. True, most researchers, analyzing the causal relationships of periodontal and gastrointestinal diseases, came to the conclusion that the pathology of the digestive organs always precedes the appearance of periodontal diseases [29]. M.V. Safronova et al. [30] revealed periodontal disease in 77.6% of patients with chronic gastritis, duodenitis, erosion, peptic ulcer, duodenogastric reflux and in 100% of patients with chronic hepatitis. In the work of E.R. Tamarova and A. R. Mavzyutov [331] emphasize that in periodontitis, cardiovascular diseases were diagnosed in 32.1% of cases, of which hypertension was diagnosed in 17.9% and coronary heart disease in 14.2%, pathology of the endocrine system (mainly diabetes mellitus) - 29.2% and 28.6% more diseases of the digestive system. That is, general somatic diseases with periodontitis accounted for 80.2%, without periodontitis, only 47.0%. At the same time, such periodontogens as Porphyromonas gingivalis, Treponema denti, T. cola, Streptococcus mutans, S. oralis, S. salivarius, S. sanguis, S. macacae, and S. sobrinus dominated.

There are also reports that AIDS, lichen planus, pancreatic cancer, leukemia, osteoporosis, etc. are associated with pathology in the oral cavity. The periodontium itself suffers from hypo- and hyperfunction of the thyroid gland, parathyroid and sex

glands, with diseases of the liver, kidneys, nervous and endocrine systems, ENT organs, collagenoses and allergic diseases.

Thus, the prevalence of periodontal diseases has increased dramatically and has acquired the significance of a general medical and social problem. To date, a lot of evidence has been accumulated about the combination of chronic inflammatory lesions of the periodontium with various diseases of the internal organs. Along with a complete dental examination, dentists have to evaluate not only the adverse effects of external (nutrition, climate) and local factors (a chronic source of microorganisms in the oral cavity), but also resort to consultations and examinations of family doctors and therapists. Therefore, doctors of these related specialties need to know the quantitative and qualitative composition of the microbiomes of individual human biotopes, and during hospitalization of patients or in cases of deterioration in their condition, exclude the possible negative effect of oral microorganisms on the course of the somatic process.

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