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Research Article

ETIOLOGICAL FACTORS IN DISEASES OF HARD TISSUES AND PERIODONTIUM IN PREGNANT WOMEN

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ABSTRACT

Pregnant women have one of the highest risks of dental disease [3]. According to a number of authors, during the physiological course of pregnancy, the prevalence of dental caries is 91.4%, periodontal tissue diseases occur in 90% of cases, lesions of previously intact teeth with a predominantly acute course of the carious process - in 38% of pregnant patients [5]. Secondary caries, progression of the carious process, enamel hyperesthesia occurs in 79% of pregnant women [11]. At the same time, the intensity of the increase in dental caries in terms of the absolute increase in the index of caries-filling-removal during the gestational period is 0.83 [2].

In 50% of pregnant women and women in labor, the so-called gingivitis of pregnant women is observed during the normal course of the gestational period already at 2-3 months of pregnancy [12]. From the second half of pregnancy, the pathological process becomes more pronounced and more often proceeds as a generalized catarrhal or hypertrophic gingivitis, and pyogenic granuloma often develops. As pregnancy

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progresses, periodontal disease progresses continuously, and only in the postpartum period does the clinical picture improve [4]. In the long term, gingivitis that occurs during pregnancy becomes chronic [9, 10]. In a pregnant woman, against the background of altered reactivity and reduced body resistance, latent odontogenic foci of infection can lead to serious complications as a result of exacerbation of the inflammatory process [7, 8].

The greatest severity of inflammatory phenomena in periodontal tissues occurs in the second trimester of pregnancy, and the critical increase in the cariogenic situation in the oral cavity occurs in the third trimester [4, 2], which not only determines the optimal timing of dental examinations during pregnancy and the postpartum period, but also the differentiation of the approach to programs for the prevention and treatment of the most significant diseases of the oral cavity for this period of pregnancy. The decisive role in the development of caries and periodontitis in pregnant women belongs to hormonal substances (somatomammotropin, progesterone, gonadotropin) produced by the placenta, changes in mineral and protein metabolism, immunological status, oral microflora [1, 5].

The timing of the increased risk of the onset and progression of periodontal diseases, as well as the increase in the intensity of dental caries in pregnant women, is not enough to state; tires. This does not negate the significance of already established factors affecting the occurrence and development of dental caries, periodontal disease during pregnancy, but is aimed at competently combining diagnostically important known and newly identified criteria into a system of practical recommendations for identifying risk groups among pregnant women. on dental health and special monitoring of them.

Immunoprotective peptides of biological media, including oral fluid, are markers of the intensity of local inflammation and are responsible for the implementation of innate antimicrobial immunity [6, 12]. In the oral fluid, a whole complex of immunoprotective peptides is isolated, among which lactoferrin, cathelicidin LL-37, and α-defensin are distinguished [14]. The inclusion of immunoprotective peptides in algorithms and models for ranking the risk of progression of dental caries during pregnancy will expand the boundaries of existing recommendations in this direction.

When studying systemic immunity in pregnant women with periodontal diseases, oral fluid and peripheral blood are used as biological media [8]. At the same time, retroplacental blood and umbilical cord blood containing fetal and maternal blood, despite the easy method of selection after the birth of a child and

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placenta, not associated with invasive manipulations, is not used as a biological medium. Meanwhile, the determination of the spectrum of inflammatory mediators, the mineral composition of retroplacental and umbilical cord blood will allow answering the questions whether inflammation of the periodontal tissues of varying severity was accompanied by the "mother-placenta-fetus" system, whether it is possible to predict from the stage of childbirth in the future the appearance of caries of milk teeth?

The purpose of this study is to optimize the system of providing dental care to pregnant women using clinical and laboratory indicators.

KEYWORDS

Gestation period, diseases of hard tissues of teeth and periodontal disease, periodontal disease, taste analyzer, chronic generalized periodontitis.

INTRODUCTION

To study the clinical and immunological indicators in the development of periodontal diseases and hard tissues of the teeth, a dental examination of pregnant women with periodontal diseases and hard tissues of the teeth was carried out, in the regional dental clinic in the amount of 25 people - the main group, as well as 15 people not in the gestation period. These patients were taken as a comparison group.

RESULTS AND DISCUSSION

The incidence of dental caries among women during pregnancy, according to the analysis of the works of some scientists, is 90.8%, increasing with preeclampsia up to 95% [6]. In 39% of women during the gestation period, previously healthy teeth are damaged by acute caries. According to many scientists, inflammatory and destructive lesions of periodontal tissues during pregnancy are observed in 65-90% of cases, and in the prenatal period their prevalence is 100% [10]. According to foreign authors, the multiplicity of lesions of periodontal tissues, starting from inflammation of the gums and

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finishing with inflammation of periodontal tissues, is 15-65%. In the work of Lakoine M.O. it was found that women during pregnancy during the gestation period suffer from gingival inflammation in 35-98%, periodontal inflammation - in 7-22% [11]. In the work of Vaget K., in a study of 345 women with pregnancy in periodontitis, it was found that the depth of pathological pocket damage was mainly (38.7%) 4-6 mm [13]. The transition of dental caries into a complicated form with its increase, re-developing caries occurs in 70% of pregnant women, an increase in the carious process during the gestation period is 0.85% [5]. A distinctive sign in the development of caries in pregnant patients is considered to be damage to the highest percentage of teeth, including diffusion of the carious process deep into the enamel and dentin, involving inflammation of the tooth pulp [8].

In pregnant patients, 80% have increased enamel sensitivity, hyperesthesia to mechanical, thermal and chemical agents of healthy teeth, the most common are wedge-shaped defects, pathological abrasion of vertical type teeth [1].

Of the total number of pregnant women, 95% of pregnant women undergo the need for dental treatment [7], orthopedic - 57%, emergency surgeries by surgeons are performed in 2.4% of patients [6].

In an analysis of 150 women during pregnancy, it was determined that the parameters of increased tension of carious teeth increased towards the end of the gestation period in relation to the first trimester [7]. In particular, scientists determined that for the duration of the moment of pregnancy of 8-12 weeks, the KPUz and KPUp-indices showed approximately 10.9 ± 0.8 and 23.5 ± 0.9, and at the time of 34-40 weeks they showed larger values are 14.1±0.9 and 26.1±0.7, in turn. The assessment of the hygienic index among the same category of women indicated its poor picture and the expediency of intermediate indicators of the gingival index to the inflammatory process on the gums of moderate severity.

At the same time, scientists found that with an increase in the duration of the gestation period, the surface of the areas of demineralization of the tooth enamel increases, as a result, it was associated with a decrease in the content of calcium and phosphorus in the mixed saliva and the release of total calcium into the biopsy of the acidic environment. Researchers come to the conclusion that it is inevitable to perform hygiene

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procedures and measures for remineralizing therapy during pregnancy.

In the studies of Zaitsev O.V. when examining 170 pregnant patients in the 2nd and 3rd trimesters, it was found that during the gestation period, chronic catarrhal gingivitis aggravates the dental condition in fact in each of the studied pregnant women [12]. Thus, the incidence of chronic catarrhal gingivitis represented 95.88%. With an increase in the period of pregnancy, the manifestations of bleeding and swelling of the gums, redness of the soft tissues in the zone of the dentinal groove increased, which led to an increase in the numerical indicators of the gum indices and an increase in the severity of inflammation of the gums.

In a large epidemiological study, which summarized 3471 women during pregnancy who lived in the city of Derbent, a number of authors Makhmudov A.R. found the necessary grounds for caries damage to the teeth of women during pregnancy [7, 3, 9]. The researchers created a prototype of providing dental care to women during pregnancy, which consists of a timely trip of women to the dentist, overcoming anxiety on the eve of caries therapy in the process of gestation thanks to special individualized dental and sanitary-hygienic education, increasing the persuasiveness of pregnant women to undergoing treatment, conducting the ART method as the choice of therapy for dental caries in pregnant women with stomatophobia.

The created program of dental care for women during the gestation period was tested by the developers in the process from 2003 to 2007, which showed its effectiveness due to an increase in the percentage of sanitized women during pregnancy from 78.91% to 92.25%.

There are indications for the duration of dental observation at 4-8, 14-18, 24-28, 35-40 weeks of pregnancy. Before the onset of pregnancy, women are strongly encouraged to begin dental treatment with the extraction of affected teeth. In the event that dental therapeutic procedures have not been performed, then therapy should be started in the second trimester of pregnancy - in the third to sixth trimester of the pregnancy period [6]. From the point of view of Kharitonov S.I. The best time for dental treatment in pregnant women is between 12 and 30 weeks [8]. At this time, the fetal organogenesis is completed, the placenta is developed as the main means of protection, fetoplacental hemodynamics is developed, the mother's secondary

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immunodeficiency is determined, which reduces its manifestation.

When examining pregnant patients, to analyze the hygienic state of the oral cavity, it is proposed to apply the Silness-Loe hygiene index (GI), during which the completeness of dental plaque on the gingival surface is assessed. To identify the carious intensity of teeth, it is commonplace to use the KPU index (the total number of teeth with caries, fillings and extracted teeth). At the same time, there is a focal violation of enamel mineralization, non-carious lesions. To assess the inflammatory-destructive lesions of the periodontium during pregnancy, it is proposed to carry out the systemic periodontal index according to Leus, the gum bleeding index according to the Cowell method and the papillary-marginal-alveolar index PMA.

In a virological study of Vagk T., it was determined that inflammatory-destructive periodontal diseases in women during pregnancy are always demonstrated in the clinic during pregnancy 18-25 and 24-30 weeks in pregnant women 25-30 years old [11]. Researchers consider obesity, poor oral hygiene with the reproduction of dental deposits, and the ability of gums to bleed as probable risk opportunities.

Discrepancies in dental morbidity in patients of the gestational period are determined by the diversity of housing areas, cultural and social opportunities, the treatment initiative of the patients themselves, and the systematic aspects of the study of women [10, 11].

The biological membrane of microorganisms as a factor in dental deposits is considered the main causative component that creates inflammatory and destructive changes in the oral cavity. It has been determined that more than 96% of microorganisms present in the environment exist in biological membranes. The biological membrane is quite united, communicating association of bacteria.

The source of the membrane is located in the thickness of periodontal tissues, dental deposits, it is inhabited by anaerobic gram-negative and microaerophilic microorganisms [12, 3]. Most of all, Bacteroides forsythus, as well as P. gingivalis and A. actinomycetemcomitans, have the greatest pathogenic dynamism in the formation of infectious periodontal diseases, C. rectus, E. rndatum, F. nucleatum, P. intermedia/nigrescens, P. micros, S. intermedium and T. denticola. The development and progression of microbial

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inflammation in periodontal tissues mainly depends on local immunological reactivity.

Microcolonies of bacteria are protected by an intermicrobial matrix, which is penetrated by channels. Nutrients, bacterial waste products, enzymes, metabolites and oxygen circulate through the channels. The structure and permeability of the matrix is regulated by many factors, among which female sex hormones are indirect [11].

During pregnancy, the secretion of female sex hormones changes in women: the level of progesterone in the blood is increased 10 times, and estrogen - 30 times compared with the body of a non-pregnant woman and a preserved menstrual cycle. Hormonal changes lead to a change in the cellular metabolism of oral microbes, a restructuring of local immune responses. Thus, an increase in progesterone is accompanied by increased vascular permeability of the gingival capillaries, gingival edema, accumulation of tissue fluid, increased secretion of prostaglandins, which creates favorable conditions for the development of gingival inflammation. In addition, the development of local inflammation in periodontal tissues, according to the generally accepted view, is affected by a change in the secretion of interleukin-6, which leads to a decrease in the resistance of gingival tissues and the intermicrobial matrix to the development of microbial inflammation.

The nonspecific mechanism of protection of the oral cavity from bacterial pathogens is represented by many mechanisms. These include mechanical mechanisms (barrier function of the mucous membranes), microbiological component (the role of normal microflora), chemical (humoral) and cellular factors of the oral fluid.

The bactericidal properties of the oral fluid, due to the content in it of a large number of antibacterial proteins - lysozyme, lactoferrin, lactoperoxidase, immunoglobulins, agglutinins and mucins; peptides of antimicrobial action: hisstatins, defensins and cathelicidin LL-37, provide mucosal or innate immunity of the oral cavity [3, 7]. The agglutinins and sIgA contained in saliva prevent the adhesion of microorganisms, lysozyme destroys the walls of bacteria, and lactoferrin deprives bacteria of the iron necessary for their vital activity. In addition, gingival fluid, which contains complement components, cytokines, immunoglobulins, and leukocytes,

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takes part in maintaining the integrity of periodontal tissues.

A special role in mucosal immunity is assigned to antimicrobial peptides - cationic proteins, which, having a wide spectrum of antimicrobial activity, perform a number of important functions as inflammatory mediators, have an immunomodulatory and cytotoxic effect, affect leukocyte chemotaxis and play an important role in the development of autoimmune diseases. processes [13, 14].

The development, course, and outcome of inflammatory processes are associated with a violation of the formation of antimicrobial peptides, an increase or decrease in their expression. However, their role in the development of inflammatory periodontal diseases, especially in pregnant women, is at the initial stages of study. This substantiates the relevance of further studies of immune mechanisms in the development of chronic periodontitis and the development of informative criteria for the diagnosis and course of these diseases in pregnant women.

Let us consider in more detail the mechanism of action of antibacterial proteins and antimicrobial peptides. Lactoferrin is a protein of the transferrin family of iron-binding proteins with a molecular weight of 80 kDa. Lactoferrin is found in the secondary granules of polymorphonuclear neutrophils, it can be found in epithelial cells, as well as in a variety of biological fluids and secretions. The first description of the mechanism of action of lactoferrin appeared in 1939. Lactoferrin binds calcium and magnesium ions of the surface membrane of gram-negative bacteria, which has a destabilizing effect, triggers autolysis and provides bacteriostatic activity of the protein. Lactoferrin, damaging the cell membrane of bacteria, creates the possibility of implementing the bactericidal effect of lysozyme by affecting the peptidoglycan of bacteria.

In addition, lactoferrin triggers a catalytic reaction for the formation of hydroxyl radicals, which makes an additional contribution to the bactericidal effect. Taken together, lactoferrin has antibacterial, antiviral, antifungal, immunomodulatory, and antioxidant properties (Caccaro R. et al., 2018).

Determination of lactoferrin content in secretory fluids, including saliva, is a non-invasive method for monitoring the inflammatory activity of local processes. Determination of the level of

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lactoferrin in the biological media of the body can serve as a marker of neutrophil activation during inflammatory processes. In inflammatory processes, its level in saliva, blood plasma, urine, breast milk can increase 10-100 times [2].

Another factor of mucosal protection is lysozyme. For the first time it was isolated by A. Fleming in 1922 from mucus obtained from the nasal cavity. An immunomodulatory effect is associated with lysozyme due to the release of muramyl dipeptide from the bacterial cell membrane. Lysozyme has a bactericidal effect against gram-negative bacteria due to increased lytic activity of the sIgA complex with C3 complement fraction, enhances the phagocytic activity of neutrophils [6, 7].

According to Zasloff M. and Tanida T., the combination of a low level of lysozyme along with a reduced concentration of immunoglobulins, lactoferrin is associated with increased sensitivity to infectious pathogens. Thus, the amount of antimicrobial proteins in the oral fluid reflects the state of local non-specific protection factors of the oral mucosa.

Antimicrobial peptides are the first line of defense of innate immunity in all types of living beings, and the high significance of AMPs is confirmed by their high content in circulating neutrophils [1]. Studies have shown that AMPs are involved in the inflammatory response by acting as chemoattractants for immune cells, including neutrophil recruitment by inducing interleukin-8 production and mobilization of immunocompetent T cells, as well as agents that enhance cell adhesion and subsequent transepithelial cell migration. [12, 13, 14].

In humans, two classical AMPs have been established - defensins and cathelicidins. Defensins have a molecular weight of 4 kD and constitute a large family of small cysteine rich cationic peptides. Defensins are responsible for killing or destroying a wide range of pathogens, which include bacteria, fungi, and enveloped viruses. Mammalian defensins, according to the results of many systematic studies based on factual arguments, are involved in the mechanisms of innate and acquired immunity and are multifunctional when interacting with host cell receptors [15].

Defensin molecules are small amphiphilic cationic peptides. They contain 29-47 amino acids rich in cysteine with a P-folded antiparallel structure. The peptides are stabilized by three intramolecular disulfide bonds between cysteine

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residues. The presence of disulfide bonds is extremely important. These bonds in the defensin molecule maintain the resistance of molecules to proteases of leukocyte and microbial origin and provide antimicrobial properties in the focus of tissue destruction and inflammation.

There are two main groups of defensins - a- and p-defensins. Recently, a tritium class of defensins, y-defensins, has been discovered. In human neutrophils, defensins contain 30-50% of granular proteins. It should be noted that defensins have been identified in tissue macrophages, small cells of the intestinal epithelium, and cardiomyocytes. It has been established that in plasma defensins nonspecifically bind to blood serum proteins with a large molecular weight: albumin, alpha 2-macroglobulin, complement [5, 4].

A-defensins, the classic "neutrophil" defensins (HNPs), were identified in the azurophilic granules of neutrophils and first described in the mid-1980s. It is neutrophil granules that are the main depot for four α-defensins (HNP1-4), two α-defensins, HD5 and HD6, were found in Paneth cells. A-defensins secreted by neutrophils can be found in biological fluids. They have an antimicrobial effect, are chemoattractants for T-lymphocytes with CD4/CD45RA and CD8, activate the secretion of interleukin-8, bind C1q, and thus carry out complement activation [11].

The first P-defensin was discovered in dialysate of hemofiltrate and described in the early 1990s. There are several isoforms of P-defensin. The HBD1 peptide consists of 36 amino acid residues [11]. The composition of P-defensins is variable, which reflects the inducible nature of their secretion. The major human P-defensin is HBD1-6. P-defensins are produced by keratinocytes, mucosal epitheliocytes, monocytes and macrophages, and dendritic cells.

Recently, another structurally distinct subfamily of y-defensins has been identified in the leukocytes of rhesus monkeys. In humans, the secretion of y-defensin is probably blocked due to mutations, but is preserved in primates [12].

It has been established that AMP secretion occurs constitutively, but when an infectious agent enters the body and inflammation occurs, AMP production can be expressed or induced. Constitutive (permanent) synthesis is more characteristic of a-defensins, and the secretion of p-defensins is most often induced. In addition, it is known that a-defensins realize their action

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inside phagosomes, while P-defensins are produced mainly by epithelial cells and accumulate in secrets. Such functional properties of defensins as antimicrobial and cytotoxic are realized due to their ability to form pores in membranes, which is then accompanied by spontaneous diffusion. Thus, defensins target the weakest link in the microbial cytoplasmic membrane.

This locus is characterized by increased permeability. Peptides accumulate on the surface of the pathogen membrane, orienting in parallel, then electrostatically interact with anionic groups of phospholipid heads, "carpet-like" cover the membrane. Upon reaching a certain critical concentration, through pores are formed in the target membrane and, as a result, the bacterium is lysed. It should be noted that these properties of defensins are due to their electrostatic interaction with bacteria. Defensins exhibit direct antimicrobial activity against bacteria, fungi, eukaryotic parasites and/or viruses.

To neutralize microorganisms, AMPs can act synergistically with proteins, lysozyme, and antibiotics entering the blood. There is an opinion that AMPs promote wound epithelialization as a consequence of stimulation of angiogenesis and reproduction of epitheliocytes. Defensins also have intracellular targets. They can intracellularly inhibit the structures responsible for the synthesis of bacterial proteins and nucleic acids.

There are certain spatial features of the secretion of defensins. The maximum secretion of defensins occurs in those cells and tissues that are involved in the body's natural defense against infection. The maximum concentrations of a-defensins (>10 mg/ml) in the human body are found in leukocyte granules [13]. In addition, high concentrations of a-defensins are also characteristic of the lymphoid cells of the small intestine. Various barrier and secretory epithelial cells of the oral cavity and small intestine also produce α- and β-defensins, depending on the circumstances, constantly or in response to infection [10]. The average concentration of defensins in these epithelial cells reaches 10–100 μg/ml [3], but due to the uneven distribution of peptides, local concentrations are higher. It should be emphasized that in the presence of an inflammatory process, it increases by 2-4 times, changing to the maximum in septic conditions and at the same time reaching a micromolar concentration. Thus, in infected or otherwise injured tissues, AMPs are most likely to be

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released at high concentrations, but their local concentration is still a subject of research.

The number of genes encoding the production of a- and P-defensins is at least 8. These genes form a cluster on chromosome 8p22-p23. The defensin gene cluster has not yet been mapped. According to Mars W.M. et al. this can be explained by the polymorphism of these peptides and differences in the number of copies of specific defensin genes. Thus, HNP1-3 is encoded by two genes HDEFA1 and HDEFA3. At the same time, Linzemeier R.M. it was found that the level of HNP in neutrophils is proportional to the number of gene copies. Moreover, the authors come to the fundamentally important conclusion that it is the established genetic component that determines the individual resistance of the organism to infections.

Since the main effect of defensins is antimicrobial, the specificity of the directed action of AMPs on bacteria and fungi is of scientific interest. Scientists were able to establish that HBD2 and HBD3 are more effective in terms of bactericidal action on microorganisms than HBD1. Moreover, aerobic bacteria are more sensitive to HBD2 and HBD3 than anaerobic microbes. HBD3 is more active against a wider range of bacteria as well as fungi. In addition, HBD3 requires a lower concentration compared to HBD2 and HBD3 to realize the bactericidal effect. Less pronounced antibacterial activity develops HBD4.

However, a feature of the action of HBD4 is its high activity against Pseudomonas aeruginosa [13]. At the same time, it should be emphasized that, according to Ericksen B., almost complete identity of peptides to each other is characteristic of HNP [12].

HNP and HBD are involved not only in local, but also in systemic responses to the inflammatory process. Yang D. et all. it was found that defensins act as active chemoattractants for monocytes, T-lymphocytes and immature dendritic cells, provide antigen-specific immune responses, macrophages are activated, and phagocytic reactions are enhanced. After conducting an experimental series of studies Biragyn A. et all. it was found that P-defensins, using Toll-like receptors, induce the "maturation" of dendritic cells, thereby regulating their functions [11, 3].

The antiviral effect of denphensins is associated with their ability to destroy the integrity of the virus envelopes. In addition, the point of view is expressed that defensins bind viral glycoproteins.

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Along with this, defensins can promote the lysis of cells damaged by the virus. HNP1 is the first defensin for which a direct antiviral effect has been studied. The antiviral activity of defensins against herpes simplex viruses HSV-1 and HSV-2, vesicular stomatitis virus, influenza, cytomegalovirus has been registered.

Cathelicidins, along with defensins, are a family of antimicrobial peptides. The molecular weight of cathelicidins is 3-5 kD. The cathelicidin group is synthesized and found in the body as an inactive precursor with N- and C-terminal domains. The number of amino acid residues is variable and ranges from 12 to 80. Most often, cathelicidins consist of 23-37 amino acid residues. In humans, only one peptide from the group, hCAP-18/LL-37, is expressed.

Its molecular weight is 18 kD. hCAP-18/LL-37 was first identified in secondary peroxides in neutrophil negative granules. Cathelicidin LL-37 acts on gram-positive and gram-negative bacteria, fungi, enveloped viruses, and protozoa. This AMP neutralizes lipopolysaccharides, acts as an angiogenesis factor and, thus, participates in re-epithelialization processes. For neutrophils, monocytes, mast cells, cathelicidin LL-37 is a chemoattractant. It regulates the production of chemokines, increases the number and sensitivity of receptors for them, promotes the activation of interleukin-8.

The study of changes in the secretion of cathelicidin LL-37 is important for studying the microbiological mechanisms of the development of dental caries. Cathelicidins are found in oral epithelial cells and are responsible for the activity of antimicrobial innate immunity. The antibacterial spectrum of this endogenous peptide extends to Streptococcus mutans, whose role is undeniable in the development of caries. Cathelicidin has a synergistic antibacterial effect with defensins. According to previously published data by Mona Doss et al. a decrease in the level of LL-37 CC is a predisposing factor to the occurrence of periodontal diseases.

Histatins are another class of AMPs and are represented by a family of 12 histidine-rich peptides. Histatins are found only in the saliva of humans and higher primates, as they are produced by the epithelium of the parotid and submandibular salivary glands. The concentration of histatins in saliva is about 45-75 μg/ml. They develop a bactericidal and fungicidal effect against bacteria and fungi. Histatins are weakly amphipathic peptides. On models of

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liposomes, it was shown that they have a weak lytic ability.

Cellular mechanisms of nonspecific immune reactions are represented by a system of cells with phagocytic and killer natural activity. The system of natural killers (NK cells), which have the ability to destroy and digest cells, is represented by monocytes and T-lymphocytes with CD16 and CD56 receptors. Natural killers have a nonspecific toxic effect on cells affected by an infectious pathogen or tumor cells. In general, natural killer immune responses are effective in fighting viruses and tumor cells.

Phagocytosis refers to the basic and ancient forms of nonspecific immune reactions of the body. Phagocytic reactions begin to take place already in saliva. For their implementation, leukocytes and lymphocytes are present in human saliva. These cells enter the saliva through the epithelium of the gum pockets. Undoubtedly, phagocytosis is most active in tissues through the participation of neutrophilic granulocytes and macrophages.

Phagocytes migrate from the blood to tissues due to chemotaxis, chemotaxis, adhere to pathogens and phagocytize them with the formation of phagosomes, phagolysosomes. Due to the cytotoxicity of hydrolases and other biologically active substances of neutrophils and macrophages, the absorbed bacteria are lysed, which forms the basis of complete phagocytosis [10].

Microorganisms, their toxins, immune complexes, as well as cytokines, etc. modulate and induce phagocytic activity. mouth. The release of hydrolytic enzymes (such as proteases, peptidases, oxidases, deoxyribonucleases and lipases) leads to the destruction of microorganisms in a matter of hours [5,9]. In addition, neutrophil granules, in addition to a wide range of hydrolases, contain low molecular weight cationic polypeptides and cationic proteins, lactoferrin, lysozyme. As a result of phagocytosis, lipids, polysaccharides and proteins of bacteria are degraded.

Hydrolytic enzymes released from leukocytes have a lytic effect both on microorganisms and on collagenase, protease of the periodontal connective tissue framework, keratase of epithelial structures, and neuraminidase of surface cell structures. This group of enzymes is called matrix metalloproteinases (MMPs) and is represented by 15-18 enzymes. Their name is due

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to the main effect - the destruction of extracellular matrix molecules [10].

In inflammatory processes of the gums, as a result of a decrease in the intensity of apoptosis, the number of phagocytes increases. There is an activation of infiltrated immune elements that attack the periodontal tissue and prolongation of their life cycle. Activated neutrophils are potentially cytotoxic to surrounding cells. They secrete a number of cytokines, which, in turn, prolong the cellular response to the pathogen.

In chronic periodontitis, an imbalance is formed between pro- and anti-inflammatory cytokines towards the predominance of the production of pro-inflammatory mediators. Pro-inflammatory cytokines are central to the pathogenesis of inflammatory periodontal diseases.

The main interleukin (IL) that supports the inflammatory process in the periodontium and is responsible for its generalization is interleukin-1, which exists in 2 forms (IL-1a and IL-1R). The action of IL-1 begins after the combination of the cytokine with a specific receptor on the cells. After interacting with endothelial cell receptors, IL-1 promotes the production of adhesive molecules that cause chemotaxis and adhesion or adherence of polymorphonuclear granulocytes of leukocytes and monocytes. Acting on fibroblasts, IL-1 promotes the production of collagenase, which leads to the degradation of collagen, a decrease in its synthesis, and stimulates osteoresorption.

In the works of Barer G. et al. and Zaitseva E.M. it has been established that with the progression of chronic generalized periodontitis, the content of IL-1 in the tissues of the gums and gingival fluid increases significantly [5, 6]. In the study of Kovalchuk L.V. et al. and Kravchenko E.V. et al. it was indicated that Th1 lymphocytes mainly accumulate in the periodontal tissues, which intensively produce interferon-y and TNF-a. This feature of the cytokine profile is accompanied by the accumulation of macrophages in tissues. Subsequently, Th2 cytokine profiles are also activated, leading to the activation of B-lymphocytes.

Destructive changes in the periodontium are associated with an increased amount of IL-1, IL-6 and y-IF. IL-1 and y-IF activate osteoclasts, IL-1 increases the synthesis of collagenases. IL-6 activates the differentiation of B-lymphocytes to plasma cells with the production of immunoglobulin G, which promotes complement

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fixation and release of chemotaxis mediators. Cytokines after the initiation of the inflammatory process in the periodontium further support the activation of the cells responsible for their synthesis, trigger the resorption of the alveolar bone. A pronounced damaging effect on the periodontium is primarily associated with a change in the secretion of IL-ip and γ-IF, an increase in the level of IL-6, IL-8 [4, 5, 6]. Chronic inhibition of IL-2 and IL-2R production leads to the development of autoimmune disorders.

Among the features of the cytokine profile, conflicting data have been accumulated regarding y-IF in chronic periodontitis. According to Wilson T.G. et al. the content of interferon-y in periodontal tissues during its inflammatory and destructive changes is much higher than in the tissues of healthy people. According to Barer G.M. et al. in the gingival fluid during the active course of periodontitis, the content of α- and γ-IF, on the contrary, is reduced, which, according to the authors, indicates a secondary immunodeficiency of the T-helper and T-suppressor types [5, 6].

IL-4 refers to anti-inflammatory cytokines. IL-4 is associated with the containment of inflammatory and destructive changes in the periodontium and reduces the manifestation of osteoporosis. Donati M. et al., Gonzales J.R. et al. in patients with generalized periodontitis, a decrease in the content of IL-4 in the gingival fluid, saliva and dental plaque was found to decrease. Single publications are also found regarding the role of IL-12 in the pathogenesis of generalized periodontitis. IL-2 is responsible for enhancing the cell-mediated immune response, effective anti-infective protection.

Dysregulation of cytokines and immunoglobulins in periodontal tissues leads to destructive changes.

Activation of osteoclasts in destructive periodontal lesions is primarily associated with the formation of IL-1 [10]. However, when IL-1 receptors are completely blocked, the area of destructive changes increases and systemic changes occur [8]. In periodontitis, increased production of TNF-α by polymorphonuclear leukocytes (PMNL), monocytes/macrophages and fibroblasts [14], a high concentration of IL-6 secreted by osteoblasts, fibroblasts, macrophages, PMNL and T- lymphocytes [11].

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