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DIAGNOSTIC AND PROGNOSTIC SIGNIFICANCE OF GINGIVAL FLUID CYTOKINES IN THE DEVELOPMENT OF INFLAMMATORY PERIODONTAL DISEASES

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Abstract
Inflammatory periodontal diseases are one of the most common dental diseases in the world, along with dental caries. In the modern concept of the development of inflammatory periodontal diseases, one of the important roles is assigned to the body's immune response to the action of periodontal pathogenic microorganisms. In modern scientific literature, the concept of cytokine development of inflammatory periodontal diseases has been formed and substantiated. Evaluation of the cytokine profile of oral and gingival fluids allows us to determine the activity and severity of the disease. Well-founded immunological and molecular genetic mechanisms for the development of inflammatory periodontal diseases, associated with the influence of cytokines, make it possible to adjust the complex treatment of inflammatory periodontal diseases, determine the direction of personalized therapy for patients, determine the effectiveness of the treatment and the prognosis of the disease.

Keywords Inflammatory periodontal diseases, gingivitis, periodontitis, gingival sulcus, gingival fluid, microbiota, cytokine profile, interleukins.

INTRODUCTION

According to WHO, inflammatory periodontal diseases (IPD) are one of the most common dental diseases in the world after dental caries. The highest incidence rate occurs at the age of 15–19 years (55–89%), as well as 35–44 years (65–98%). According to the data [32,41], the adult population level in various cities of the Republic of Uzbekistan in the age group of 15-18 years is 69 - 80 %, and in the age group 35-44 years 92 - 99%.

The main reason for the development of IPD is the association of opportunistic microorganisms of dental plaque and their metabolic products, which can have a direct or indirect effect on periodontal tissue [2,21,36,38].

The microbiota of the gingival sulcus is represented by more than 500 strains of bacteria.

However, out of the entire variety of microorganisms, only 3 to 20 of them are periodontopathogenic. The most common are actinobacilus actinomycetemcomitans , porphyromonas gingivalis , bacteroides forcythus , spirochetes , prevotella intermedia , eikenella corrodens , veilonella recta , treponeva denticola , capnocytophaga in various associations and others [11,21,47,50]. Depending on the form of inflammation in periodontal tissues, the species composition of the microbiota also changes. Thus, with catarrhal gingivitis, the predominantly coccal flora predominates (s. salivarius (66.7%), s. epidermidis (61.9%), s. Heamoliticus (57.7%), peptostreptococcs (52.3%)), with mild chronic periodontitis - bacillary morphological variant [17,37,44].

Depending on the duration of exposure, dental plaque microorganisms, having antigenic properties, can cause both inflammation in periodontal tissues and a chain of immunopathological reactions. Lipopolysaccharides of gram-negative bacteria and mucosaccharides of gram-positive bacteria have the greatest antigenic activity [4,16,21].

The Main Findings and Results

An important role, in addition to microbial invasion in the development of inflammatory periodontal diseases, is played by both general somatic pathology (diseases of the gastrointestinal tract, cardiovascular system, endocrine system, etc.), and local periodontopathogenic factors, such as (the composition of saliva, dental deposits, the presence of orthopedic and orthodontic structures, pathology of the dental system, etc. [4,7,10,18,21,34].

It is known that general and local factors that can reduce the body's immune defense play a significant role in the development of inflammatory periodontal diseases. Violations of the barrier properties of the epithelium can facilitate the penetration of microorganisms into tissues and stimulate the development of the inflammatory process. Immunocompetent cells, such as leukocytes, macrophages and lymphocytes, are activated and produce various enzymes and inflammatory mediators, which leads to damage to periodontal tissues [22,48].

In chronic catarrhal gingivitis and other forms of periodontitis, the body's immune response can be mediated by the activation of various types of lymphocytes, including T-lymphocytes to the immune response [16,21,40]. With prolonged exposure to pathogens on periodontal tissue and an increase in the inflammatory process, immunopathological reactions may occur with the participation of autoimmune mechanisms of periodontal damage. With prolonged exposure of the pathogen to periodontal tissue and progression of the severity of the process, a transition occurs from the inflammatory nature of periodontal tissue damage to immunopathological reactions with an autoimmune mechanism of periodontal damage associated with the activation of T2 helper cells [3,25].

Overall, understanding the interactions of microorganisms, the immune system, and other factors in the development of periodontal disease helps to better understand disease mechanisms and develop effective treatment and prevention strategies.

In the initial stage of inflammation, the number of macrophages that trigger the immune response increases, the chemotaxis of immune cells and the phagocytic activity of neutrophils are activated. However, as the process becomes more chronic, the picture changes. In patients with chronic forms of inflammatory periodontal diseases, there is a decrease in the phagocytic activity of immune cells. In chronic catarrhal gingivitis in the acute stage, the number of functional phagocytes, their phagocytic activity and bactericidal function decreases [10]. In patients with chronic generalized periodontitis, a profound depression of these indicators is observed [1].

Some studies indicate increased chemotactic activity of neutrophils in moderate to severe periodontitis. Changes in the cytological picture in inflammatory periodontal diseases are also noted, such as a decrease in segmented neutrophils and

changes in phagocytic activity depending on the severity of the disease [8].

Indeed, changes in the immune system during inflammatory periodontal diseases can be quite diverse. An increase in the number of lymphocytes in the inflammation site in mild and moderate forms of chronic catarrhal gingivitis and generalized periodontitis has been noted in several studies [3,5,27].

Regarding humoral immunity, there is evidence indicating a decrease in the content of total T-lymphocytes and the Th / Ts indicator , which indicates the development of an immunodeficiency state. With gingivitis and periodontitis, a decrease in the number of B-lymphocytes is also observed [2,35].

Regarding immunoglobulins, different studies provide conflicting results. Some indicate an increase in the concentration of IgA, IgM and a decrease in IgG in the initial forms of the disease, and then a change in the ratio as the condition worsens. Other studies indicate a significant increase in the levels of all immunoglobulins, except IgE , in gingivitis, but a decrease in the concentrations of IgA, IgM , IgG in chronic periodontitis [35].

One of the central links in the pathogenesis of inflammatory periodontal diseases are cytokines, which explains cytokine IPD development concept. Cytokines play an important role in the pathogenesis of inflammatory periodontal diseases. They are endogenous regulators that coordinate the interaction of various components of the immune system and other body systems. The production of cytokines can be aimed at both immune defense and tissue destruction at the site of inflammation [23, 28].

Studies show that the content of cytokines in oral and gingival fluids does not always correlate with their levels in the blood, which indicates the activation of local immunity [39]. Increased levels of pro-inflammatory cytokines (for example, IL-1β, IL-6, IL-8, IL-17, IL-18, IF-γ, TNFα) and a decrease in anti-inflammatory cytokines (for example, IL-4 and IL-10) were detected in chronic catarrhal gingivitis and generalized periodontitis [15,29,30,45].

IL-1β plays an important role in the development of the primary immune response to the introduction of pathogenic periodontal microbiota. Its functions include the initiation and regulation of inflammatory processes, activation of various cells of the immune system and stimulation of the synthesis of other cytokines. The level of IL-1β in the gingival fluid correlates with the depth of the periodontal pocket and contributes to the generalization of the inflammatory process [5, 7].

Molecular genetic predisposition may also influence the course and severity of inflammatory periodontal diseases. Studies of IL-1β gene polymorphism show differences in the distribution of alleles in patients with different forms of periodontitis. For example, some studies indicate more pronounced polymorphism of the IL-1β gene in patients with severe forms of periodontitis [5,7,12,18,20].

Tumor necrosis factor-α (TNFα) plays a significant role in the development of inflammatory periodontal diseases. This cytokine, produced by macrophages and monocytes, performs a number of important functions, including enhancing the proliferation of lymphocytes, increasing the synthesis of acute phase proteins, increasing the permeability of the vascular endothelium, activating free radical oxidation and suppressing delayed-type hypersensitivity. It has been established that the concentration of TNF-α increases in the gingival fluid even before the first clinical manifestations of periodontal diseases [19,49].

The level of TNFα in the gingival fluid increases even before the first clinical signs of periodontal disease appear. This cytokine has a cytotoxic effect and, together with other cytokines such as IL-1β and IL-6, activates the production of the enzyme collagenase and other factors that contribute to the destruction of collagen in periodontal tissues . It also activates osteoclasts and blocks osteoblasts, thereby promoting the formation of periodontal pockets [4, 46].

Increased concentrations of IL-6 also play an important role in the development of inflammatory processes in the periodontium. It is involved in lymphocyte differentiation, receptor expression, and the production of other cytokines such as IL-2. IL-6 is also responsible for the production of IL-2 by T lymphocytes, which regulates the immune response [10,33].

CONCLUSION

With different degrees of severity of inflammatory periodontal diseases, the concentrations of anti-inflammatory cytokines, such as IL-4 and IL-10, change. These cytokines promote the humoral immune response and can block proinflammatory cytokines such as IL-1β and TNFα [9,14,24,31,42].

The information provided concerns changes in the immune system during inflammatory periodontal diseases. It is important to note that the diversity and inconsistency of data on immune reactivity are associated with different methods for assessing immune activity, the presence of systemic pathologies and types of inflammatory reactions [6,13].

The study of the immunological and molecular genetic mechanisms of the development of inflammatory periodontal diseases associated with the influence of cytokines plays an important role in the understanding and treatment of these diseases. The concept of cytokine origin of inflammatory periodontal diseases (IPD) allows for a more in-depth study of the processes occurring in periodontal tissues. Analysis of the cytokine profile of oral and gingival fluids can indeed help in assessing the activity and severity of the disease, which in turn helps in choosing the optimal treatment strategy for each individual patient. Personalized therapy based on cytokine profiles can improve treatment outcomes and disease prognosis [27].

Thus, the available scientific data on the cytokine profile of inflammatory periodontal diseases make it possible to develop individualized approaches to treatment, determine the effectiveness of the treatment and improve the prognosis of the disease. This opens up new prospects for the development of more accurate and effective methods for diagnosing and treating periodontal diseases.

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