



CLINICAL SIGNS OF PERIODONT TISSUE DISEASES IN CHILDREN WITH ADENOVIRUS INFECTION.

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Abstract. Клинический диагноз заболеваний пародонта в значительной степени зависит от признаков, таких как потеря эпителиального прикрепления зуба, глубина зондирования кармана, кровоточивость при зондировании, индекс зубного налета, подвижность зуба, поражение фуркаций и рентгенологическая оценка костных структур. Однако, эти показатели не отображают текущее состояние болезни и не дают информацию об активности или риске развития заболевания.

Keywords. Зубы, пародонт, периодонт, воспаление, аденовирус, прикус, гингивит.

Microorganisms living in symbiosis with humans are of great importance for the health of the human body and play an important role in the pathological conditions of the body. Changes in the microbiome contribute to the pathogenesis of many diseases and reflect a person's state of health or illness. Thus, monitoring changes in the microbiome is a promising potential new criterion in the diagnosis and prognosis of diseases[1].

Periodontal diseases are one of the most urgent and studied problems in dentistry. The results of a study conducted by the WHO scientific association demonstrate that the level of periodontal diseases is at a high level and is evolving in the age group from 20 to 44 years (65-95%) and at the age of 15-19 years (55-89%).

Periodontitis is a chronic inflammatory disease associated with changes in the subgingival microbiota. A severe course of the disease can lead to tooth loss and a significant decrease in the patient's quality of life. Imbalance in the microbiome of the oral cavity, along with environmental factors and heredity, are the main causes influencing the occurrence and progression of this disease [3].

In the initial stage of periodontitis and with its progression, pathogenic bacteria colonize the periodontal pocket, form subgingival biofilms that attach mainly to the surface of the tooth root, causing inflammation in periodontal tissues [4].

In severe forms of the disease, the destruction of periodontal tissues is noted, which leads to progressive loss of bone tissue and, ultimately, to mobility and tooth loss. The infectious process in periodontitis causes an inflammatory reaction of the human immune system and exacerbation of other chronic diseases [1].

Although the disease can be stopped, the periodontal condition must be constantly monitored after initial treatment because the disease can recur and progress without obvious

symptoms. The etiology of this disease is not fully understood, and it can be caused by chronic diseases such as diabetes, obesity, acquired immunodeficiency syndrome and stress, which contribute to the development of periodontal inflammation. For example, excessive blood glucose levels cause a pro-inflammatory cascade during the formation of the disease[5].

Smoking leads to a significant narrowing of microvessels, masking the clinical signs of bleeding during probing [6]. Previously occlusive injury (damage to the supporting apparatus of the tooth due to the action of chewing forces) It was considered the main factor leading to periodontitis, which was observed in animal models, but evidence of this phenomenon in humans has not been determined [7,8]. Thus, traditional, used clinical criteria for predicting the course of the disease may be useful, but they cannot adequately predict the relationship between the initial manifestations and the progression of the disease. Without a reliable way to predict the progression of the disease, the identification of patients in need of treatment occurs only after obvious tissue damage.

The microbiome of the oral cavity in periodontitis. The clinical diagnosis of periodontal diseases largely depends on signs such as loss of epithelial attachment of the tooth, depth of probing of the pocket, bleeding during probing, plaque index, tooth mobility, furcation lesion and X-ray evaluation of bone structures. However, these indicators do not reflect the current state of the disease and do not provide information about the activity or risk of developing the disease [8].

Clinical diagnosis has its limitations and does not allow clinicians to determine the cause, pathogenesis or prognosis of the disease in the case of advanced periodontitis. Therefore, it is believed that the use of available technologies such as molecular analysis can help in determining the qualitative and quantitative composition of the periodontal microbiota. Accurate determination of the microbiome composition of periodontal pockets can play an important role in the development of effective and adequate therapy[9].

In a healthy periodontal condition, the number of oral bacteria averages about 10⁹, whereas in the case of periodontitis, this number exceeds 10^{8.7} [10]. Evaluation of the composition of the subgingival biofilm by microbiological and molecular methods revealed a connection with a large number of microorganisms, some of which are capable of destroying periodontal tissues [11]. They proposed the concept of bacterial complexes associated with the severity of periodontitis and divided them into five colors: yellow, red, green, orange and purple.

The researchers came to the conclusion that initially non-pathogenic bacteria belonging to the yellow, green and purple complexes act as initiators of biofilm formation [13]. However, it has also been found that these types of microorganisms impart adhesive properties to bacteria from the orange complex, which can lead to the creation of favorable conditions for the growth of bacteria such as *Porphyromonas gingivalis*, *Treponema denticola* and *Tannerella forsythia*, which belong to the red complex and cause periodontitis of varying severity.

In addition to the "red complex" bacteria, *Aggregatibacter actinomycetemcomitans* is also found in periodontal pockets, which is classified as a purple complex and is associated with the occurrence of aggressive forms of periodontal inflammation, for example, localized juvenile periodontitis or treatment-resistant periodontitis (refractory periodontitis). These are gram-negative bacteria, serotypes A, B, and C of which play an important role in the rapid progression of the disease [14].

Other complexes have a low or moderate effect on the development of periodontitis [12]. Among many other bacteria involved in the development of the disease, *Prevotella intermedia*, *Campylobacter rectus*, *Peptostreptococcus micros*, and *Spirochetes* species are found [15]. In the Russian classification, periodontal pathogens are divided into two orders. First-order periodontopathogens such as *P. gingivalis*, *A. actinomycetemcomitans*, and *T. forsythia* contribute to the rapid progression of the disease, as they have an intracellular life form and are contained in the gum epithelium and periodontal tissues, and their virulence factors lead to tissue destruction [4,6].

On the other hand, periodontopathogens of the second order (*T. denticola*, *Fusobacterium nucleatum* and *Prevotella intermedia*) play a less important role in the development of periodontal diseases. However, they can form associations with *P. gingivalis* and *T. forsythia*, more pathogenic bacterial species, which contributes to the spread of inflammation in the subgingival region. If only *P. intermedia* is found in the patient, this may indicate the onset of the inflammatory process, while the presence of associations with other periodontal pathogens indicates the progression of the disease [7,8]. It has also been shown that various viral agents, such as herpes viruses, are actively involved in the process of aggressive periodontitis [9]. In addition, individuals with primary and acquired immunodeficiency have many different fungal agents, including *Candida albicans*, which plays an important role in interactions with other periodontal pathogens that enhance the clinical course of the disease [2]. Methods of diagnosis of periodontal pathogens.

The ideal method for diagnosing periodontitis should allow, firstly, screening of the microbiota, secondly, predicting the course of diseases, and thirdly, monitoring the effectiveness of therapy [8]. Currently, there is a gradual shift away from analyzing the effects of specific pathogens on the development of periodontal diseases towards analyzing the entire microbiome.

To study the role of bacteria in the development of periodontitis, new diagnostic methods are required to detect increasingly complex relationships between microorganisms, environmental factors, and human health. Most types of microorganisms cannot be cultivated in bacteriological laboratories, since oral bacteria cannot recreate their trophic relationships with each other, prevailing in their natural environment. Therefore, most species are not detected by standard microbiological methods[2,3].

Cultivation of microorganisms. For a long time, cultivation methods were considered the gold standard in the diagnosis of periodontal pathogens. Like any diagnostic methods, traditional microbiological methods have their advantages, but also a number of limitations. Most pathogens present in deep periodontal pockets are anaerobic and, accordingly, require specific cultivation conditions, sampling and transportation conditions, and failure to follow strict rules can potentially lead to an erroneous diagnostic result. Difficulties also include the selection of suitable culture media, low concentrations of isolated bacteria, long periods of bacterial growth, and waiting times before making an accurate diagnosis.

Also, the microbiological method does not allow for species differentiation between closely related taxa. In addition, this method is not suitable for the identification of many clinically significant microorganisms, for example, *T. forsythia* [4]. Despite the large number of disadvantages, however, it is impossible to abandon this method, since it is used to determine sensitivity to antibiotics, which is of great importance in prescribing antibacterial drugs for the



treatment of patients. Thus, traditional methods based on cultivation do not fully meet the requirements of modern dentistry, but it is not possible to completely abandon them.

Polymerase chain reaction (PCR). The modern need for accurate, rapid identification and quantification of periodontal pathogens required the development of other effective methods. In addition to the microbiological method, the method of flow cytometry, DNA-DNA hybridization, immunochemical analyzes, and others were used.

However, these methods have low specificity and sensitivity in the identification of periodontal pathogens [5]. The advent of PCR has led to the creation of a more accurate tool for identifying the total number of pathogens by developing species-specific primers that amplify only target sequences [6]. For example, various PCR diagnostic test systems have been developed for more accurate and rapid detection of multiple periodontal pathogens.

The most well-known in our country is the domestic Multident-5 test system manufactured by GenLab LLC for multiplex PCR with primers for the five main anaerobic periodontopathogens: *A. actinomycetemcomitans*, *T. forsythia*, *P. intermedia*, *P. gingivalis* and *T. denticola*. The Dentoscreen Complex and the DNA Express kit are also used to isolate DNA from biological material and subsequent analysis of isolated DNA by PCR [8].

It is important that in addition to the ability to detect anaerobic bacteria of the oral cavity, PCR makes it possible to detect the DNA of viable and non-viable cells, thereby providing more complete information about the oral microbiota, which makes it possible to correct the current state of the disease [8]. However, PCR also has some limitations in the form of DNA polymerase inhibitors present in clinical samples - hemoglobin, heparin, and ethylenediaminetetraacetic acid (EDTA), alcohols, detergents, and salts present during DNA isolation, which can reduce or even inhibit the effectiveness of the reaction. Another limitation is the need for expensive specialized equipment in well-equipped laboratories [8].

Over the years, the PCR technique has undergone many modifications, which has made it possible to expand its capabilities. For example, RT-PCR (reverse transcription) is a method for detecting RNA molecules in a sample with a pre-known sequence region complementary to the primer, PCR-RFLP (restriction fragment length polymorphism) is a PCR reaction in combination with restriction analysis of amplification products, and others. Real-time PCR (or quantitative PCR, eng. Realtime PCR, qPCR, qRT-PCR) with species-specific primers provides an accurate quantification of individual bacterial species and their total number in plaque samples.

This method allows us to determine which types of bacteria forming the biofilm of the oral cavity are dominant, which makes it possible to use effective antimicrobial therapy. Real-time PCR is used for qualitative and quantitative assessment of dental plaque parodontopathogens and the contents of periodontal caramans [9].

An example of the application of this method is the use in our country of a set of Dentoflora, which allows us to determine the total amount of bacterial 16S rDNA of six periodontopathogens (*A. actinomycetemcomitans*, *P. gingivalis*, *P. intermedia*, *T. denticola*, *T. forsythia* and *C. albicans*) and human chromosomal DNA [15]. Determining the number of individual microorganisms allows us to get a more complete picture of the ecosystem of the oral cavity and identify the predominance of specific bacteria or their complexes [3].

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