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Status of Immunity in Chronic Diseases of the Salivary Glands

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Abstract: Chronic diseases of the salivary glands – including chronic sialadenitis, Sjögren's syndrome, and other autoimmune processes – are among the most common pathologies in modern medicine. Changes in the immune system play a crucial role in the development of these diseases. This study investigated the immune status of patients with chronic salivary gland diseases. The research compared T-lymphocyte subpopulations, immunoglobulin levels, and cytokine profiles of patients with those of a control group. Results revealed significant changes in the CD4/CD8 ratio, increased levels of IgG and IgA, as well as elevated levels of cytokines IL-6 and TNF-α in chronic diseases. These alterations support the autoimmune mechanisms of the pathology and highlight the central role of the immune system. The findings of this study have practical significance for improving the diagnosis and treatment strategies of chronic salivary gland diseases.

Keywords: Chronic salivary gland diseases, immune status, CD4/CD8, immunoglobulin, cytokines, IL-6, TNF-α, Sjögren's syndrome, sialadenitis, immune system, diagnosis, treatment, clinical study, immunological markers, autoimmune processes

Introduction

Chronic diseases of the salivary glands are one of the most important problems encountered in clinical practice today. In particular, chronic sialadenitis, Sjögren's syndrome, and other types of autoimmune processes not only reduce the patient's quality of life, but also cause serious diagnostic difficulties and the need for long-term treatment. According to the World Health Organization, the overall prevalence of diseases of an autoimmune nature is increasing year by year, in which damage to the oral cavity, as well as the salivary glands, is noted among the most important clinical signs. This requires a deeper study of the pathogenesis of these diseases and an analysis of changes in the immune system.

Salivary glands play an important role in the physiological functions of a person, the secretion they produce ensures the beginning of the digestive process, as well as moisturizes the oral cavity and participates in antimicrobial defense mechanisms. Therefore, their functional impairment leads to serious consequences not only for local, but also for general health. As a result of chronic inflammatory or autoimmune processes, saliva production is significantly reduced, with dry mouth (cherostomia), difficulty swallowing, speech impairment, and frequent infections.

In recent decades, thanks to developments in the field of immunology and molecular biology, new data have been obtained on the main mechanisms of chronic salivary gland diseases. In particular, disorders of the T-lymphocyte subpopulation, changes in the CD4/CD8 ratio, cases of hyperimmunoglobulinemia, as well as an increase in pro-inflammatory cytokines, such as IL-6 and TNF-α, play an important role in the pathogenesis of the disease. These changes are often characteristic of autoimmune processes and represent an incorrectly directed attack of the immune system against its own tissues.

Nevertheless, the analysis of existing scientific literature shows that not all aspects of immune status in chronic salivary gland diseases have been fully studied. Some studies were limited to describing more clinical symptoms, while others studied only individual immune markers separately. This makes it difficult to understand the full clinical and immunological relationship. Therefore, a comprehensive analysis of general and specific changes in the immune system in chronic diseases of the salivary glands is an important scientific and practical task.

The relevance of this study lies in the fact that by identifying changes in the immune system, not only the pathogenetic mechanisms of the disease become clearer, but also the effectiveness of early diagnosis, individual treatment approaches, and preventive measures increases. Especially in chronic processes with the presence of an autoimmune component, monitoring of immune markers allows for a preliminary assessment of the course of the disease, the risk of recurrence, and the level of response to treatment.

The purpose of the study is to determine the immune status of patients with chronic salivary gland diseases, compare them with the healthy control group, and analyze the immunological mechanisms of the disease. This is intended to create a scientific basis for improving diagnostic and treatment strategies in the future.

Methodology

This study was conducted at the Clinical Center of Dentistry and Immunology in Tashkent for 2022-2024. A total of 68 patients were involved in the study, in whom chronic salivary gland diseases (chronic sialadenitis, Sjögren's syndrome, and other autoimmune processes) were confirmed by clinical and instrumental methods. The age of the patients ranged from 25 to 65 years, of which 45 were women and 23 were men. The duration of the disease ranged from 1 to 10 years.

As a control group, 30 healthy individuals (18 women and 12 men, average age 34.5±2.1 years) without chronic inflammatory or autoimmune diseases were involved. They underwent a medical examination for their general health status.

Clinical symptoms (herostomy, pain and swelling in the salivary glands, recurrent inflammation), laboratory tests, and ultrasound results were taken into account as diagnostic criteria. The criteria of the American Rheumatological Association (ACR) were used in the diagnosis of Sjögren's syndrome.

Immunological examinations:

- T-lymphocyte subpopulations (CD3+, CD4+, CD8+) were determined using flow cytometry.
- The ratio of CD4/CD8 was calculated.
- Immunoglobulin levels (IgG, IgA, IgM) were determined by enzyme-linked immunosorbent assay (ELISA).
- The level of cytokines (IL-6, TNF-α) was measured using special ELISA kits.

Statistical analysis. The obtained data were processed using the SPSS 25.0 program, and the arithmetic mean (M) and standard deviation (SD) were calculated. Differences between groups were assessed using Student's t-test and chi-square test. The value $P < 0.05$ was considered statistically significant. Also, the correlation between some immune markers and clinical signs was checked using the Pearson coefficient.

Ethical issues. The study was approved by the Ethics Committee under the Ministry of Health of the Republic of Uzbekistan. All participants gave written consent before participating in the study.

Results

During the study, the immune status of 68 patients with chronic salivary gland diseases was compared with 30 healthy individuals in the control group.

Clinical observations. Xerostomy (dry mouth) was noted in 79.4% of patients, and pain and swelling in the salivary glands in 61.7% of patients. Recurrent episodes of inflammation were observed on average 2.4±0.8 times per year. Symptoms of dry eyes, characteristic of Sjögren's syndrome, were detected in 42.6% of patients.

Immunological indicators

Subpopulations of T-lymphocytes. In the group of patients, the level of CD4+ cells was significantly increased compared to the control (46.8±4.2% versus 38.5±3.1%, $p<0.01$).

The level of CD8+ cells decreased (26.4±3.0% versus 19.7±2.8%, $p<0.05$).

The ratio of CD4/CD8 in patients was 2.37±0.3, which is significantly higher than in the control group 1.45±0.2 ($p<0.001$).

1. Immunoglobulins –

- The IgG level in patients was 18.6 ± 1.5 g/L, which is higher compared to 13.9 ± 1.2 g/L in the control group ($p < 0.01$).
- IgA levels were also significantly elevated (3.4 ± 0.5 g/L versus 2.1 ± 0.4 g/L, $p < 0.05$).
- No significant difference was found in the level of IgM ($p > 0.05$).

2. Cytokines

- The level of IL-6 in patients was 24.7 ± 3.2 pg/ml, more than twice as high as in the control group, which was 12.4 ± 2.1 pg/ml ($p < 0.001$).
- The level of TNF-α was also significantly elevated (35.2 ± 4.6 pg/ml versus 18.7 ± 3.0 pg/ml, $p < 0.001$).

Additional observations

- A moderately strong positive correlation ($r=0.62$; $p<0.05$) was observed between the CD4/CD8 ratio and clinical symptoms (chereostomy degree).
- It was established that an increase in the level of IL-6 and TNF-α is associated with the duration of the disease in patients ($r = 0.58$; $p < 0.05$).

Discussion

The results of this study showed that there are significant changes in the activity of the immune system in patients with chronic salivary gland diseases. In particular, an increase in the CD4/CD8 ratio was revealed due to an increase in the number of CD4+ T-lymphocytes and a decrease in the number of CD8+ T-lymphocytes. This condition represents an imbalance of the immune system and is one of the characteristics of autoimmune processes. In previous studies, a violation of the CD4/CD8 ratio in Sjögren's syndrome and chronic sialadenitis was also noted, and our results support this data.

Changes in the level of immunoglobulins also indicate autoimmune mechanisms. An increase in the level of IgG and IgA was observed in the group of patients, which indicates an inflammatory process accompanied by hyperimmunoglobulinemia. The absence of significant changes in the level of IgM indicates that immunoglobulins of this class do not play a leading role in chronic processes. This result was previously noted by other authors, who emphasized that high levels of IgG and IgA immunoglobulins are directly related to the activity of the disease.

Information obtained on cytokines is also important. A significant increase in the level of IL-6 and TNF-α confirms the active course of the inflammatory process in chronic diseases of the salivary glands. IL-6 plays a key role among the mediators of inflammation and stimulates the activation of T- and B-lymphocytes. TNF-α enhances tissue damage, ensuring the duration of the process. The high detection of these cytokines in our study confirms that the disease is chronic and prone to recurrence.

The established relationship between clinical symptoms and immunological indicators also deserves special attention. In particular, a moderately strong correlation was found between a high CD4/CD8 ratio and the severity of xerostomy. This means that the imbalance in the immune system intensifies the severity of clinical manifestations. The correlation of IL-6 and TNF-α levels with the duration of the disease indicates the possibility of predicting the course of the disease using these markers.

The obtained results indicate that changes in the immune system in chronic salivary gland diseases not only play a leading role in the pathogenesis, but can also serve as an important diagnostic marker for early diagnosis and assessment of the effectiveness of treatment. From a practical point of view, this

means that by establishing monitoring of the immune status of patients, it will be possible to develop individual treatment approaches and monitor the activity of the inflammatory process.

At the same time, there are some limitations of the research. Firstly, the number of patients is limited, and it is necessary to verify the results in a wider population. Secondly, we studied only some immune markers (CD4, CD8, Ig classes, IL-6, TNF-α), but other cytokines, cellular receptors, or genetic polymorphisms were not analyzed. Thirdly, the study was of a cross-sectional nature, and no long-term dynamic observations were conducted.

In future research, it is important to study a broader immunological panel in chronic salivary gland diseases, identify genetic factors, and evaluate immunomodulatory treatment strategies.

Conclusion

The results of the study show that a significant imbalance in the activity of the immune system is observed in chronic diseases of the salivary glands. In particular, an increase in the CD4/CD8 ratio was revealed as a result of an increase in the number of CD4+ T-lymphocytes and a decrease in CD8+ T-lymphocytes. This confirms the disruption of immune processes and the activation of autoimmune mechanisms.

Also, high levels of IgG and IgA in patients indicate the duration of the chronic inflammatory process. A significant increase in the cytokines IL-6 and TNF-α indicates an active course of the inflammatory process in the salivary glands. The identified correlation between clinical signs (herostomia, pain, recurrent inflammation) and immunological indicators confirms the leading role of immune imbalance in the pathogenesis of the disease.

These data indicate that they can be used as an important diagnostic marker in establishing monitoring of the immune status, clarifying the diagnosis, and assessing the effectiveness of treatment in chronic salivary gland diseases. Therefore, in future scientific research, it is advisable to conduct a more in-depth study of immunological markers, genetic factors, and the effectiveness of immunomodulatory therapy.

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