

## FEATURES OF HUMORAL IMMUNITY INDICATORS IN THE BLOOD SERUM OF PATIENTS WITH ADENOVIRAL CONJUNCTIVITIS BEFORE AND AFTER TREATMENT

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### ABSTRACT

Inflammatory eye diseases of viral, bacterial and mixed etiology are widespread and are a serious medical and social problem, accounting for more than 40% of all outpatients. The most common agents that cause damage to the organ of vision are adenoviruses (ADVs). Adenoviral eye damage occurs in 10-12% of all cases of adenoviral damage to the body. In addition, adenoviruses remain the most common causative agents of hospital ophthalmic infections. In addition to acute forms, adenoviral eye infection can also occur in the form of chronic and recurrent forms, the proportion of which is currently difficult to estimate.

Target: To study the indicators of humoral immunity in the blood serum of patients with adenoviral conjunctivitis before and after treatment.

**Key words:** Adenovirus, conjunctivitis, immunity, ophthalmic infection.

### INTRODUCTION

Inflammatory eye diseases of viral, bacterial and mixed etiology are widespread and are a serious medical and social problem, accounting for more than 40% of all outpatients. The most common agents that cause damage to the organ of vision are adenoviruses (ADVs). Adenoviral eye damage occurs in 10-12% of all cases of adenoviral damage to the body. In addition, adenoviruses remain the most common causative agents of hospital ophthalmic infections. In addition to acute forms, adenoviral eye infection can also occur in the form of chronic and recurrent

forms, the proportion of which is currently difficult to estimate. Along with the nervous and endocrine systems, the immune system plays the most important role in maintaining balance. It is the dominant and guiding force that controls the process every second by recognizing, limiting the spread, neutralizing and eliminating many microorganisms coming from the external environment. The activity of the immune system is carried out in several stages, and with each subsequent stage the specificity of protection increases.

The immunopathogenesis of acute and chronic eye infections is a complex scientific and practical problem, many aspects of which are only just beginning to be understood by researchers. Adenovirus infection has a profound effect on the synthesis of macromolecules in host cells. With adenoviral eye lesions, a change in the patient's immune status occurs, the nature of which depends on the type-specific properties of the virus, the place of its reproduction, and interaction with immunocompetent cells. Against the background of adenovirus infection, immune deficiency develops, which is caused by many factors, including apoptosis-induced decrease in the number of T-lymphocytes, the presence of an antagonistic effect of tumor necrosis factor (TNF), as well as the expression of so-called virus-associated RNA genes, which help suppress the antiviral effect of interferons (IFN) and other cytokines.

The widespread spread of adenoviral infection, its high contagiousness, damage to working-age population groups, and the development of corneal complications with decreased visual acuity force us to look for new approaches to the treatment of this disease. Ineffective treatment of acute viral, including adenoviral, lesions of the mucous membrane of the eyes leads to the transition of the process to a chronic form. The disease takes a sluggish long course, with short periods of remission and frequent relapses, which significantly reduces the quality of life and causes long-term inconvenience to the patient.

**Target:** ANDTo study the indicators of humoral immunity in the blood serum of patients with adenoviral conjunctivitis before and after treatment.

**Materials and methods:**

All patients with adenoviral conjunctivitis Depending on the method of treatment received, they were divided into two corresponding groups:

The main group - 60 patients with adenoviral conjunctivitis, who, along with traditional treatment, were treated with the antiviral drug Virostav 1.0 mg - 10.0 ml, 1 drop 4-5 times a day for 10 days;

The comparison group included 60 patients with adenoviral conjunctivitis who received traditional treatment.

It is known that the basis of antiviral protection is provided by the mechanisms of cellular immunity. Antibodies produced locally or circulating in the blood (humoral immunity) can block the spread of viruses that are released from dead infected cells and can infect other cells. However, as a rule, antibodies alone are not enough to completely neutralize the virus.

The dominant role in the processes of immune functioning of the eye belongs to cytokines. Cytokines are biologically active substances that are produced by various cells. Corneal endothelial cells, iris and retinal pigment epithelial cells, ciliary body cells and Müller cells are responsible for the secretion of these substances.

In recent years, the discovery of cytokines and the study of their role in the pathogenesis of a wide range of diseases have determined the priorities of their study in various pathologies, including infectious diseases. In clinical practice, the study of cytokine status makes it possible to assess the nature of the process and predict the outcome of the disease in many infections, to objectively assess the effectiveness of therapy, especially in cases of using drugs with immunomodulatory and immunocorrective activity, and cytokines reflect the individual primary reaction to an etiotropic agent.

Cytokines are a group of polypeptide mediators involved in the formation and regulation of the body's defense reactions; they are involved in virtually every link of immunity. Cytokines are characterized by a complex network nature of functioning, in which the production of one of them affects the formation or manifestation of the activity of a number of others. Due to these features of the biosynthesis and regulation of cytokines, they are not always detected in the circulating blood.

According to most authors, it is pathological disruptions in the cytokine system in inflammatory eye diseases of infectious and autoimmune origin that determine the chronic and recurrent course of the disease, the severity of its outcomes and the insufficient effectiveness of treatment. In recent years, a fairly large number of studies have been carried out on the role of cytokines in various eye diseases.

### **Results:**

First of all, we analyzed the main antiviral cytokines IFN- $\alpha$  and IFN- $\gamma$ , the results of which are shown in Tables 1. and 2.

**Table 1.****Indicators of IFN- $\alpha$  before and after treatment in blood serum (pg/ml)**

Group	IFN- $\alpha$	
	before treatment	after treatment
Main group	35.5 $\pm$ 1.16	22.8 $\pm$ 0.82
Comparison group	35.9 $\pm$ 1.21	27.8 $\pm$ 1.26

According to table 1. it is clear that before treatment, IFN- $\alpha$  levels in the blood of patients in both the main and comparative groups increase compared to the control group. At the early stage of the development of a viral infection, before the emergence of the primary humoral immune response, the most important protective antiviral mechanism is IFN- $\alpha$ . In addition, IFN- $\alpha$  protects activated T lymphocytes from apoptosis.

After appropriate treatment, patients in the main group (22.8 $\pm$ 0.82 pg/ml) there is a decrease in the frequency of expression of this cytokine by 1.56 times compared to the indicators before treatment (35.5 $\pm$ 1.16 pg/ml), and in the comparative group there was also a decrease in concentration IFN- $\alpha$  after treatment (27.8 $\pm$ 1.26 pg/ml) 1.29 times than the original data (35.9 $\pm$ 1.21 pg/ml).

When assessing the cytokine status before treatment, patients in both groups showed higher production of IFN- $\gamma$  than healthy individuals, which plays an important role in protection against viruses, attracting macrophages and monocytes to the site of inflammation.

IFN- $\gamma$  in our study tended to decrease both in comparison with healthy volunteers and in the dynamics of the infectious process of each group.

**Table 2.****Indicators of IFN- $\gamma$  before and after treatment in blood serum (pg/ml)**

Group	IFN- $\gamma$	
	before treatment	after treatment
Main group	35.2 $\pm$ 1.42	26.1 $\pm$ 1.05
Comparison group	35.5 $\pm$ 1.36	30.5 $\pm$ 1.24

After treatment in patients of the main group (26.1 $\pm$ 1.05 pg/ml) there was a 1.35-fold decrease in the expression of the type 2 IFN gene when compared with the values before treatment. In the comparison group, the levels of this cytokine before treatment were 35.5 $\pm$ 1.36 pg/ml, and after treatment the indicators decreased slightly by 1.16 times and amounted to 30.5 $\pm$ 1.24 pg/ml. The dynamics of changes in the level of IFN- $\gamma$  transcription in both the main and comparative

groups are similar to those of IFN- $\alpha$ . Acting as the main agent that activates macrophages, IFN- $\gamma$  plays the role of a “controller” of viral infection.

The next indicator we studied was the pro-inflammatory cytokine IL-8, a powerful mediator of inflammation belonging to the group of chemokines. This cytokine is produced under the influence of bacterial endotoxins and cytokines, mainly under the influence of tumor necrosis factor (TNF) and IL-1, as well as IL-3 (Table 3.).

**Table 3.****Indicators of IL-8 before and after treatment in blood serum (pg/ml)**

Group	IL-8	
	before treatment	after treatment
Main group	77.7 $\pm$ 5.26	64.5 $\pm$ 5.02
Comparison group	77.5 $\pm$ 5.18	71.9 $\pm$ 7.15

The study of IL-8 synthesis at the transcriptional level before treatment revealed a significant difference in its main (77.7 $\pm$ 5.26 pg/ml) and comparative groups (77.5 $\pm$ 5.18 pg/ml), compared to healthy volunteers (63.8 $\pm$ 4.96 pg/ml). Induction of IL-8 synthesis by cells of the inflammatory focus, caused by the structural components of the pathogen, as well as the stimulating effect of other cytokines, leads to the activation and recruitment of neutrophils to the focus of inflammation. The increase in IL-8 gene expression in the studied groups is apparently associated with the need to concentrate protective immune factors around the invading viruses for their faster destruction.

In addition, in the dynamics of the development of the inflammatory process within each of the groups, there is a tendency for a gradual decrease in the level of IL-8 expression, so in the main group (64.5 $\pm$ 5.02 pg/ml) decreases by 1.2 times and approaches the indicators of the control group (63.8 $\pm$ 4.96 pg/ml), and in the comparison group (71.9 $\pm$ 7.15 pg/ml) 1.08 times.

The immune response to the entry of various viruses, including adenoviruses into the human body includes the production of specific immunoglobulins (Ig) - IgA, IgM and IgG - to the structural protein of the nucleocapsid (N-protein), the glycoprotein responsible for penetration into the cell (S-protein), and other antigens.

The first immunoglobulin studied was IgA, the results of which are shown in Table 4.

**Table 4.****IgA indicators before and after treatment in blood serum (pg/ml)**

Group	IgA	
	before treatment	after treatment
Main group	1.93±0.08	1.59±0.08
Comparison group	1.92±0.09	1.78±0.1

IgA is present in the blood and secretions of mucous membranes. Antibodies of the IgA class appear in the first days after infection, their concentration increases in the acute period, which was confirmed in our study. In the main group after treatment (1.59±0.08 pg/ml) there is a decrease in IgA by 1.21 times, compared with the indicators at the time of hospitalization (1.93±0.08 pg/ml), and in the comparison group it decreased by only 1.08 times. It must be emphasized that, according to various authors. The appearance and increase in the concentration of IgA antibodies can be observed both during primary infection and during reinfection and exacerbation of latent infection.

Next, we studied the content of IgM in the blood serum, the results of which are shown in Table 5.

**Table 5.****IgM indicators before and after treatment in blood serum (pg/ml)**

Group	IgM	
	before treatment	after treatment
Main group	1.91±0.1	1.72±0.09
Comparison group	1.92±0.1	1.89±0.1

The concentration of IgM antibodies in the main group before treatment was 1.91±0.1 pg/ml, and after treatment decreased by 1.11 times and amounted to 1.72±0.09 pg/ml. In the comparative group before and after treatment, no statistically significant differences were found. In the blood, IgM is found in the form of pentamers consisting of 5 monomers connected by a J-chain. WITH IgM is synthesized in the body during the primary immune response; they are low-affinity, but high-avidity due to the large number of active centers. In combination with an antigen, they activate complement more effectively compared to IgG. IgM monomers are B cell receptors.

Another immunoglobulin, the concentration of which changes after adenovirus infection, is IgG class antibodies, the results are presented in Table 6.

Table 6.

**IgG values before and after treatment in blood serum (pg/ml)**

Group	IgG	
	before treatment	after treatment
Main group	10.6±0.23	9.21±0.13
Comparison group	10.5±0.23	10.1±0.21

Class G immunoglobulins make up the bulk of immunoglobulins in blood serum. IgG antibodies to the adenovirus appear several days after infection. Their concentration increases rapidly during the period of acute infection. IgG antibodies appear in large quantities during the secondary immune response, so the bulk of antibodies against bacteria and viruses are IgG. Immunity to adenoviruses is unstable.

From the data in Table 4.6. it is clear that the blood serum IgG concentration in the comparative group (10.1±0.21 pg/ml) after treatment decreased by only 3.81%, compared to the values before treatment (10.5±0.23 pg/ml), while in the main group after treatment (9.21±0.13 pg/ml) there was a decrease in this indicator by 13.1% than before treatment (10.6±0.23 pg/ml ).

**Conclusions:** Thus, based on the results of the studies, it was found that The cytokine response we observe during adenoviral eye infection has some characteristic features. IFN- $\alpha$ , IFN- $\gamma$  and IL-8 are the main cytokines involved in antiviral immunity, therefore the surge in the frequency of gene expression of these cytokines at the initial stage of the disease reflects an adequate tissue response in response to adenoviral infection. In all studied indicators of humoral immunity in the blood serum before the start of treatment, an increase was observed, and after using the drug Virostav along with traditional treatment, it was revealed that the indicators of IgA by 10.7%, IgM by 8.99%, IgG is 8.81% lower than after traditional treatment.

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