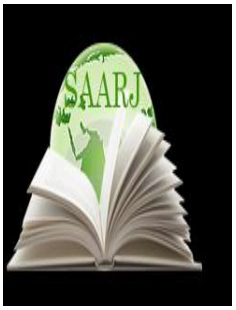

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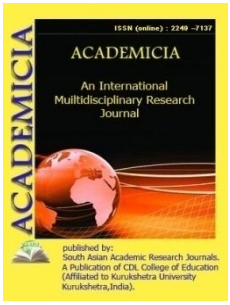

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CLINICAL CURRENT AND ANTI-VIRAL THERAPY OF ADENOVIRAL KERATOCONJUNCTIVITIS

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ABSTRACT

This study presents the clinical efficacy of the antiviral drug "Virostav" in patients with adenoviral keratoconjunctivitis. On the background of therapy with Virostav, complete recovery with restoration of normal vision was revealed in 69.2% of patients, and partial recovery with subsequent complete restoration of vision in 30.8% of patients. The effectiveness of the drug with complete recovery of patients with adenoviral conjunctivitis was 76.9%. The convenient and ready-to-use drug Virostav has a pronounced therapeutic effect in the complex treatment of patients with both adenoviral keratoconjunctivitis and adenoviral conjunctivitis, this is the basis that the drug Virostav is promising in the treatment of patients with viral eye lesions.

KEYWORDS: *Adenoviral Keratoconjunctivitis, Visometry, Interferon, Eye Drops, Virostav, Viral Eye Damage, Antiviral Drug, Biomicroscopy, Clinical Efficacy.*

INTRODUCTION

Viral lesions of the organs of vision remain the most important problem in practical ophthalmology due to their wide spread and high frequency of outbreaks. The most common viral agents of eye disease are adenoviruses - adenoviral infections. Among them, the most common are adenoviruses of serotype 8, 11, 19 (epidemic keratoconjunctivitis), adenoviruses of serotype 3, 4, 6, 7 (pharyngoconjunctival fever), as well as enteroviruses [5].

As a rule, viruses often infect the mucous membranes, and viruses in various parts of the eye are especially dangerous. The process most often involves the cornea, as a result of which keratitis occurs, which in the future is the cause of corneal opacity, persistent decrease in vision, as well as the development of severe complications [2].

Currently, adenoviruses and herpes simplex viruses are the most common causes of corneal damage. According to the world's leading ophthalmologists, 66.8% of all cases of corneal pathology are associated with them, 55.1% - of all ulcerative lesions of the cornea, more than 60% - of blindness. A viral lesion of the eye has its own peculiarity - in most cases it proceeds with a frequent relapse of the disease. Moreover, the course of each subsequent relapse is more severe than the previous one, which requires more intensive and long-term treatment and can contribute to the development of persistent corneal opacity, as well as complicated forms of keratitis - corneal ulcers, its perforation, which requires surgical treatment - corneal transplantation. Such patients lose their ability to work for a long time or become disabled [1, 3].

Treatment of viral eye diseases is a difficult task in practical ophthalmology. Traditionally, antiviral drugs such as acyclovir and others are used for herpes viral lesions of the eyes [6].

Interferons also play an important role in the treatment of viral infections. Interferons as natural antiviral agents have been used for many years to treat viral lesions of the eyes. Due to the action of interferon around the focus of the introduction of the virus, a barrier is formed from cells uninfected with the virus, and therefore the spread of infection is limited. Interferon is also capable of modulating the activity of immunocompetent cells. Human leukocyte interferon has been widely used in the past for the treatment of viral keratoconjunctivitis, but its isolation from donor blood is currently difficult due to the epidemic situation. Recently, recombinant interferons have been used in medicine, including ophthalmology. It is believed that the safety of the spread of blood-borne infections can be fully guaranteed only if the leukocyte interferon prepared on blood cells is replaced with recombinant interferon obtained by genetic engineering [4].

Antiviral therapy for adenovirus infection is associated with certain difficulties, since today there are no drugs in the world that selectively affect the pathogens - adenoviruses. With these infections, drugs of broad antiviral action are usually used - interferons. One of them is the preparation of interferon alpha-2 - Okoferon eye drops. The active substance of Okoferon's drop is interferon alpha-2b of a recombinant person 1,000,000 IU. The drug exhibits immunomodulatory and antiviral activity. In order to avoid possible physicochemical interaction of Okoferon with other ophthalmic agents, it is advisable to apply it 30 minutes before or 30 minutes after instilling other medicines into the eyes [7].

In ophthalmological practice, a drug has recently been widely used - Virostav eye drops, the active agent of which is idoxuridine. Virostav - modern eye drops for the treatment and prevention of viral eye diseases. The main indications for the use of the drug are keratitis and keratoconjunctivitis.

Considering that the mechanism of the antiviral action of Virostav and Okoferon is the same - the drugs act on the basis of interferon alpha-2, we assumed that the use of Virostav in the complex therapy of viral keratoconjunctivitis will allow us to study the clinical efficacy in a comparative aspect.

The aim of the work was to evaluate the clinical efficacy of the antiviral drug Virostav in the complex therapy of viral conjunctivitis in comparison with other antiviral eye drops.

MATERIALS AND METHODS

We observed 23 patients with various forms of clinical course of adenoviral lesions of the eyes: adenoviral conjunctivitis (AVK) - 10 patients: 4 (40.0%) men, 6 (60.0%) women), adenoviral epidemic keratoconjunctivitis (EKC) - 13 patients, including 5 (38.5%) men and 8 (61.5%) women. Patients with adenoviral conjunctivitis made up group I, and patients with epidemic adenoviral keratoconjunctivitis made up group II (Fig. 1).

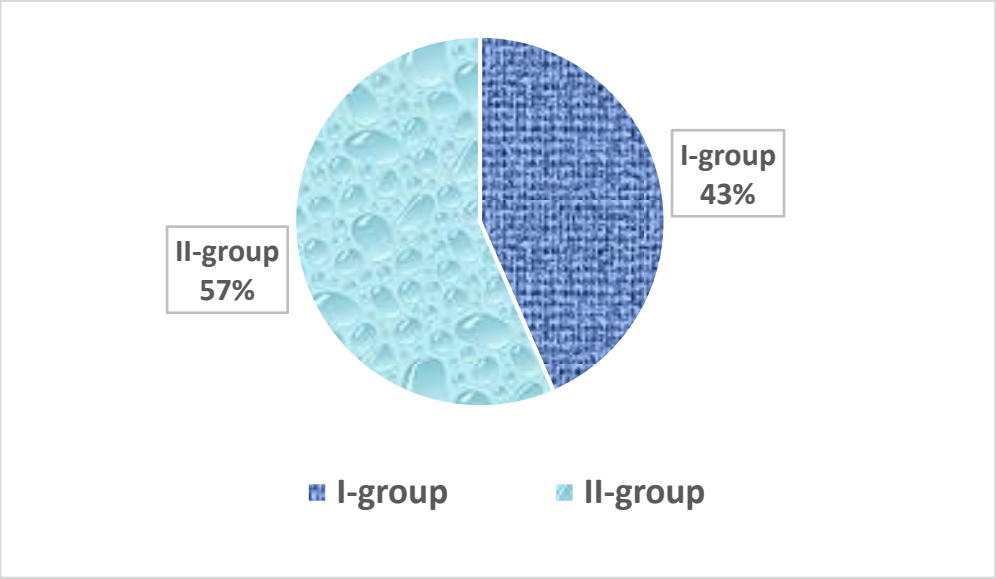

Figure 1. Distribution of examined patients by groups

The age of the examined patients varied from 18 to 55 years in the first group from 18 to 51 years), and in the second - from 19-55 years. The average age of patients in the first group was 35.4 years, and in the second - 37.0 years.

Patients of the first group received traditional therapy with the inclusion of the antiviral drug Okoferon (0.1% solution, 5.0 ml) in the form of eye drops in the treatment regimen. Patients of the second group received Virostav antiviral eye drops (0.1% solution 10.0 ml).

Eye drops Okoferon (0.1%) in patients of the first group were instilled 2 drops into the conjunctival sac of the eye every 2 hours, but not less than 6 times a day. With a decrease in the symptoms of the disease, the volume of instillations was reduced to 1 drop. The course of treatment averaged 7-10 days.

Eye drops Virostav (0.1%) in patients of the second group were instilled in the following sequence - 1 drop into the conjunctival cavity every hour during the day and every 2 hours at night. After sustained improvement, every 2 hours during the day and every 4 hours at night. The treatment was continued for another 3-5 days after complete healing, confirmed by the absence of fluorescein staining of the cornea.

According to indications, patients in both groups received additional treatment depending on the clinical form of the infectious process.

Examination of patients included: collection of anamnesis, results of clinical research, biomicroscopy of the eye, conjunctiva, cornea. General and special methods of ophthalmological examination were used. Of the generally accepted general research methods, visometry, biomicroscopy and side illumination were used. Of the special research methods, immunological (determination of fluorescent antibodies in conjunctival scrapings), algesimetry (determination of corneal sensitivity) and virological (polymerase chain reaction) methods for determining viral eye lesions (viral conjunctivitis and keratoconjunctivitis) were used.

Statistical processing was performed using a computer program. To assess the statistical significance of differences between comparable mean values, the correctness of the answer was determined by the Student's test (t). The level of significance of this response (P) was determined according to the Student's distribution table (P-coefficient of reliability). Differences were considered significant at $P < 0.05$.

Results of the study

For patients with adenoviral conjunctivitis (group I), acute onset of the disease and bilateral eye damage were most typical. Patients often complained of pain, sensation of a foreign body in the eye, lacrimation. The eyelids of the patients were edematous, the conjunctiva was moderately or significantly hyperemic, the lower transitional fold was thickened, folded, sometimes there were punctate hemorrhages. In half of the patients, regional adenopathy of the parotid lymph nodes was found.

For patients with epidemic adenoviral keratoconjunctivitis (group II), the following clinical picture was characteristic: acute onset, usually both eyes are affected - first one, after 1-5 days - the second. Patients complain of pain, sensation of a foreign body in the eye, lacrimation, regional adenopathy is noted on day 1-2 of the disease. After 5-9 days from the onset of the disease, characteristic point infiltrates appear under the corneal epithelium (Table 1).

TABLE 1 CLINICAL CHARACTERISTICS OF ADENOVIRAL CONJUNCTIVITIS AND EPIDEMIC ADENOVIRAL KERATOCONJUNCTIVITIS IN PATIENTS WITH VIRAL EYE DISEASE

Indicators	The nature of the damage	Adenoviral conjunctivitis %	Epidemic adenoviral keratoconjunctivitis, %	P
Onset of the disease (acute)		100%	100%	> 0,05
Eye damage	unilateral	10,0%	7,80%	> 0,05
	bilateral	90%	92,3%	> 0,05
Eye pain		70,0%	61,5%	> 0,05
Sensation of a foreign body in the eye		50,0%	46,1%	> 0,05
Photophobia		30,0%	30,8%	> 0,05
Lachrymation		40,0%	38,5%	> 0,05
The eyelids are swollen		10,0%	15,4%	> 0,05
Conjunctival hyperemia	moderate	20,0%	15,4%	> 0,05
	significant	10,0%	23,1%	< 0,05

Regional adenopathy	50%	46,2%	> 0,05
Pinpoint hemorrhages	60,0%	69,2%	> 0,05
Point infiltrates under the epithelium	20,0%	30,8%	> 0,05
The lower transitional fold is thickened	70,0%	69,2%	> 0,05

As can be seen from the table, the clinical picture of adenoviral conjunctivitis and epidemic adenoviral keratoconjunctivitis were very similar, the difference between the clinical parameters was not statistically significant (the exception was significant conjunctival hyperemia in the second group, P <0.05).

In the examined patients of both groups with confirmed viral eye damage, purulent discharge from the conjunctiva was not detected.

Among patients with adenoviral keratoconjunctivitis, conjunctival hemorrhages often appeared (69.2%). In this group, 4 (30.8%) patients had a severe course of the disease with a pronounced allergic inflammatory reaction, severe irritation of the mucous eyes, clearly noticeable edema of the eyelids and conjunctiva, profuse lacrimation and severe photophobia. In patients, the conjunctiva was edematous, loosened, membranes formed on the mucous membrane, the separation of which was accompanied by bleeding. In 15.4% of patients, epitheliopathy was noted on the cornea of the eye. At the first signs of subepithelial punctate keratitis or the formation of films, with epitheliopathy and tear insufficiency, appropriate symptomatic and pathogenetic drugs were added to the treatment.

When carrying out additional therapy for adenoviral conjunctivitis, the time for normalization of the conjunctiva with the disappearance of the phenomena of eye damage was reduced to 6.8 days. The results of treatment in a comparative aspect with a group of patients receiving another drug in the form of eye drops are presented in table. 2.

TABLE 2 RESULTS OF THE TREATMENT OF ADENOVIRAL CONJUNCTIVITIS AND KERATOCONJUNCTIVITIS WITH THE USE OF EYE DROPS OKOFERON AND VIROSTAV

Indicators	Viral eye damage	Okoferon (I-group)	Virostav (II-group)	P
Average duration of therapy, day	adenoviral conjunctivitis	6,8±1,10	7,1±1,32	> 0,05
	epidemic adenoviral keratoconjunctivitis	9,65±1,56	10,1±2,03	> 0,05
Disappearance of hemorrhages, day	adenoviral conjunctivitis	6,5±0,72	6,9±0,89	> 0,05
	epidemic adenoviral keratoconjunctivitis	10,9 ±2,07	11,5±2,21	> 0,05
Disappearance of hyperemia, day	adenoviral conjunctivitis	5,9±0,45	6,3±0,57	> 0,05
	epidemic adenoviral keratoconjunctivitis	6,7±0,69	7,4±0,77	> 0,05
The disappearance of	adenoviral	8,34±1,24	9,0±1,53	> 0,05

photophobia, day	conjunctivitis			
	epidemic adenoviral keratoconjunctivitis	9,64±1,43	10,2±1,55	> 0,05
Complete recovery, %	adenoviral conjunctivitis	80,0%	76,9%	> 0,05
	epidemic adenoviral keratoconjunctivitis	70,0%	69,2%	> 0,05

As can be seen from the table, in case of epidemic adenoviral keratoconjunctivitis, when prescribing combination therapy with the inclusion of the drug Virostav, the duration of treatment was 10.1 days.

Conjunctival edema disappeared on day 6 in all patients, conjunctival hyperemia disappeared on day 11, and the follicular reaction completely disappeared in all patients on average on day 12 of treatment. It should be noted that as a result of complex treatment, local manifestations of the disease also disappeared.

CONCLUSION

The results of these studies of the clinical efficacy of the drug - Virostav eye drops in comparison with the drug Okoferon in the treatment of adenoviral keratoconjunctivitis showed that the administration of the drug Virostav according to the proposed scheme has no less pronounced therapeutic effect in the complex therapy of adenoviral keratoconjunctivitis. Virostav does not have an irritating effect and is well tolerated by patients. There is a reduction in the duration of treatment, respectively, the number of complications and relapses decreases. The clinical efficacy and safety of patients' therapy was assessed by the reduction or disappearance of clinical symptoms of eye damage. This indicator is naturally associated with a decrease in viral load - viral replication. in the treatment of viral keratoconjunctivitis with the drug "Virostav" in 69.2% of cases, complete recovery was noted and in 30.8% of cases, a relative delay in recovery with subsequent complete recovery was revealed, the effectiveness of the drug in adenoviral conjunctivitis was 76.9% and 33.1%, respectively.

Thus, the results of the study showed that the use of eye drops of the drug "Virostav" revealed a high efficiency of therapy for both adenoviral conjunctivitis and adenoviral keratoconjunctivitis. Virostav, possessing a highly effective therapeutic effect in the complex treatment of adenoviral conjunctivitis and keratoconjunctivitis, is a highly economical drug and very convenient to use as a finished drug.

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