RESULTS OF CONSERVATIVE TREATMENT OF KERATOCONUS

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Abstract. *The paper describes the study on the ratio of antibodies in the blood serum of patients with keratoconus to a number of neuroantigens and markers of autoimmune processes. Obtained results allowed the authors to predict the prognosis of the disease development and suggest medical treatment of keratoconus with peptide bioregulators (52 patients). The control group comprised* 146 *patients. Due to this medical treatment the arrest of keratoconus progression was proved to be statistically significant.*

Key words: *keratoconus, immunology, antiidiotype, prognosis of progression, treatment, cytamins, biolan, peptide bioregulatores.*

Keratoconus is the central dystrophy of the cornea with its characteristic cone-shaped deformation resulting in the significant decrease of vision in young patients.

Etiology and pathogenesis of this disease is not yet totally clear. Currently, the most recognized hypothesis says that disturbed heredity and metabolism are main factors responsible for keratoconus development. N. A. Puchkovskaya and Z. D. Titarenko proved in their book (6) that different etiologic factors could lead to a lower activity of glicose-6-phosphatedegidrogenase and inhibition of the glutathione reduction reaction. This work describes in details further pathologic processes which finally cause death of cells and atrophy of the cornea. In their research, the two authors studied corneal disks with keratoconus removed during penetrating keratoplasties.

We clinically examined immunity of 117 patients with keratoconus. Determined were serum levels of autoantibodies (a-AB)-markers of autoimmune processes (a-AB to phosphadites, DNA, collagen IV, cytoplasmic antigens of neurophils, and Fc-fragments of antibodies) as well as levels of a-AB and applicable antiidiotypic antibodies (AIAB) to antigens S100 and GFAP of the nervous tissue and to the growth factor of nerves (GFN). Also, we calculated the value of the coefficient K which is the ratio of a-AB/AIAB (1). Normally, this value makes up 0.8-1.2 ($p<0,05$).

Increase in the level of serum antibodies at least to one of the mentioned neuroantigens was recorded in 81.2% of our patients. Empirically set up normal "limits" for the K coefficient (for antibodies to antigens of nervous tissue) were typically found either higher and lower these limits ($p<0,05$). The highest values of K were recorded during active progression of keratoconus. On the arrest of the disease development these values became normal. From the prognostic point of view, the K value lower its norm appeared to be a favorable indicator. All these findings allowed us to presume that in patients with keratoconus idiotypic antibodies were insufficiently "shielded" by applicable antiidiotypes causing their pathogenic action.

Physiological level of antibodies-markers of autoimmune processes was higher in 42.5% of patients and lower in 29.5% of them; both conditions had an adverse effect on the progression of keratoconus.

Employing methods of multiple correlation and regressive analysis we revealed the most important indicators - KS100, K GFN, and levels of markers of autoimmune processes (C). On the basis of these indicators and immunologic data (1), the equation of linear regression was obtained that allowed to calculate the prognosis of keratoconus progression for each particular patient. In comparison with the actual progression, our calculated prognosis has proved to be correct in 72.7% of cases.

These research data as well as a well-known combination of keratoconus with general diseases (polyglandular endocrine pathology, atopic dermatitides, pollinosises, osteogenesis imperfectia, etc.) helped to select proper medications and the treatment scheme.

A set of peptide bioregulators developed by Russian scientists included CYTAMINS, (ophthalamin, cerebramin, epiphamin, chondramin) and BIOLAN (3, 4, 5).

The medical treatment was prescribed to 52 patients for 1-5 years (on the average - two treatment session **per** year). The control group comprised 146 patients.

We compared the following factors in the two groups: the patients age, their age at the moment of **disease** onset, the level of the disease manifestation during the very first visit to a doctor, and the total duration of the follow-up period.

In tables (I-V), please see a detailed comparative analysis of the examined patients for all above mentioned factors:

Table I.

Patients' age.

Patients' age (years)	*Patients with keratoconus (%)*	
	Treatment	*Control group*
Under 13	0	1
Within 14-30	93.8	49.5
Over 30	6.2	49.5
M±6	*24 ±5*	*29 ±8*
T	*0.53*	

Table II.

Patients' age at the moment of disease onset.

The age at the disease onset (years)	*Patients with keratoeonus (%)*	
	Treatment	*Control group*
Under to 13	28	35
At 14-30	72	61
Over 30	-	8
M±S	*16±5*	*16±6*
T	*0*	

As the table I shows, patients differ very much from each other in their age, and those from the treatment group are younger than those from the control one. Young patients are known to have their keratoconus progressing faster.

The table II shows that in terms of the disease onset the groups are identical.

Table III.

Duration of the disease.

Duration of the disease	*Patients with keratoeonus (%)*	
	Treatment	*Control group*
For up to 5 years	44	25
For 6-10 years	25	19
For more that 10 years	31	56
M±6	*8±6*	*15±8*
T	*0.7*	

Table IV.

Keratoeonus stage during the first visit to a doctor.

*TIS**	*Patients with keratoconus (%)*	
	Treatment	*Control group*
Up to 2.0	72	74
Within 2.01 -3.0	22	25
Above 3.01	6	1
M±6	*1.68 ±0.64*	*1.71 ±0.52*
T	*0.04*	

The difference in patients, in terms of the disease duration, is quite considerable. Note, that the treatment group with a more intensive progression of keratoconus has a shorter duration of the disease.

The table IV shows that during the first visit to a doctor the stage of the disease was practically identical in both groups of patients.

Table V.

Total duration of the follow-up period.

Duration of the follow-up period (months.)	*Patients with keratoconus*	
	Treatment	*Control group*
M±6	*27±16*	*25 ±15*
m	*0.09*	

The Table V shows the total follow-up period was identical in both groups.

Thus the detailed comparison of the two groups indicates much older patients and longer duration of the disease in the control group.

Development of the special topographic index of the keratoeonus stage (TIS) (2) for the first time permitted us to quantitatively characterize progression of keratoeonus in different age groups depending on the duration of the disease as well study changes in its progression due to the given treatment.

Case follow-up for 5 years of 402 patients with keratoconus (1) showed that 1/3 of all cases had a progressive character of the disease, and doctors could see both its progressive and non-progressive forms. More frequent and faster progression of keratoconus is observed during the first 10 years from the onset of the disease.

Our research (1) further confirms that keratoeonus is most intensively progressing during the first 5-10 years after its onset and that after 10 years the number of its progressive forms goes rapidly down, though some isolated progressive cases could be met with after 30 and even 40 years after the onset of initial signs of the disease.

The obtained data on the rapid progression of keratoeonus on its earlier stage and especially in young people allowed us to consider patients under 30 years of age with total duration of the disease for up to 10 years THE RISK GROUP OF ACTIVE PROGRESSION OF KERATOCONUS.

Naturally, the treatment was, in the first place, prescribed to this category of patients. Besides, this particular feature served as a basis for the comparative analysis of two groups of patients and was also taken into account when assessing final results of treatment.

For the qualitative evaluation of keratocunus progression in both groups we used the above mentioned topographic index of the keratoeonus stage (TIS) computed with the help of special program on the basis of the equation of linear regression and topographic data of the cornea (2).

In this work we used the TIS derivative - the criteria of progression I (CP1) which characterizes the rate of progression in one eye during a year (1). As the progression of keratoeonus in both eyes was often unsymmetrical, one eye was considered one case. Comparative data on the progression of keratoeonus in two groups of patients are presented in the Table **VI.**

Table VI.

Progression of keratoeonus in the treatment and control groups.

CPl	*Patients with keratoeonus (%)*	
	Treatment	*Control group*
Non-progressive keratoconus (CP1<0.1)	69	70
Progressive Keratoconus (CPl > 0.1)	31	30
M±6 (for progressive keratoeonus)	*0.25 ±0.08*	*0.34 ±0.30*
T	*0.30*	

As follows from Table VI:

- Performed treatment significantly reduces the rate of keratoeonus progression.
- Patients from the treatment (1) and control (2) groups differ very much from each other: patients from the 1st group are younger and duration of their disease is shorter as compared to the 2d group, i.e. the disease progression in the 1st group could be much faster than in the 2d group. Due to the treatment given to patients from the 1st group the progression rate of their keratoeonus not only went down to the same value as in the 2d group but proved to be even significantly lower. This finding further supports the significance of final treatment results.
- The number of patients with a progressive character of the disease did not change with a lapse of time. Probably, our treatment scheme do not lead to the conversion of progressive forms of keratoeonus into the non-progressive ones, however the progression rate goes considerably down.

Clinical examination of immunity of treated patients demonstrates normalization of immune indexes in 31.3% of cases and their marked improvement in 52.8% of cases. This fact makes it is possible to presume that one of mechanisms that ensures efficiency of peptide bioregulators (of the animal origin) is the normal idiotypes/antiidiotypes ratio with the directivity to S100 и GFN proteins as well as a lower serum level of autoimmune antibodies markers of autoimmune processes. We believe that the delay in the keratoeonus progression due to the suggested treatment could also be attributed to some other factors including improvements in biomechanical properties of the cornea.

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