The purpose of this study was to investigate the content neurospecific markers protein S-100 and neuroenolaza in blood serum and tear fluid of patients with ocular ischemic syndrome.

Material and methods. We observed 43 patients aged 57 to 79 years, mean age 67.3 ± 2.7 years. Control group consisted of 11 volunteers without ophthalmic symptoms. The main group consisted of 32 patients with OIS. The neurospecific proteins S100 and NSE were investigated in blood serum and tear fluid.

Results. The study found that in patients of the control group the content of protein were within the normal range: S -100 in the tear fluid – 0.0662 ± 0.00335 mkg/l, in the blood serum 0.0508 ± 0.00241 mkg/l. In patients of the main group the indicators of protein in the tear fluid were elevated in all patients - 3.12 ± 0.246 mkg/l (p<0.005). The normal levels in blood serum of marker S-100 was in 30 patients - 0.0589 ± 0.00303 mkg/l, while, in 2 patients protein S-100 were raised fluid and averaged 0.2175±0.00725 mkg/l. It was found that in patients of the control group content of protein NSE in the tear fluid and blood serum were within normal values - 15.86 ± 0.148 Ng/ml, 15.60 ± 0.202 Ng/ml respectively. In the main group the amount of protein NSE tended to increase in the tear fluid in 23 patients and averaged 33,012 ± 3,2626 Ng/ml (p<0.005), a significant decrease the quantity of protein was observed in 9 patients, which amounted to 5.166 ± 0.8301 Ng/ml. At normal levels in the blood serum protein NSE detected in 30 patients and averaged 14.48 ± 0.263 Ng/ml, whereas, in 2 patients there was a significant increase of content of protein NSE and was 27.47 ± 3.068 Ng/ml.

Conclusions. Thus, changes in the concentration of S100 and neuroenolaza in the tear fluid in patients with ocular ischemic syndrome allow to identify as marker of nerve cells damage of the eye, contributing to the definition in conjunction with other signs of stage and etiology of the disease.

INTRODUCTION

It was found that blood circulation in ocular ischemic syndrome (OIS) vessels of optic disk suffers much faster than the flow in the central retinal artery. Considering of the increased blood supply papillomacular beam and temporal areas of the optic disk, the upper and lower segments are in the worst conditions in chronic hypoxia, and most likely in these areas will develop processes of neurodegeneration before (Makkaeva, 2009).

For detailed study and control of processes of neuronal degeneration was investigated protein S100, presenting in high concentration in nervous system cells. According to the literature, increasing the concentration of this protein in blood serum report as a marker of nerve cells damage. It has been shown that in an early phase of cerebral infarction, microglial cells in peri-infarction zone express proteins S-100, and actively proliferate, and the expressed proteins are not more than three days after infarction. This suggests that the constant activation of microglial population is early response of nervous tissue to ischemia and can be used as an early marker of damage (Alfred, Fonteh, & Biringer, 2006).

Among neurospecific proteins, in addition to the marker S100, the most studied is the neuron - specific enolase (neuroenolaza, NSE). Neyroenolaza - an enzyme of carbohydrate metabolism, presenting in the cells of neuro-ectodermal origin, neurons of the brain and peripheral nervous tissues. Increasing neurospecific proteins in the blood indicates damage to the nervous tissue, and allows to give intravital assessment of the central nervous system and the dynamics of the neurodegenerative process in ischemic brain lesions. However, up to date neurobiochemical diagnostics used in acute cerebrovascular disorders, but not in lesions of the vision (Blinov, 2004; Martynova, Skvortsov, Petrov, & Chekhonin, 2007).

Tear fluid is an active biological system, which characterizes the composition of the metabolic processes of the eyeball occurring not only in the tissues washed it, but in the body as a whole, an important consideration is the fact that tear easily accessible for research. Unlike most other body fluids it can be quickly and easily get to study (Dzhengurova, 2007).

According to the literature, violation of metabolic processes in the organ of vision and the corresponding changes of the tear fluid may occur long before the manifestation of disease, which opens up opportunities for early diagnosis and prevention.

In this context, the study of ischemic lesions of the eye based on neurobiochemical changes of blood and tears in conjunction with standard methods is an urgent problem, because early detection and monitoring of levels of S-100 and neuroenolaza will identify and confirm the presence of nerve tissue damage at an early stage when successful treatment is possible.

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LEVEL OF MARKERS OF NEURODEGENERATION IN PATIENTS WITH OCULAR ISCHEMIC SYNDROME

Purpose
To explore content of neurospecific markers protein S-100 and neuroenolaza in blood serum and tear fluid in patients with ocular ischemic syndrome.

Material and methods
We observed 43 patients aged from 57 to 79 years, mean age 67.3 ± 2.7 years. From these, 12 (27.9 %) are women and 31 (72.09 %) are men. Observation period - from 6 months to 3 years. In the control group (group 1) were 11 volunteers without ophthalmic symptoms, identical age category. The main group (group 2) consisted of 32 patients with OIS including impaired circulation in the blood vessels of the retina and optic nerve.

The study was conducted with the Declaration of Helsinki, ethical approval of the National Committee (37-02/19 – 27.06.2014) of the Republic of Uzbekistan under the Ministry of Health of the Republic of Uzbekistan. Patients are acquainted and signed a written informed consent.

All patients underwent a comprehensive eye examination, which included visiometry, tonometry, static computer perimetry, biomicroscopy, fundus ophthalmoscopy, and optical coherence tomography. To exclude cancer and detect ischemic brain lesions performed magnetic – resonance tomography with tractography and angiography.

Laboratory blood tests were included: general analysis of blood, general urine analysis, detailed biochemical analysis of blood, lipid profile, rheumatoid panel, hemostasiogram and immunofluorescent blood test for TORCH infection.

Indicators of neurospecific proteins S100 and NSE investigated in blood serum and tear fluid using chemiluminescent immunoassay on automated electrochemiluminescent immunoanalyzer Cobas e 411 (Roche Diagnostics, Switzerland). All patients on the indication consulted narrow specialists: neurologist, neurosurgeon, internist, cardiologist and angi surgeon.

Statistical processing of the results was performed by the program Statistica 8.0.

Results and discussion
The study revealed in patients of the control group indicators of the protein S-100 in the tear fluid totaled 0.0662 ± 0.00335 mkg/l, which was within the normal range (N ≤ 0.105 mkg/l).

In patients of the main group indicators of the protein in the tear fluid were raised in all patients and averaged 3.12 ± 0.246 mkg/l (p<0.005). In the serum marker S-100 were observed at normal level in 30 patients - 0.0589 ± 0.00303 mkg/l, while, in 2 patients indicators of protein S-100 were raised and averaged 0.2175 ± 0.00725 mkg/l (p <0.005). There was a significant increase in 31 times the content neurospecific protein S-100 in the tear fluid of the main group patients compared with controls. Tendency to increase the content of this protein in the tear fluid was relatively unexpressed in patients without concomitant diseases (18 patients) - 2.100 ± 0.196 mkg/l. In the presence of patients with concomitant diseases such as diabetes type II and hypertension (14 patients) the content of the marker increased 45 times, which compose 4.521 ± 0.112 mkg/l. Perhaps during the development of local changes in the retina and optic nerve, such as diabetic and hypertensive neuroretinopathy, marker level also rises. It should be noted that in these patients when correctly administered both basic and ophthalmic diseases visual functions remained high and amounted to 0.61 ± 0.13.

To the level of the marker in the tear fluid also influenced stages of the disease, while in the early stages of acute ischemia indicators increase sharply, averaged 3.963 ± 0.143 mkg/l. As the transition process in the chronic form, and possibly incorporating compensatory mechanisms protein content gradually decreased and after a month was 1.990 ± 0.185 mkg/l.

It was found that in patients of the control group content of protein NSE in the tear fluid and blood serum were within normal values - 15.86 ± 0.148 Ng/ml, 15.60 ± 0.202 Ng/ml respectively.

In the main group the amount of protein NSE tended to increase in the tear fluid in 23 patients and averaged 33.012 ± 3.2626 Ng/ml (p<0.005), a significant decrease the quantity of protein was observed in 9 patients, which amounted to 5.166 ± 0.8301 Ng/ml. At normal levels in the blood serum protein NSE detected in 30 patients and averaged 14.48 ± 0.263 Ng/ml, whereas, in 2 patients there was a significant increase of content of protein NSE and was 27.47 ± 3.068 Ng/ml. At normal levels in the blood serum protein NSE detected in 30 patients and averaged 14.48 ± 0.263 Ng/ml, whereas, in 2 patients there was a significant increase of content of protein NSE and was 27.47 ± 3.068 Ng/ml.

Unlike marker S100, for the content neuroenolaza in the tear fluid did not affect comorbidities organism rather indicators protein depended on the etiology of the disease. Thus, in patients with ischemic neuropathy and ischemic central retinal vein thrombosis was noted elevated levels of NSE in 206%. With the development of ischemic syndrome due to inflammation - the central retinal vein thrombosis and anterior ischemic neuropathy vasculitis etiology - neuroenolaza levels decreased in 32,25%.

Analysis of the data quantity of protein NSE in the blood serum showed that the content of the marker in the majority of patients remained in the normal range, it indicates the integrity of the blood-brain barrier (Grigoriev, 2010). Increasing the level observed in patients with concomitant neurological disorders - the development of vascular encephalopathy with the presence of multiple ischemic lesions, atrophy of frontal - temporal areas on both sides.

We noted a significant increase in the amount of neuroenolaza 206% in the tear fluid in 23 patients of the main group, but significant correlation between the number of indicators neurospecific proteins S100 and neuroenolaza in blood serum and tear fluid in these patients not revealed.

The tendency to increase the markers S100 and NSE in the tear fluid, remain, while in the normal range in blood serum may indicate that the processes of neurodegeneration and ischemia in these patients developed mainly in the organ of vision. It should be noted that in two patients, where was recorded increased content of protein S100 213 times and NSE 13,56 times, were cause neurodegeneration of the brain, which confirmed MRI and the clinical diagnosis of neurologists.

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The obtained data show a significant increase in the content of neurospecific protein S100 in the tear fluid (at 37 - 40 times) in patients with chronic OIS, at the time in the general circulation recorded the normal values. In the literature, there is evidence of elevated levels of this protein in the blood serum in patients with glaucoma (Kamenskikh, Zaharova, Kolbenev, Kamenskikh, & Sidelnikova, 2013), but missing some information about content of the protein S100 in the tear fluid. To the local increase amount of this marker promotes development in the organ of vision ischemic and hypoxic processes, which is typical for OIS enhancing damage of glial cells in the nervous tissue, which leads to increased development of markers of neurodegeneration S100 (Shakeri, Mahdkhah, & Panahi, 2013). Increasing the content of protein S100 in the nerve tissues is one of the indicators predict extensive brain damage. The concentration of S100 depends on the degree of brain damage and provides significant information about the management and treatment of patients with brain disorders. When an injury protein S100 from damaged brain cells released into the systemic circulation and can be determined in the blood within a few minutes after the injury. Level S100 in such situations may be used to exclude light traumatic brain injuries with high sensitivity (98.8 %) and specificity (99.7 %). Values of protein S100 below 0.105 mg / l I minimize the likelihood of intracranial injury and correlate with negative results computed tomography (Routi, 2009). In patients after cardiac surgery with cerebral complications express of protein continues in the postoperative period. Level of S100 greater than 0.5 mkg / l after 2 days heart surgery indicates the presence of the patient neurological complications (Jacques, 2013). Therefore, can be conjecture that the increase levels of protein S100 in the tear fluid indicates to damage of nerve fibers of the eye and can be used as an early marker for the prediction of neurodegenerative processes in the eye.

During MR tractography in 15 patients of the main group had changes in fiber optic tract. Thus, in 4 patients (26.6 %) showed thinning fibers large occipital forceps, 5 patients (33.3 %) revealed a partial tear of the upper row of fibers in place of attachment to the beam optic radiation, in 2 patients (13,3 %) medial fiber optic bundle visualized in part, were circumcised. Thinning of the lateral fibers of the right optic beam was observed in 2 patients (13,3%), differentiated in small amounts in 2 patients (13,3%).

Figure 1: A partial tear of the upper row of fibers in place of attachment to the beam optic radiation

Source: Authors

Figure 2: A partial tear of the upper row of fibers in place of attachment to the beam optic radiation (top view)

Source: Authors

In processing of the data found: 5 patients (15,6%) had hypertension III; 5 patients (15,6%) with diabetes type II; 2 patients (6,25%) with chronic cerebral ischemia (stroke history); 3 patients (9,37%) with cerebral arteriosclerosis. The analysis revealed that the changes in the MR tractography detected in patients with elevated levels of protein S100 and NSE in the tear fluid, whereas patients with the amount of protein within the normal the changes of the optic tract fibers were not detected. It should be noted that patients with lesions of the optic tract fibers had normal values neurospecific protein S100 and NSE in blood serum. Consequently, the significant correlation between data of tractography and the levels of protein S100 and NSE were not observed.
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Conclusion
Thus, changes in the concentration of protein S-100 and neuroenolaza in the tear fluid of patients with ocular ischemic syndrome allow us to identify them as a damage marker of nerve cell of eyes, contributing to the definition in conjunction with other signs of stage and etiology of the disease.

Changes in the concentration of protein S-100 and neuroenolaza may suggest significant damage of nerve tissue in OIS, which justifies the neuroprotective therapy.

Increased protein S-100 and neuroenolaza in the tear fluid and blood serum determined neurodegenerative processes caused by the brain and the organ of vision; it was confirmed by MR tractography and clinical data.

REFERENCES