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Research Article

Prognostic Value of the Specific Marker of Neurodegeneration in Optic Neuritis

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Abstract

Introduction: Early diagnosis of optic neuritis (ON) is essential to prevent or limit the structural damage and permanent loss of visual function.

Aim of the Study: The aim of this study was to estimate prognostic importance of the neuron-specific enolase (NSE) in the blood serum and tears in diagnosis of the optic neuritis.

Materials and Methods: The clinical-diagnostic examination has been performed at the patients with optic neuritis (ON), including colorimetric analysis of the fundus of eye, optic coherent tomography (OCT) and VEP, as well as analysis of the NSE content in the blood serum and in the lacrimal fluid.

Results: There was revealed reduced content of NSE in the lacrimal fluid in the patients with acute stage of ON and increased content of NSE in the patients with ON at the stage of transition into atrophy of the optic nerve disk. The results of work prove rationality of the NSE in the lacrimal fluid as additional diagnostic marker of the optic nerve injury induced by inflammatory process.

Keywords: *Diagnostics; Tear; Neuron-Specific Enolase*

Introduction

The determination of the specific marker of apoptosis in blood seems to be of great importance for diagnosis and prognosis of the optic nerve diseases. The gradual destruction of neurons in neurodegeneration results the production of the neurospecific enzymes and their isoenzymes. From the damaged cells they come into the extracellular space that allows definition of depth and intensity of structural-functional disorders of the biomembranes in the central nervous system at their increase [1,2].

Among the known neurospecific proteins the neuron-specific enolase (NSE) appeared to be most investigated and adequately describing membranous functions of the blood-brain barrier, now it is used for diagnosis of the acute conditions characterized by cerebral ischemia and hypoxia of a brain [3]. NSE is a common marker of all differentiated neurons. According to the literature data, at diseases of nervous tissue the qualitative and quantitative definitions of this proteins in the blood serum give the valuable information on the intensity degree of neuron damages and disorders of whole integrity of the blood-brain barrier. The increase of the enzyme content in the blood plasma and cerebrospinal fluid indicates about damage of the brain [3,4]. One of the perspective directions is the study of this factor in blood and lacrimal liquid and their comparative analysis at various stages of the neuritis of optic nerve (ON).

The contents of the tear do not differ from the composition of the blood plasma and in many respects characterizes metabolic processes developing in a body of sight that is one more factor resulting in consideration about rationality of studies of tear for the diagnostic and medical purposes [1,5].

Aim of the Study

The aim of this study was to estimate prognostic importance of the NSE in the blood serum and tears in diagnosis of the optic neuritis.

Material and Methods

Three groups of the patients with ON at the age of from 15 till 55 years (on the average 27 ± 1.4 years) are examined. The first group was included 17 patients (24 eyes) at the acute stage of ON. The second group was composed of 13 patients (18 eyes) with ON at the stage of transition in the atrophy of the disk of optic nerve (OPD). Control group- 3 consisted of 10 healthy people (20 eyes).

At selection of the contingent there was excluded ON of demyelinyzing etiology, as well as patients having trauma of brain, the patients with epilepsy and other accompanying diseases.

All contingent were performed complex examination including standard ophthalmological methods (visometry, tonometry, perymetry for colours, ophthalmoscopy), special methods of investigation: magnetic resonance imaging (MRI) of the brain and orbita with tractography, optic coherent tomography (OCT) (Zeiss, Spectral Domain Technology), examination of the visual evoked potentials (VEP) (Neuron-spectrum 4-VPM), colorimetric analysis of the fundus of eye.

The consultations of otorhinoraringologist, neuropathologist, neurosurgeon, infectionist, therapeutist and rheumatologist were carried out.

Examination of the tear was performed in all contingents of the patients. Tears were studied in the morning after awakening to exclude influence of hygiene procedures on its contentse. The collection of lacrimal fluid (LF) (0.15 ml) was made with the help of cannula from the lacrimal lake and inferior conjunctival fornix without touching conjunctiva and cornea. The collection of blood was made from the elbow vein in quantity 5 ml and was centrifuged for the serum isolation. The collected samples of tear and blood serum (BS) were inserted into the test-tube and were sent immediately for testing. The level of NSE in tear and BS were measured by standard technique on the automatic electrochemiluminescent immunoanalyzer Cobas e 411 for chemiluminescent immunoanalysis (Roche Diagnostics, Switzerland). The concentration of C-reactive protein was determined by the ELISA test system "IBL" ("BioKhimMak", Russia).

All the data was processed employing the variation statistical methods using the software Statistica for Windows 6.0. For data with normal distribution, inter-group comparisons were performed using student's t-test, the mean (M) and standard error (SE) of the mean were calculated, the difference was considered reliable when $p < 0.05$.

Results and Discussion

At biomicroscopy the anterior piece of an eye was without changes. At the direct ophthalmoscopy in group 1 of patients the disk of optic nerve was of round or oval form, of bright pink color, the borders were poorly defined, the number of vessels passed through the edge of disk increased to 16.4 ± 2.2, arteries had normal calibre, veins were dilated, the edema of peripapillary zone was noted and macular reflex was smoothed (100%).

In the second group the disk of optic nerve (OND) was of pale colour, the borders were poorly defined, the number of vessels passing through the edge of disk decreased to 13.1 ± 2.0, arteries were narrowed, veins were of normal calibre, macular reflex was smoothed. In the third (control) group the eye fundus was without pathology.

The data about the colorimetric analysis of the fundus of eye of the studied contingent are presented in the table 1. Thus, colorimetric analysis of the fundus of eye showed that in the patients with hyperemia of OND the red color prevailed - 78%, in the patients of the se-

cond group this parameter decreased to 38%, but the parameters of dark blue and green colour raised. The gradient of transition in the first group was low, in the second group this parameter increased. In the acute stage of disease the dilatation of the vessels was observed, at transition into the stage of ischemia the narrowing of the vessels was observed, it indicates about onset of OND atrophy.

Fundus of eye		Healthy individuals (n = 20)	Study groups	
			I	II
Colour of optic disk	Red	46%	78%	38%
	Green	26%	7%	24%
	Dark blue	33%	15%	28%
Borders of optic disk, units		18.2 ± 0.33	4.2 ± 0.41*	20.2 ± 0.36*
Swelling optic disk, mm		0	2.3 ± 0.12*	1.4 ± 0.04*
Caliber of arteries		24.2 ± 0.7	28.3 ± 0.3*	16.1 ± 0.2
Caliber of veins		38.1 ± 0.5	52.6 ± 0.2	32.3 ± 0.4
The ratio of the arteries to the veins		2/3	1/2	2/3
Number of vessels		12 - 14	18.3 ± 1	11.2 ± 2
Peripapillary retinal edema		0	4.1 ± 0.2	2.2 ± 0.4

Table 1: *Colorimetric analysis of the fundus of eye.*
*Note: *: Significant difference when compared with the control group (p < 0.05).*

In the patients of the first and second group the concentric narrowing of fields of sight in white and in red colour was observed. In 15 (50%) patients of the first and second group the perimetry in the red colour was failed as at the given pathology the color sensation is broken.

In the first group during examination of the fundus of eye there was revealed increase of the parameter of neuroretinal zonule (NRZ) with use of OCT by 3.5 ± 0.3 mm^3, at norm of 1.48 mm^3 in 18 (75%) eyes, the volume of physiological excavation was zero, in 16 (66,6%) of cases there was observed edema on the macular zone. In the second group in connection with transition of the acute stage into the stage of atrophy the parameter of NRZ decreased mainly in the upper and temporal quadrants, and also the area of a disk OND reduced to 1.9 ± 0.2 mm^2 at norm 2.26 mm^2.

On the data of VEP the parameter of the latency P100 in the first group increased in comparison with the second group and achieved, on the average, 122 ± 10.7 ms at norm 102 ms. The amplitude of VEP decreased considerably in the second group in comparison with the first group to 4.26 ± 3.27 μV (in norm 8,4 μV). The decrease of amplitude testified to decrease of quantity of functioning axons.

On the MR tractography in the patients of the second group there was defined thinning of the visual fibres, whereas in the first group these changes were not observed.

The analysis of the results of NSE investigation (Table 2) showed significant changes of this parameter depending on the stage of pathological process. Thus, the NSE activity varied depending on the stage and rate of disease progressing. The normal NSE parameter was 15.7-17.0 ng/ml. In the first group in 18 eyes with hyperemia OND the parameter NSE in the tears accounted for, on the average, 0.81 ± 0.15 ng/ml ($p < 0.05$), in 6 eyes with expressed hyperemia and OND edema the parameter NSE was 7.25 ± 0.20 ng/ml. In the BS the parameter was, on the average, 13. 67 ± 1. 44 ng/ml, at norm 15.7-17.0 ng/ml. Thus, at the initial stages of ON the parameter of NSE was reduced in comparison with norm 19 times ($p < 0.05$). During progression of disease the parameter NSE raised considerably, but nevertheless,

it remained below than norm 2.3 times ($p < 0.05$). Hence, at the stage of hyperemia and swelling of OND the parameter NSE reduced below than norm in the LF, but in the BS it remained within the limits of normal variables, that prove diagnostic value of the used method.

Parameters	Study group 1 (n = 24)	Study group 2 (n = 18)	Healthy individuals (n = 20)
CRP in LF, mcg/mL	182.0 ± 7.81*	157.0 ± 6.72	5.56 ± 0.23
CRP in serum, mcg/mL	8.2 ± 0.23	7.6 ± 0.31	5.6 ± 0.24
NSE in LF, ng/ml	4.02 ± 0,17*	24.86 ± 3,84*	15,7 ± 0,2
NSE in BS, ng/ml	13.67 ± 1,44*	14.76 ± 1,23*	16,8 ± 0,12

Table 2: *Indicators of blood and lacrimal fluid of patients with optic neuritis.*
*Note: *: Significant difference when compared with the control group ($p < 0.05$).*

In the second group the parameter NSE increased in the LF and accounted for, on the average, 24.86 ± 3.84 ng/ml, though in the BS he remained within the limits of norm. Thus, at ischemic and atrophic-gliosis stage of disease this parameter raised considerably in the LF.

At the analysis of parameter NSE in the BS in the control and studied groups the reliable distinctions and the pathological deviations were not found out.

The analysis performed had shown the tendency to increase of the contents NSE in the LF during progressing disease. During transition of disease from the acute stage into the stage of ischemia the level of NSE raised in the LF 1.43 times from norm ($p < 0.05$).

In the control group the parameter of NSE in the LF and BS remained within the limits of norm (LF- 15.7 ± 0.2 ng/ml, BS- 16.8 ± 0.12 ng/ml).

The parameter of NSE in LF in the first group was lower than norm 4.29 times ($p < 0.05$). On all probability, it is caused by increase in hypoxia and intensification of the glycolysis process in the neural cells. In the second group in the patients with ON at the stage of transition into atrophy of OND the parameter of NSE increased 1.43 times ($p < 0.05$), probably, it was connected to the beginning destructive processes in the neural tissue with gradual destruction of neurons at neurodegeneration, that results in the output of NSE from the damaged cells into the extracellular space. The level NSE allows finding out depth and intensity of structural and functional disorders of biomembranes in increase of this parameter.

The following regularity of NSE change should be noted depending on the rate of disease progressing: at a sharp stage of disease the decrease of NSE level was recorded to 4.02 ± 0.17 ng/ml ($p < 0.05$), and at transition into the chronic stage there was revealed gradual increase of NSE to 24.86 ± 3.84 ng/ml ($p < 0.05$).The analysis of NSE parameter at transition into the stage of atrophy was characterized by its increase by 43%.

The correlation between NSE levels in the BS and the stages of diseases in our researches was not revealed. Hence, the study of NSE in the BS does not give the reliable information about the development of the pathological process.

According to our data of investigations there was noted the inverse correlation between parameters of NSE in the LF and visual functions. The higher parameters of the acuity of vision were noted there was lower parameter NSE than norm by 25%, in reduction of visual acuity the parameter NSE increased by 46%.

The changes on the fundus of eye looking like hyperemia and OND edema were characterized by reduction of NSE in the LF in the first group of the patients. The growing pale of OND and vascular narrowings were characterized by gradual increase in NSE in LF in the second

group of the patients. At the patients with changes at tractography looking-like as thinning fibres of large occipital forceps there was noted increase of parameter NSE in the LF by 43%.

Conclusion

At the acute the parameter of NSE reduces, on the average, 4,02 ± 0,17 ng/ml, and at gliosis-atrophic stage increases to 24,86 ± 3,84 ng/ml, that, probably, connected to the intensified disintegration of neural fibres. Alongside with the clinical signs for the evaluation of the prognosis of damages in ON it is necessary to measure NSE parameter as subclinical marker of the neurodegenerative process.

The comparative analysis has shown the rather increased level NSE at ON at the stage of transition into atrophia in comparison with the acute form of disease.

The analysis of NSE at the patients with ON is the informative diagnostic criterion of the evaluation of neuronal damage of the optic nerve. The definition of NSE in the lacrimal fluid should be included into the complex examination of the patients with ON as additional marker of the inflammatory process available already at the early stages.

Bibliography

1. Brjevskiy SA and Somov EV. "The lacrimal liquid is the biological material for diagnostic investigations". The actual problems of children ophthalmology: Materials. SPb (1995): 28-31.
2. Zhukova IA., *et al*. "Neurospecific enolase as a nonspecific neurodegenerative process marker". *Bulletin* of *Siberian Medicine* 10.2 (2011).
3. Chekhonin VP., *et al*. "Immuno-enzymatic analysis of the neurospecific enolase on the basis of monoclonal antibodies in the assessment of permeability of the blood-brain barrier in the neuro-psychic diseases". *Ros Psychiatr* 4 (2000): 15-19.
4. Chekhonin VP., *et al*. "Immunological analysis of the neurospecific antigens". Moscow: Medicina (2000): 415.
5. Chekhonin VP., *et al*. "Selective accumulation of the monoclonal antibodies to the neurospesific enolase in the cerebral tissue in the rats with occlusion of the middle cerebral arteria". *Bulletin of Experimental Biology and Medicine* 138.4 (2004): 343-347.

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