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regulatory index $CD4^+/CD8^+$) by means of expressed decrease of helper line of immunity, testifying suppressor character of immune response. Identical picture was observed in the patients with chronic herpetic injure of eyes. So there was 1.2 fold decrease of $CD3^+$ lymphocytes, 1.1 fold $CD20^+$ lymphocytes, and 1.3 fold decrease of IRI ($CD4^+/CD8^+$). As a result of the performed therapy patients with primary episode of the disease with ophthalmic Herpes had some positive dynamics (1.03 fold rise of $CD3^+$ and $CD20^+$- lymphocytes, 1.2 fold increase of IRI level by means of significant increase of helper subpopulation of T-lymphocytes, while in cases of relapse of chronic disease we observed its absence ($CD4^+$ lymphocytes — 19.37±0.37 before and 19.37±0.31 after the therapy) or even negative dynamics of some values of cell-mediated immunity ($CD8^+$- lymphocytes –18.44±0.49% before and 17.89±0.34% after the therapy). In relation to that there is notable reliable increase of immune regulatory index in the primary episode (0.98±0.04 before and 1.13±0.03 after the therapy) and absence of IRI dynamics in relapse cases (1.07±0.03 before and after the therapy — 1.09±0.03).

Analysis of the obtained data showed the highest values of ACL to TAG of cornea and vascular membrane both in the primary episode and relapse of chronic ophthalmic Herpes (7.00±0.50%; 7.44±0.35%; 6.03±0.35% and 7.48±0.41%, respectively), reliably different from the normal values. Less expressed pathologic disorders were also observed in crystalline lens and corpus vitreous of eyes both in primary episode (3.76±0.18% and 3.28±0.21%, respectively), and recurrent ophthalmic Herpes (3.48±0.20% and 3.83±0.22%, respectively). Values change ratio in relation to the values before the therapy showed that more expressed dynamics of recovery of pathologic impairments was noted in the primary episode (1.4 fold to ACL to TAG of cornea, 1.3 ACL to TAG of crystalline lens and vascular membrane) in comparison with the relapse (1.2 fold to ACL to TAG of cornea and vascular membrane, 1.1 fold ACL to TAG of crystalline lens).

Conclusion. Thus, the obtained results show the presence of deep secondary immune deficiency status with expressed misbalance of immune regulatory subpopulations of lymphocytes ($CD4^+$ and $CD8^+$- lymphocytes), with expressed decrease of IRI indicating suppressive character of immune reaction of an organism and deep destructive alterations in the tissues of eyes, confirmed by high values of ACL to TAG of cornea, vascular membrane, crystalline lens and corpus vitreous. After the performed common pathogenetic therapeutic measures the more expressed dynamics of the recovery of pathologic impairments was noted in the primary episode of ophthalmic Herpes, then in chronic recurrent forms of the disease.

References:

1. Dolgikh T. I. Immunologic characteristics of first time herpetic infection./Dolgikh T. I., Yershov A. V., Minakova Y. U., Zapariy N. S.//Infectious diseases, 2010; 8 (1): 25–28.
2. Isakov V. A. Herpes viral infection./Isakov V. A., Romantsev M. T., Ribalkin S. B.//Recommendations for doctors. — St.Petersburg, 2006; 95.
3. Kuskova T. K. Family of herpes viral at the modern stage./Kuskova T. K. Belova Y. G.//MSMSU, Moscow, GP. 2004; 5: 48–58.
4. Makarova T. Y. Herpetic infection. Clinic, diagnostics, therapy/Khabarovsk, 2007; 112.
5. Khodjayeva A. S. Herpes-viral infections, variants of clinical manifestations, diagnostics and therapy//Med. Jour. Uzbekistan. 2010; 1: 50–54.

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Application of the new diagnostic complex of biomarkers in patients with Alzheimer's disease and vascular dementia

Abstract: The article presents data on new methods of diagnostics of Alzheimer's disease in a comparative perspective with using the ischemic scale of Khachinsky. In this regard, we studied 147 patients, who were divided into 3 groups. In the research we found that the use of our diagnostic method increases the diagnostic value of using ischemic scale of Hachinski.

Keywords: Alzheimer's disease, scale of Khachinsky, beta-amyloid protein, apolipoprotein E4, dehydroepianderosteron sulfate.

Alzheimer's disease is a progressive neurodegenerative lesion with individual characteristics of the course and severity of symptoms, as well as multiple converging etiopathogenetic mechanisms. The etiology of this lesion is not fully understood. Some researchers suggest that the convergence of such risk factors as advanced age, presence of epsilon 4 genotype lipoprotein E, obesity, insulin resistance, vascular factors, dyslipidemia, hypertension and inflammatory markers [1, 475–481] launches pathophysiologic cascade which lead to pathology of Alzheimer's type and developing of dementia [2, 1364–1370]. Modern understanding of Alzheimer's disease is based on the gradual biological changes that occur, apparently, decades before the first symptoms. Today, great importance is given to potential biomarkers that can detect biological changes [3, 49–70]. Nowadays there is no biomarker which for self-use in clinic

could be a decisive factor in the diagnosis of Alzheimer's disease. This is primarily due to the definition of cross-known biomarkers correlated as with the course of Alzheimer's disease as with other pathologies of the nervous system. In this regard, we have put forward the hypothesis of the complex use of the most important biomarkers for early diagnosis and monitoring the effectiveness of therapy and identifying groups of risk for Alzheimer's disease. The essence of the hypothesis is a one-time determination of a number of biomarkers in patients (degydroepianderosteron sulfate (DHEA-S), apolipoprotein E4 (ApoE-4) and beta-amyloid protein (Aβ1–42)) and according to discriminatory levels of these compounds developing an appropriate diagnosis or putting the patient to the risk of developing Alzheimer's disease. When creating this hypothesis, we proceeded from the known data of modern research, a model describing the pathogenesis of Alzheimer's disease, which can be used for potential therapeutic approaches [4, 30025–30035].

We combined our proposed diagnostic complex biomarkers with ischemic Khachinsky scale [5, 315–326]. Ischemic scale Khachinsky [6, 1084–1085] includes criteria for assessing the patient's condition and conduction etiology of the pathological process. According to the scale Khachinsky, score more than 7 points suggests a vascular cause of dementia, and less than 4 points — does not confirm the vascular etiology of the process, 4–7 score does not allow one to determine the probable cause of dementia. The most significant signs of ischemic scale Khachinsky that differentiate vascular dementia from Alzheimer's disease, is an acute onset, progression and stepfluctuating course of the disease, presence of hypertension, previous stroke and focal neurological symptoms. Ischemic Scale Khachinsky helps to differentiate vascular dementia from Alzheimer's disease, but its value for the diagnosis of vascular dementia without strokes, as well as of mixed dementia remains low. Using this scale is possible only for one option — vascular dementia with strokes.

The aim of this work was to correlate the expression of biomarkers (beta amyloid protein (Aβ1–42), apolipoprotein E4 (ApoE-4), dehydroepianderosteron sulfate (DHEA-S)) in patients with varying degrees of intensity by Khachinsky scale.

We studies 147 patients with verified diagnosis of Alzheimer's disease (n=17), early Alzheimer's disease (n=30) and chronic cerebral ischemia (n=100).

The average age of patients with Alzheimer's disease was 71,05±1,15 years, with early AD — 57,2 ± 0,92 years, with chronic brain ischemia — 67,18±1,06 years. In Alzheimer's disease, women accounted for 47,1±12,1% of the number of studied patients, with the diagnosis of early Alzheimer — 50,0±9,1%, with chronic brain ischemia — 61,0±4,9%. In Alzheimer's disease patients under the age of 60 years were not found, and the distribution of patients in the age period 61–70 years and older than 70 years were approximately equal. At an early stage of Alzheimer's disease a significant portion of patients (73,3±8,1%) was under 60 years (age between 40–60 years), while there were no patients over 70 years. In chronic brain ischemia, most patients were older than 70 years (40,0±4,9%), but the proportion of patients in the age groups 40–60 years and 61–70 years was also significantly (25,0±4,3% and 35,0±4,8%, respectively).

Test biomarkers were determined in blood serum. Determination of beta-amyloid 1–42 protein (Aβ1–42) was performed using of commercial kits for ELISA studies Human amyloid beta 1–42 (Aβ1–42) ELISA Kit (EASTBIOPHARM, China), determination of apolipoprotein E4 was performed using commercial kits Human Apolipoprotein E4 (Apo-E4) ELISA Kit (EASTBIOPHARM, China), the definition of dehydroepianderosteron sulfate (DHEA-S) was carried out using commercial kits ImmunoFA-DGEA-S (Immunotex, Russia).

Results and Discussion

The results of expression of biomarkers (beta amyloid protein (Aβ1–42), apolipoprotein E4 (ApoE-4), dehydroepianderosteron sulfate (DHEA-S)) in patients with varying degrees of intensity are given on a scale Khachinsky listed in the table (Table 1).

Table 1. – Results of biomarkers` rates in patients with varying severity on a scale Khachinsky (n = 147)

			Early AD (n = 30)	Correlation coefficient	AD (n=17)	Correlation coefficient	Chronic cerebral ischemia (n=100)	Correlation coefficient
Number of points on the scale Khachinsky	Less 4	Number of patients (abs), %	50,0±9,13% (15)		47,1±12,1 (8)		–	
		Aβ1–42, pg/ml	390,8±11,21	–0,268	600,0±16,58	0,018	–	
		ApoE-4, ng/ml	29,75±1,09	–0,371	59,2±2,31	–0,504	–	
		DHEA-s, mmol/l	0,16±0,01	0,277	0,13±0,01	0,408	–	
	4–7	Number of patients (abs),%	50,0±9,13% (15)		52,9±12,1 (9)		–	
		Aβ1–42, pg/ml	404,6±12,98	0,137	637,7±25,77	0,203	–	
		ApoE-4, ng/ml	31,3±1,33	0,23	63,7±2,83	0,674	–	
		DHEA-s, mmol/l	0,13±0,01	0,574	0,2±0,02	–0,199	–	
	Более 7	Number of patients (abs),%	–		–		100,0% (100)	
		Aβ1–42, pg/ml	–		–		313,6±4,78	0,142
		ApoE-4, ng/ml	–		–		21,2±0,44	0,087
		DHEA-s, mmol/l	–		–	0,142	1,14±0,09	–0,022

In patients with chronic cerebral ischemia score was greater than 7, the average was 10,9±0,13. This allows you carry this contingent of patients safely to the group with vascular neurodegenerative disease. In patients with early AD points were from 50,0±9,13%, in the «gray zone» from 4 to 7, what doesn`t allow, according to the scale Khachinsky, to diagnose neurodegenerative disorders. However, determination of biomarker complex (Aβ1–42, ApoE-4 and c-DHEA) showed that the levels of these diagnostically significant proteins are comparable to values in patients with early stage AD: Aβ1–42 above 400 pg/ml, ApoE 4 above 31,0 ng/mL DHEA-to below 1,0 mol/l; patients with vascular cause of pathological states of the brain — Aβ1–42 above 313,6±4,78 pg/ml, ApoE 4 above

21,2±0.44 ng/mL DHEA-c 1,14±0,09 m.mol/l. Thus, differences in performance between two groups are significant (between Aβ1–42– 29,0%, ApoE-4–47,6%, DHEA-S — 8,7 times) allows surely include patients with a score 4–7 by scale Khachinsky to a group with symptoms of Alzheimer`s disease.

In patients with AD number of patients with the distribution of points in the «gray zone,» i. e. in the range from 4 to 7, have been significant — 52,9 ± 12,1%. Here, the markers have been correlated with those values characteristic of already developed AD: Aβ1–42 above 600 pg/ml, ApoE-4 above 60.0 ng/mL DHEA-S is below 1.0 mmol/L. That is, the use of complex biomarkers not only help the distribution of patients in a particular group whose scores on a scale Khachinsky not to allow confidently diagnose the cause of a neurodegenerative condition, but also to diagnose a specific pathology under the discriminatory levels of expression of the markers.

Conclusion

In favor of the effectiveness of complex biomarkers with a score on a scale Khachinsky used work says that a significant number of patients who fall into a "gray zone" of the scale (4–7), where it is difficult to determine the cause of neurodegenerative disease. The proportion of these patients in our study was 51.06% in the group diagnosed with early AD and AD. Thus, the use of diagnostic complex biomarkers in patients with neurodegenerative disorders improves the efficiency and diagnostic value of using of scale Khachinsky.

References:

1. Be la Monte S. M. Insulin resistance and Alzheimer's disease, BMB Reports, 42 (8), 2009.
2. Diaz M. C., Rosales R. L. A Case Report on Dyskinesia Following Rivastigmine Patch 13,3mg/24hours for Alzheimer's Disease: Perspective in the Movement Disorders Spectrum Following Use of Cholinesterase Inhibitors, 94 (34), 2015.
3. Schneider J. A., Montine T. J., Sperling R. A., Bennet D. A. Neuropathological Basis of Alzheimer's Disease and Alzheimer's Disease Diagnosis, 28, 2012.
4. Kann O. The interneuron energy hypothesis: implications for brain disease, Neurobiol. Disease, S0969–9961 (15), 2015.
5. Szigeti K. New Genome-Wide Methods for Elucidation of Candidate Copy Number Variations (CNVs) Contributing to Alzheimer's Disease Heritability, Methods Mol. Biol, 1303, 2015.
6. Khachinsky V., Oveisgharan S., Shankle W. R. Atrial fibrillation and the Khachinsky ischemic scale-reply, Arch. Neurol., 69 (8), 2012.

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Morphological researches of liver at chronic intoxications with drugs and alcohol and their combination

Abstract: The received results help to recommend for differential diagnostics CDI and CAI research of such parameters of a hepatic tissue, as a share of parenchyma, having on fatty vacuoles and on intralobular infiltrates, perimeter and the area of section of a portal tract, extent of the focuses of destruction of a boundary plate along perimeter of a portal tract, average quantity of ductules in a portal tract, shares of a cut of the portal tract, occupied with cells of inflammatory infiltrate and vessels, shares of fibroblasts, macrophages, lymphocytes, neutrophiles and plasmatic cells as a part of inflammatory infiltrate.

Keywords: liver, drugs, alcohol, morphological changes.

One of the most typical diseases of drug-adductors (especially at intervenous injections of drugs) a chronic hepatitis of viral etiology is considered. However the data of the public literature about character and distribution of liver damages at drugs intoxication, as a rule, are not full and extremely contradictory. For instance, a role of drugs in liver damage pathogenesis is still unclear. There are not found the data about liver damages at combined intoxication with drugs and alcohol. There is questionable issue of differences in duration and morphology of viral hepatitis on the background of drug-adduction and at patients, not abusing drugs [1].

In the present time the forensic-medical diagnostics of drugs intoxication is based in complex of morphological data and results of these substances presence in the biological fluids and tissues of corpse. The forensic-chemical research helps to find out not only a type of drug, but also the duration, passed from the last time drug injection and an injected dosage according to the drug concentration in tissues, blood and urine. The interpretation of patomorphogenesis and tanatogenesis at drug-adduction is complicated by variety of effects of psychotropic drugs and impurities, and also defeat of many systems with disorder of intersystem bonds at various levels of an organism [3; 7].

Under the modern data, replication of hepatitis viruses comes to light at 97,8% of the addicts taking heroin intravenously. Prevalence of an infection of a virus of a hepatitis B among addicts makes actual studying of its specificities in this population [4].

According to forensic-chemical researches and morphological signs it is possible to draw a conclusion on rather frequent combination of a narcotism with abusing alcohol. In the literature there are data that abusing alcohol raises activity of a chronic virus hepatitis C, in particular, due to the strengthening of step necrosis [5]. Accordingly there should be accelerated development of cirrhosis too. Besides, acceleration of fibrosis and a cirrhosis can be somewhat caused in addicts by the raised frequency of mix-hepatitis (B+C) in this population. According to our supervision and the literature data [4], mix-hepatitis is differed from monoetiological by strengthening of necrotic and inflammatory processes that is shown, first of all, by high activity of a portal hepatitis.

At this stage of our researches we used histomorphometric method of research of a liver tissue at a chronic alcoholic intoxica-

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