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Cognitive Criterion For Early Diagnosis Of Alzheimer`S Disease

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Abstract

The article presents modern approaches to the early diagnosis of AD. Alzheimer's disease (AD) is a widespread disease worldwide. According to experts from the World Health Organization, asthma is the most common cause of dementia in the elderly and senile. None of the currently known biomarkers with independent use in the clinic can fulfill the role of a decisive factor in establishing the diagnosis of AD. This is primarily due to the cross-determination of known biomarkers correlated with the course of asthma in other pathologies of the nervous system. In this regard, we hypothesized the integrated use of the most important biomarkers for early diagnosis, monitoring the effectiveness of therapy and identifying AD risk groups. The essence of the hypothesis is the simultaneous determination in patients of a number of biomarkers (dehydroepiandrosterone sulfate (DHEA-s), apolipoprotein E4 (Apo-E4) and beta-amyloid protein (Aß 1-42) and, when discriminating levels of these compounds are established, the development of the corresponding the diagnosis or classification of a patient at risk for developing AD. The study aimed compare clinical and laboratory data in the early diagnosis of AD. Laboratory tests were carried out using the enzyme immunoassay determination of the level of DHEA (dehydroepiandrosterone) before and after the oxidation of the catalyst with Fe2+. When studying the DHEA level in blood serum before and after oxidation with a catalyst, the level of DHEA was insignificant or absent in patients with AD, while the level of DHEA in patients without AD increased sharply. The new diagnostic method proposed by us showed a differential diagnosis of AD.

Keywords - *Alzheimer's disease, vascular dementia, cognition, DHEA, Khachinsky scale*

1. Introduction

Cognitive impairment (CI), especially dementia - one of the most common causes of disability in patients of all ages. Cognitive impairment creates significant challenges for patients, their families and friends, and clinicians who provide their health care. Early recognition allows for diagnosis and appropriate treatment, education, psychosocial support, and engagement in shared decision-making regarding life planning, health care, involvement in research, and financial matters. Alzheimer's disease (AD) refers to the primary degenerative dementia and characterized by a progressive decline of cognitive functions, primarily memory, as well as the development of behavioral disorders. AD is the most common cause of dementia in the elderly and senile age. This issue is in the interests not only of neurologists and of general practitioners, internists, psychiatrists, geriatricians. According to WHO [4], cerebrovascular disease and dementia take third place among the causes of death of the world after heart disease and malignant neoplasm. Most publications and clinical studies relating to each of these clinical entities separately, but at the same time, there is growing evidence that in patients with AD and in patients with vascular dementia (VD) are detected and neurodegenerative and vascular changes [2]. Clinically both neurodegeneration and cerebrovascular pathology potentiate each other and cause the development of more severe intellectual-mental disorders [3]. Such coexistence of two disease entities usually determined as a mixed vascular neurodegenerative dementia [4].

2. Methodology

Objective: The purpose of the research was examining the values of clinical and laboratory data, and establishing the relationship between them in the early diagnosis of Alzheimer's type of dementia

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2.2. Sample of the study: A total of 40 patients (17 men and 23 women) under the age of 65 (average age 61, 3±5,7 years) years with dementia of Alzheimer's type (DAT), 40 vascular dementia (VT) and 25 healthy individuals. The study was conducted in the department of neurology of the Tashkent Medical Academy for 2015-2017. To assess the development of cognitive impairment (CI) Khachinsky scale was used. The following methods during neuropsychological examination for quantitative and qualitative assessment of the obtained results were used: Mini-Mental State Examination (MMSE), a battery of tests to assess frontal dysfunction (FD).Following the criteria proposed Yahno N.N., CI was divided by the severity into light (LCI), moderate (MCI) and heavy (HCI) [1]. HCI diagnosed if: MMSE score was less than 10 and/or a score of less than 11 by BTFD.MCI diagnosed if the MMSE score of 11 to 20 by MMSE, and/or FD was 12 to 14 points. Criteria for LCI: MMSE 20-23 points, BTFD 15 points if there is an error in the performance of other neuropsychological tests in the absence of complaints of cognitive function disorder or having the character of cognitive complaints in the absence of any abnormalities in neuropsychological testing. Laboratory tests were carried out using enzyme immunoassay determination of the level of DHEA-S before and after the oxidation catalyst with Fe2+.

3. Finding and results.

Patients in the study had no significant differences in the parameters family history, nature, and severity of premorbid personality characteristics, somatic and exogenous burdens the time of entry into the study. Patients were randomized by age and gender distribution, education level. There were no statistically significant differences in terms of pathogenetic therapy, received about cognitive impairment. Clinic AD in the study group was characterized by the presence of neurological deficits and a progressive decline in cognitive function. In the study of patients 16,7% were diagnosed LCI, at 36,7% - MCI, 46,6% - HCI. Complaints on cognition actively impose only 65,8% of patients (Table 1). Absence of complaints of cognitive nature correlated with the severity of the CI (r=0,279; p=0,002), severity of disregulatory violations (r=0,273; p=0,009), apathy (r=0,221; p=0,015), impulsivity (r=0,236; p=0,009), abuse of alcohol intake history (r=0,343; p<0,001).

Diseases / Complaints	AD	VD
Memory decline	92,3	75
Sleep disorder	61,5	65
Decline of mood	32,7	63
Emotional desire	40,3	76
Reduction of work capacity	50	61
Low attentiveness	73	52
Head-turning	44,2	75
Fast fatigue	69,2	51
Disproportionate ideas	80,7	48
Nausea	30,7	44
Noise in the head	44,2	78
Headache	57,7	73
Tactile	46,1	46
Increased blood pressure	15,3	83
Urinary incontinence	11,5	42
Forced cry	9,6	51
Movement disorders	17,3	46

Figure1. Differences in complaints of patients amongst AD and VD

Groups	DHEA, μmol/l	
	before oxidation	after oxidation
AD	2,13±0,12	2,41±0,15
VD	2,38±0,19	3,90±0,23
Control group	3,05±0,08	5,64±0,12

Figure 2.DHEAresults in the patients with AD, VD, and control group

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			Early AD (n = 32)	Correlation coefficient	AD (n=19)	Correlation coefficient	Chronic cerebral ischemia (n=109)	Correlation coefficient
POINTS	Less than 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	–	
	More than 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

Figure 3. Variability of biomarkers` rates in patients with varying of severity on Khachinsky scale

At the stage of moderate dementia, significant differences in the parameters of the functioning of the groups are not revealed. In hematological oxidation, ELISA study of serum led to a sharp increase in DHEA levels in the control group, while the serum of patients with AD it was not observed or was not significant the increase of DHEA level.

Evaluation of cognitive neuropsychological disorders showed that the most frequent disorders were dyssomnia (70, 8%), emotional liability (63, 3%), anxiety (65, 0%), depression (58,3%) and apathy (44,2%). It was determined that the main group of patients suffering from Alzheimer's disease with early-onset dementia mild degree had significantly worse performance ($p<0, 05$) the overall functioning, they were more prominent violations in communications, orientation, ability to act independently in all areas.

4. Discussion

The formation of amyloid beta occurs through the sequential formation of dimers, oligomers and, in the end, polymers; the method depends on the concentration: the initial slow phase of nucleation can be catalyzed by apoliprotein E4, ions (such as Fe3 +) or glycosaminoglycans, which probably induce the formation of p-fibers. Amyloid aggregation can be the cause of the inflammatory response, which is included in the pathological process. Activation of microglia and astrocytes is associated with the formation of neuritic plaques [7,8,9]. This is accompanied by an increase in the concentration of inflammatory mediators, such as C ^, in the cascade of complement and cytokines (tumor necrosis factor

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a, interleukin 1 p, transforming growth factor p1 and interleukin [10,11]. The toxicity of oligomers with respect to cells is largely due to oxidative stress, disruption of calcium homeostasis, oxidative damage to DNA, lipids, and proteins. The presence of Ap increases oxidative stress with the formation of intracellular superoxide radicals and H202. Cumulative damage results include oxidation of lipids and proteins. Thus, the toxic effect of Ap largely depends on the induction of the inflammatory response and intracellular damage and is associated with inducing factors, in particular with concentrations of DHEA-c and Apo-E4 [12].

This study has allowed establishing a high incidence of cognitive disorders in patients with dementia of the Alzheimer type. Neuropsychological analysis of patients with presenile dementia, Alzheimer's type showed that the syndrome of mild dementia was determined first of all by gradually increasing of dysmnestic intellectual disorders. Memory disorders formed relatively slowly, more slowly than in AD, mnestic-intellectual disorders progressed. The disease most often begins in the presenile age (65 years).

The results of neuropsychological studies of patients with mild dementia of the Alzheimer`s type (DAT) allowed to talk about what's syndrome disorders of higher neurological functions have determined a decrease in the control, programming and arbitrary regulation of activity. Also, the observed defects in the spatial organization of neurological functions that are manifested in the sensitized conditions, organization and kinetic motion (dynamic praxis) [13]. Violation of memory consists of the following components: a narrowing of the scope of the direct memory increased the influence of interfering in the activities of reproduction, violations of election during playback. Almost all patients DAT at this stage of dementia observed relative safety of various components of the speech function except the nominative function of speech (in naming latency was expressed more than in the group of healthy subjects). It was noted in the preservation of visual and auditory gnosis [14, 15]. Patients in this group actively complained of memory loss. They were not always accurate in-time orientation. In the study of blood analysis, changes in the level of serum DHEA after oxidation correlated with the cognitive and mental state of the patients. These results showed that the comparison of the serum levels of DHEA in the patient before and after the oxidation can be a useful tool for the diagnosis of AD.

5. Conclusion

1. Based on the study patients, it was found that the formation of cognitive impairment due to biological factors, their severity depends on the severity of dementia. The mechanism of neurological symptoms, functioning disorders is heterogeneous, depending on the biological causes and social conditions of the functioning of patients.
2. Violations of the higher brain functions of speech, gnosis, and praxis are the neuropsychological basis of dementia. Disorders of speech and gnosis contribute to the formation of painful ideas (r = 0,891), violation perception (r = 0,798), eating disorders (r = 0,688), affective disorders (r = 0,566).
3. With an increase in the severity of dementia takes a significant ($p < 0,05$) increase in the intensity and frequency of behavioral disorders aberrant behavior (r = 0,850), agitation / aggression (r = 0,623), conduct disorders of night and day activity (r = 0,723).
4. Determining the level of DHEA in the blood serum of patients, as well as reaction with an oxidizing Fe2 + may be adopted as one of the biochemical markers in early diagnosis of AD forms, which may be recommended for screening.

References

[1] Gavrilova SI, Levin OS Diagnosis and treatment of dementia in clinical practice - M .: MEDPRESS-INFORM, 2016.
[2] Panegyres P.K., Berry R., Burchell J. Early Dementia Screening // Diagnostics (Basel). – 2016. – Vol. 6(1). – P. E6–E11.
[3] Press release on the Alzheimer's & Brain Awareness Month International Survey. – USA, 2014. – P. 39–42.

ISSN: 2005-4238 IJAST

[4] Tolibov D.S., Rakhimbaeva G.S. Prevalence and risk factors for dementia of the Alzheimer's type - T .: Vestnik TMA. 2017.
[5] Tolibov D.S., Hadjaeva M.H. Analysis of clinical and neuroimaging parallels of Alzheimer's disease - T .: Materials of science conference. 2016.
[6] M. H. Tabert, J. J. Manly, and J. J. Manly, "Neuropsychological prediction of conversion to Alzheimer's disease in patients with mild cognitive impairment," Archives of General Psychiatry, vol. 63, no. 8, pp. 916–924, 2006.
[7] Z. S. Khachaturian, "Diagnosis of Alzheimer's disease," Archives of Neurology, vol. 42, no. 11, pp. 1097–1105, 1985.
[8] G. McKhann, D. Drachman, M. Folstein, R. Katzman, D. Price, and E. M. Stadlan , "Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA work group under the auspices of Department of Health and Human Services Task Force on Alzheimer's disease," Neurology, vol. 34, no. 7, pp. 939–944, 1984.
[9] Z. Nagy, M. M. Esiri, and M. M. Esiri, "Accuracy of clinical operational diagnostic criteria for Alzheimer's disease in relation to different pathological diagnostic protocols," Dementia and Geriatric Cognitive Disorders, vol. 9, no. 4, pp. 219–226, 1998.
[10] S. J. Tabrizi, D. R. Langbehn, and D. R. Langbehn, "Biological and clinical manifestations of Huntington's disease in the longitudinal TRACK-HD study: cross-sectional analysis of baseline data," The Lancet Neurology, vol. 8, no. 9, pp. 791–801, 2009.
[11] Howard JM (1985) A theory of the control of the ontogeny and phylogeny of Homo sapiens by the interaction of dehydroepiandrosterone and the amygdala. United States Copyright Office, Registration Number: TXu00022058.
[12] Bologa L, Sharma J, Roberts E (1987) Dehydroepiandrosterone and its sulfated derivative reduce neuronal death and enhance astrocytic differentiation in brain cell cultures. J Neurosci Res 17, 225-234.
[13] Sunderland T, Merril CR, Harrington MG, Lawlor BA, Molchan SE, Martinez R, Murphy DL (1989) Reduced plasma dehydroepiandrosterone concentrations in Alzheimer's disease. Lancet 2, 570.
[14] Mohan PF (1989) Dehydroepiandrosterone and Alzheimer's disease. Lancet 2, 1048-1049.
[15] Svec F, Lopez A (1989) Antiglucocorticoid actions of dehydroepiandrosterone and low concentrations in Alzheimer's

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