Criteria for Early Diagnosis of Alzheimer's disease (Ad)

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Abstract

The article presents modern approaches to the early diagnosis of AD. The aim of the study was to 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-S before and after the oxidation of the catalyst with Fe^{2+}. 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: *Cognitive impairment (CI); Alzheimer's disease (Ad); Vascular Dementia (VD); Mini-Mental State Examination (MMSE); DHEA*

Introduction

Cognitive impairment (CI), especially dementia - one of the most common causes of disability in patients of all ages. In the structure of the CI dominated by Alzheimer's disease (AD) and vascular dementia (VD). Alzheimer's disease (Ad) refers to the primary degenerative dementia and characterized by 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 takes third place among the causes of death of the world after heart disease and malignant neoplasms. 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. 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 dementia.

Methods

We study 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), and 25 healthy individuals. The study was conducted in the department of neurology of the Tashkent Medical Academy for the 2015-2017. To assess the development of cognitive impairment Khachinsky scale was used. 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 (BTFD).

In accordance with the criteria proposed Yahno N.N., CI were 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 BTFD was 12 to 14 points. Criteria for LCI: MMSE 20-23 points, BTFD 15 points if there is 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 Fe^{2+}.

Results

Patients in the study had no significant differences in the parameters family history, nature and severity of premorbid personality characteristics, somatic and exogenous burdeness the time of entry into the study. Patients were randomized by age and gender distribution, education level [5]. 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 deficit 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 imposes 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

Table 1: *Complaints of patients.*

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. There were not statistically significant differences in the parameters of daily activity in the monitored groups. 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.

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

Table 2: The results of the biomarker determination in the patients.

			Early AD (n = 32)	Correlation coefficient	AD (n=19)	Correlation coefficient	Chronic cerebral ischemia (n=109)	Correlation coefficient
Number of points on the scale Khachinsky	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

Table 3: Results of biomarkers` rates in patients with varying severity on a scale Khachinsky (n = 160).

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. There was an early loss of the criticism to his condition with severe personality changes as the trans-restructuring nature, which was determined not characteristic traits of avarice previously treated patients, rigidity, self-centeredness, conflict and suspicion. 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. In addition, the observed defects in the spatial organization of neurological functions that are manifested in the sensitized conditions, organization and kinetic motion (dynamic praxis). 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 the preservation of visual and auditory gnosis. 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 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.

Conclusions:

1. On the basis of 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 Fe^{2+} may be adopted as one of biochemical markers in early diagnosis of AD forms, which may be recommended for the purpose of screening.

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