

Features of Cognitive Status in Patients with Venous Cerebral Dysfunction on the Background of Chronic Cerebral Ischemia

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ABSTRACT

A total of 282 patients with CCI of I and II stages were studied against the background of Hypertension (HD) and Atherosclerosis (ATH) or their combination, in the period from 2015 to 2018. Among the studied there were 134 (47.5%) men and 148 (52.5%) women aged 50 to 76 years (average age 54.7 ± 5.1 years). All patients were divided into groups depending on the presence of cerebral venous dysfunction (VCD). All patients underwent a standard neurological examination. The initial integrative assessment of the mental status of our patients was carried out using the generally accepted MMSE scale and the 10-word technique according to A.R. Luria to assess the state of auditory memory for words, fatigue, attention activity, memorization. Along with clinical and neurological studies, in addition to EEG recording, studies of cognitive evoked potentials (P300) were included in the block of studies.

KEYWORDS

Chronic Cerebral Venous, Cognitive Impairment, Neurological Studies.

Introduction

Cerebrovascular pathology is one of the main areas of modern clinical neurology, which is associated with the widespread prevalence of vascular diseases of the brain, a high mortality rate from acute cerebrovascular accidents (ACA) and severe persistent disability after a previous illness (1).

Underestimation of the venous part of the cerebral circulation prevents the correct understanding of the pathogenesis and clinical picture of chronic cerebral ischemia (4, 5).

Research work in recent years has shown that in chronic cerebrovascular accident, an important pathogenic significance is also an insufficiency of blood flow to the brain in the basin of the affected artery, and obstruction of venous outflow [5]. There are observations that describe the predominant localization of the pathological process in the venous system of the brain with a slight lesion of the arterial system [4, 5, 6].

An important place among the clinical manifestations of vascular pathology of the brain is occupied by impaired cognitive functions. Moreover, the severity of cognitive impairment can vary significantly depending on the stage of the process and the severity of the underlying vascular disease. More and more attention is now being paid to less severe cognitive impairment. This reflects the general trend in modern neuroscience to maximize the optimization of early diagnosis and treatment of cognitive impairment.

Thus, the identification of the clinical features of cognitive impairments is important for determining the etiology of impairments.

Purpose of the Study

To study the features of cognitive cerebral dysfunction against the background of intracranial venous insufficiency.

Materials and Methods

A total of 282 patients with chronic cerebral ischemia (CCI) of I and II stages were studied against the background of hypertension (HD) and Atherosclerosis (ATH) or their combination, in the period from 2015 to 2018. Among the studied there were 134 (47.5%) men and 148 (52.5%) women aged 50 to 76 years (average age 54.7 ± 5.1 years). The patients were examined and treated in the neurological department of the Somatic Hospital in Tashkent.

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All patients were divided into groups depending on the presence of cerebral venous dysfunction (VCD). According to the results of a study using a questionnaire to identify VCD (2), all patients were divided into 3 groups, depending on the severity of their VCD. Group I consisted of 61 patients (21.6%) with grade 1 VCD, group II consisted of 101 patients (35.8%), group III consisted of 75 patients with grade 3 VCD (26.6%). A control group (CG) - 45 people with CCI without signs of VCD was composed of the surveyed in whom VCD was not detected.

All patients underwent a standard neurological examination (analysis of patients' complaints, an objective examination, including the study of the neurological status). A clinical questionnaire was used in the study to identify signs of venous cerebral dysfunction [2]. The initial integrative assessment of the mental status of our patients was carried out using the generally accepted MMSE scale and the 10-word technique according to A.R. Luria to assess the state of auditory memory for words, fatigue, attention activity, memorization.

Along with clinical and neurological studies, in addition to EEG recording, studies of cognitive evoked potentials were included in the block of studies. (P300). Cognitive evoked potentials (CEP) were chosen due to the fact that they allow assessing endogenous events occurring in the brain and associated with the recognition and memorization of the presented stimuli (3).

The patients also underwent neurophysiological research methods: MRT of the brain with venography (RTM) of the brachiocephalic veins and venous sinuses of the brain.

To analyze the data obtained, the Statistic software package was used using the Statistic 8.0 and Excel applied programs. The distribution of characteristics for normality was assessed using the Kolmogorov-Smirnov test. To identify the differences between the indicators in the compared groups with a normal distribution, the Student's t test was used, in cases where the distribution did not meet the criteria of normality, its nonparametric analogue, the Mann-Whitney test, was used. The critical level of significance (p) when testing statistical hypotheses in the study was taken equal to 0.05. When describing the results of the study, quantitative data are presented in the form $M (\pm \sigma)$, where M is the arithmetic mean, σ is the standard deviation, qualitative data are presented as absolute values, percentages and shares.

Research Results

When studying the severity of cognitive impairment (CI) according to the MMSE scale in patients with chronic cerebral ischemia (CCI), depending on the degree of VCD, it was noted that, in three groups of patients with moderate CI, it was significantly higher than in CG. Also, significant differences in the point severity of MCI according to the MMSE scale were significantly higher in patients in group 2 compared to group 1, and in group 3 compared to group 1 (Table 1).

Table 1. The severity of CI depending on the degree of VCD (results according to the MMSE questionnaire)

CI degrees	VCD I	n=	61	VCD II	n=	101
	MMSE (scores), $M \pm \sigma$	n	%	MMSE (scores), $M \pm \sigma$	n	%
Light CI	22,3+0,2	42	68,85%	22,1+1,2	55	54,46%
Moderate CI	17,1+ 1,1	19	31,15%	15,6+ 0,4 *	46	45,54%
CI degrees	VCD III	n=	75	Контрольная группа	n=	45
	MMSE (scores), $M \pm \sigma$	n	%	MMSE (scores), $M \pm \sigma$	n	%
Light CI	20,3+0,7 *	29	38,67%	22,6+0,2	34	75,56%
Moderate CI	13,1+ 1,5 * ^	46	61,33%	18,6 + 1,2	11	24,44%

Note: hereinafter* - significant difference between CG and groups: ^ - difference between groups 1 and 3, # - differences between groups 1 and 2, & - between groups 2 and 3.

In the study of memory according to the Luria test "10 words", a significant difference was found between the number of words played in the control group and in the groups of patients with VCD II and VCD III, between both VCD III and VCD I in the time interval of 10 and 20 minutes (Table.2).

Table 2. Average number of words on the test for memorization of 10 words (according to Luria A.R.), $M \pm \sigma$

study interval	VCD I	VCD II	VCD III	Control group
Immediately after learning	5,9±0,3	5,1±0,33	4,8±0,22 *	6,5±0,21
After 10 minutes	4,7±0,29	3,9±0,35 *	3,8±0,3 * ^	5,1±0,26
After 20 minutes	4,0±0,29	3,1±0,38 *	2,9±0,33 * ^	4,3±0,28

Also, the complex of studies included EEG registration, studies of cognitive evoked potentials (P300) (Goodin D.S., Aminoff M.J. 1986). Cognitive evoked potentials (CEP) make it possible to assess endogenous events occurring in the brain and associated with the recognition and memorization of the presented stimuli (Gnezditskiy V.V. 1997).

According to the results obtained, it can be seen that in the study of neurophysiological methods in patients with VCD and CG, significant differences were noted in the main CEP parameters - in the latency of all CEP parameters in the VCD III group, in the latencies of N1 and N2 indicators in the group with VCD P300. For the rest of the studied parameters, the differences between the first group and the CG were unreliable (tab.3).

According to the study, it was noted that a more significant decrease in the amplitude and an increase in the latency of the P300 peak was observed with the progression of VCD, which indicated a greater severity of cognitive impairments these data were consistent with the data of neuropsychological examination.

Table 3. CEP parameters in patients with VCD and CG

Methodology P300	Latency parameters (ms), $M \pm \sigma$			
	perception	identification	making decisions	RAM size
Groups of subjects	N1	P2	N2	Ampl N2/P3
VCD I	235,5±1,3	347±2,1	109±1,9	19,8±0,9
VCD II	242,5±1,3	354±2,2	110,3±2,4	18,1±0,5
VCD III	243,8±1,5 * ^	355,3±2,2 * ^	113,4±1,6 *	17,8±0,7 *
Control group	233,6±1,6	333,7±2,1	104,8±2,6	20,7±0,8

When comparing P-300 indices in patients with VCD in comparison with the control group, the following results were obtained. From the presented table 3, it can be seen that the main intergroup CEP indicators had differences. When comparing P-300 indices in patients with VCD in comparison with the control group, the following results were obtained. From the presented table 3, it can be seen that the main intergroup CEP indicators had differences. For the rest of the studied parameters, the differences were not significant. When comparing CVP indices in patients with VCD I and with VCD II, we noted an increase in latency indices for all leads, but they were not reliable (Table 3).

Thus, neuropsychological examination and cognitive evoked potentials are important methods for assessing the state of higher mental functions in patients with VCD against the background of CCI, which makes it possible to assess the degree of involvement of the affected parts of the brain in the pathological process, as well as the functional state of the brain as a whole. In the study of the cognitive potential in the examined patients, it was found that more severe cognitive impairment corresponded to a more pronounced degree of VCD severity. Therefore, recording cognitive evoked potentials can provide additional information about the state of the cognitive sphere in patients with CCI with existing venous cerebral dysfunction.

When examining the results of MRT of the brain in patients with venous cerebral dysfunction against the background of CCI, diffuse changes in the intensity of the signal from the white matter of the brain were found - periventricular, subcortical leukoaraiosis, single or multiple ischemic foci 115 mm in size, external and internal cerebral atrophy. The examined patients did not have large foci of ischemia. Patients with VCD III were distinguished by a greater severity of periventricular VA of all localizations compared with the group of patients with ICP I and ICP II ($p < 0.05$).; symmetry of atrophic changes in the brain (the absence of significant differences in the index of the lateral ventricular bodies, the linear dimensions of the anterior horns and bodies of the lateral ventricles on the right and left); the predominance of single and small (up to 5 mm) ischemic foci in the substance of the brain in patients with VCD III compared with controls, 43.4% versus 10.7%, respectively, $p < 0.05$, in the deep sections of the white matter of the frontal lobes (50% and 13.5%, respectively), the head of the caudate nucleus (48.6% and 9.1%), the thalamus (12.7% and 1.8%) and the pons of the brain (5.0% and 0.5%), i.e. in structures that are functionally important for the

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development of CI.

Patients with DCV III, in comparison with patients with the control group, were characterized by a greater ($p < 0.05$) severity of asymmetric internal cerebral atrophy with predominant involvement of the left hemisphere (mean values of the index of the lateral ventricular bodies, linear dimensions of the anterior horns and bodies of the lateral ventricles were significantly higher on the left than on the right);

According to MRT venography (RTM), asymmetry of the main venous collectors was revealed in most patients; the jugular veins and cerebral sinuses, predominantly on the right side, were dilated in 45.1% of patients, on the left side - in 22.5%. Analysis of RTM data showed that in 48.2% of cases, an anomaly in the development of the brain drainage system was revealed. So, in 21.5% of cases, hypoplasia of one of the transverse sinuses was diagnosed, aplasia of the transverse sinus was detected in 9.4% of patients. In all cases, anomalies in the development of venous sinuses were noted compensatory expansion of the contralateral sinus, and in some cases, the superior and inferior petrous sinuses were visualized, which are normally difficult to identify.

Thus, in chronic cerebrovascular disease, along with changes in the arterial link of blood flow, changes in the regulation of venous circulation are also indicative. In chronic cerebral ischemia, both a comparative expansion of the IJV and a relative decrease in the intensity of blood flow in them are noted.

In assessing the effectiveness of the effect of drugs on cerebral venous circulation in the complex therapy of patients with chronic cerebral ischemia, two statistical indicators were used - the level of regulation (average values of indicators) and the dispersion of values around this level.

During the course of therapy with venoprotectors of patients with grade I VCD against the background of complex CCI therapy, an improvement in the MMSE score, the Luria test results (in the time interval - after 20 minutes, the memorization test), and the indicators of the volume of working memory in the study of cognitive evoked potentials (P300) (tab. 4).

Table 4. Estimation of variance after a course of treatment with the appointment of "venotonics" in patients with grade I ICP.

Indicators	Without "venotonics"			Reception of "venotonics"			EC
	E1	E2	E3	E1	E2	E3	
MMSE scale (points)	24,8	23,7	1,04	23,9	22,3	1,07	103,00%
Luria's test "10 words", (min)	17,8	16,9	1,05	18,3	15,1	1,21	115,00%
RAM size N2/P3	187,1	145,3	1,28	200,3	96,5	2,07	114,00%

Note: E1 - assessment of variance in patients before treatment; E2 - assessment of the spread in patients after the second course of treatment; E3 - assessment of dispersion in patients after the second course of treatment with the appointment of "venotonics"; Ke - efficiency coefficient.

An analysis of the data in the group of patients with grade I VCD against the background of CCI, who received medications affecting the regulation of cerebral venous blood flow for 2-3 months of complex therapy, shows that that if before treatment, with relatively stable average values of hemodynamic parameters, an increase in variance was noted compared to the comparison group, then after complex treatment with the inclusion of venoprotectors, a more distinct decrease in the variance of indicators of cognitive status is noted, than when exposed only to the arterial segment of the cerebral circulation. At the same time, the average indicators of cerebral blood flow were stable.

In other words, after treatment of patients with VCD against the background of CCI with the inclusion of agents affecting the regulation of venous cerebral blood flow, the level of regulation of cerebral circulation and cognitive potential increases. In the initial stages of the disease, positive changes are observed after the first course of therapy; with more pronounced disorders of the regulation of the functions of systemic hemodynamics, a longer period of treatment is required.

Conclusion

Thus, in the study of the cognitive potential in the examined patients, it was found that more severe cognitive impairments corresponded to a more pronounced degree of VCD severity. Therefore, recording cognitive evoked potentials can provide additional information about the state of the cognitive sphere in patients with CCI with existing venous cerebral dysfunction. Therapy with venoprotectors in patients with chronic cerebrovascular diseases has a systemic effect and improves the condition of the entire vascular system of the brain, including its venous component. The drugs have a pronounced anti-inflammatory effect on the venous endothelium, improve its barrier function, help preserve the structural integrity of the venous vessels, and improve their functional state.

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