Specific Aspects of Changes in Cognitive Function in Cerebral Circulatory Disorders

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ANNOTATION

Violation of higher brain functions is one of the most frequent and disadaptive complications of cerebrovascular diseases. Cognitive impairments, especially pronounced ones, can lead to significant restrictions in work, social life, and self-care of patients. In all cases, the quality of life is significantly reduced not only by the patients themselves, but also by their closest relatives.

KEYWORDS: *risk factors, dementia, neuropsychological syndrome, cognitive impairment.*

Patients with cognitive impairment are not able to fully comply with the doctor's recommendations for the treatment of the underlying vascular disease that led to brain damage. For those who have had a stroke, the effectiveness of rehabilitation measures is reduced. That is why cognitive impairments in cerebrovascular diseases are always associated with a less favorable prognosis. The material costs of the family increase significantly. This is due to the need to care for the patient.

Quantitative and qualitative characteristics of cognitive impairment are extremely important in the diagnostic work of neurologists, therapists and doctors of other specialties. As is known, at least 90% of the area of the cerebral cortex is occupied by the so-called secondary and tertiary cortical fields, the primary function of which is to ensure the cognitive process. Identification and clinical analysis of the features of cognitive impairments are necessary for the correct syndromic and topical diagnosis in vascular diseases of the brain, the correct assessment of the severity of neurological symptoms.

Vascular cognitive impairments include disorders of higher brain functions (memory, praxis, gnosis, speech, control functions) due to acute cerebrovascular accidents (ACV) and/or chronic cerebrovascular insufficiency. According to the results of international epidemiological studies, vascular etiology is the third most common (after Alzheimer's disease and the degenerative process with Lewy bodies) cause of dementia in the elderly and senile age [1]. The prevalence of cerebrovascular diseases in the spectrum of non-dementia cognitive impairment requires clarification. According to some data, cerebrovascular diseases are the most common cause of mild and moderate cognitive impairment and are ahead of degenerative brain diseases in this category of patients in terms of incidence [2].

Prevalence of cognitive impairment after stroke

According to the generally accepted classification, cerebrovascular diseases include stroke and chronic forms of cerebrovascular insufficiency.

The problem of cognitive impairment after a stroke has been actively studied since the late 1990s. As the results of numerous epidemiological studies conducted in different countries of the world have shown, the prevalence of dementia after a stroke varies from 4 to 40% [3-10]. Such a scatter of data is explained by the characteristics of the sample, primarily by differences in the age of patients and the severity of the stroke. In addition, each researcher has his own approach to the problem of pre-

stroke cognitive impairment. In addition to clinically defined dementia, in a significant number of patients after stroke, a decrease in cognitive functions goes beyond the average age standards, but does not cause restrictions in everyday life (non-dementia cognitive impairment, which are divided into mild and moderate) [11-13].

Higher rates of dementia after a stroke are naturally observed in older patients, with a larger infarct volume and a greater severity of neurological symptoms [3, 5–7, 10]. However, a number of studies have shown that cognitive disorders are detected even after mild stroke, including after a transient ischemic attack [14].

A statistical relationship was established between the likelihood of developing clinically significant cognitive impairment and stroke localization. Thus, usually more pronounced disorders of higher brain functions are observed in left-hemispheric stroke [5-7].

The main risk factors for dementia after stroke are divided into stroke-related and non-stroke-related (Table 1). The presence of risk factors for the development of dementia after a stroke, not associated with stroke, indicates the complex nature of cognitive impairment. Stroke in such a situation plays the role of a trigger that decompensates for previous brain damage (vascular or otherwise), but is not the only cause of cognitive impairment.

A separate problem is the so-called pre-stroke cognitive disorders. Clinical practice and research results suggest that in some stroke patients, cognitive impairment can be suspected retrospectively even before stroke. Thus, the IQCODE scale (The Informant Questionnaire on Cognitive Decline in Elderly - a third-party questionnaire on cognitive decline in an elderly person) suggests the presence of pre-stroke dementia in 26% of patients, and before stroke cognitive impairment - in 64% of patients with post-stroke cognitive impairment. dysfunction. At the same time, the diagnosis of cognitive disorders in these patients was first established only after suffering a stroke. There is an opinion that the decline in memory and other higher brain functions in old age is an inevitable and normal phenomenon. This is the reason why patients with cognitive disorders rarely seek medical advice [12, 15]. Cognitive disorders in combination with emotional and motor disorders form the core of the clinical picture of chronic cerebrovascular insufficiency. Due to the anatomical and physiological features of cerebral circulation in chronic insufficiency of blood supply to the brain, the subcortical basal ganglia and deep sections of the white matter of the brain are primarily affected. It is in these cerebral structures that the so-called silent infarcts are usually localized, which develop without a stroke clinic, but when they recur, they form a syndrome of progressive brain damage by the type of dyscirculatory encephalopathy. The deep sections of the white matter surrounding the lateral ventricles of the brain, with the development of diffuse changes in the white matter associated with microangiopathy (periventricular leukoaraiosis), suffer at the earliest stages [16-19].

Both the subcortical basal ganglia and the periventricular white matter play a strategic role in cognitive processes. The defeat of these structures leads to functional isolation of the frontal lobes of the brain with the formation of secondary frontal dysfunction (the phenomenon of dissociation) and, as a result, to cognitive and emotional disorders of the frontal nature [20, 21].

Based on these pathogenetic features, cognitive disorders are naturally considered the earliest clinical manifestation of chronic cerebrovascular insufficiency. According to N.N. Yakhno et al., the frequency of occurrence of cognitive impairments at stages I-II of dyscirculatory encephalopathy is 89% [22, 23]. Similar results were obtained in the study by I.V. Damulina et al. [16]. However, it should be borne in mind that none of the existing diagnostic tools for cognitive dysfunction (neuropsychological tests) is 100% sensitive. In addition, at a high premorbid level, the patient's cognitive functions may remain within the average statistical norm, despite a decrease compared to the individual norm. Most likely, the real prevalence rate of cognitive impairment in dyscirculatory

encephalopathy is even higher.

Linear features of vascular cognitive impairment

In the structure of vascular cognitive impairments, one can single out the so-called focal neuropsychological syndromes associated with local brain damage as a result of stroke, and cognitive impairments that have developed as a result of diffuse brain damage (encephalopathy).

The symptomatology of focal cognitive impairment is varied and depends on the localization of the ischemic (or hemorrhagic) focus in a particular case. At the same time, various types of aphasia, agnosia, apraxia, amnesia, and violations of control functions develop (Table 2).

Table 2. Neuropsychological syndromes in different localizations of stroke

Strokelocalization	Characteristicneuropsychologicalsyndromes
Anteriorfrontallobes	Violation of control functions (planning and control)
Posterior sections of the left frontal lobe	Motor aphasia, kinetic (motor) apraxia
Leftparietallobe	Conduction aphasia, ideomotor apraxia, digital agnosia, body schema disorder, writing disorder (alexia, agraphia)
The junction of the parietal and occipital lobes on the left	visuo-spatial agnosia, constructive apraxia, acalculia
Rightparietallobe	Anosognosia, syndrome of ignoring half of the space
Lefttemporallobe	Sensoryaphasia, amnesticaphasia
Righttemporallobe	Amusia, arrhythmia, dysprosody
Leftoccipitallobe	Visual object agnosia, isolated alexia
Rightoccipitallobe	Prosopagnosia, coloragnosia
Hippocampus, thalamus, mediobasal frontal regions	Amnesia

If local cognitive impairments are heterogeneous and depend on the localization of focal vascular lesions of the brain, then the changes associated with diffuse lesions of the brain are more uniform. As already noted, these disorders are based on leukoaraiosis and “silent” infarctions of typical (subcortical) localization, which lead to functional isolation and secondary dysfunction of the anterior parts of the brain [16, 18, 22, 24].

In the cognitive sphere, damage to subcortical structures with secondary frontal dysfunction will manifest itself with the following clinical signs:

- bradyphrenia (slowness of the pace of cognitive processes), difficulty concentrating attention, distractibility, increased fatigue during mental work;
- difficulties with switching attention and changing the paradigm of activity, inertia, akairiya, perseveration;
- lack of cognitive control, impulsiveness in making decisions, reduced criticism, tactlessness, antisocial behavior (usually with significant severity of cognitive impairment in general);
- memory impairment by type of lack of reproduction (difficulties in extracting the necessary information from the memory at the right time. Tips or providing multiple choice can facilitate the playback process);
- visual-spatial disorders (usually with significant severity of cognitive impairment in general): constructive dyspraxia, spatial dysgnosia.

General neuropsychological characteristics of vascular cognitive impairments not associated with local brain damage make it possible to focus on them as an "indicator" symptom of chronic vascular brain damage. That is, cognitive impairment of the nature described above in patients with arterial hypertension, another vascular disease, allows us to speak about the diagnosis of discirculatory encephalopathy. However, for reliable verification of the diagnosis, it is necessary to conduct neuroimaging, which will establish the presence of a vascular lesion of the brain in the form of multiple infarcts and/or severe leukoaraiosis.

Mixeddementia

Numerous clinical and morphological comparisons indicate a high comorbidity of cerebrovascular diseases and the most common neurodegenerative disease, Alzheimer's disease [25]. This phenomenon is based on the commonality of risk factors and the mutual influence of the vascular and neurodegenerative processes at the pathogenetic level.

Alzheimer's disease and cerebrovascular diseases have the same risk factors (old age, carriage of the apolipoprotein E4 gene, arterial hypertension, abdominal obesity, hyperlipidemia, diabetes mellitus) [25].

Chronic cerebral ischemia and hypoxia are risk factors for the development of cerebral amyloidosis, the main pathogenetic event of Alzheimer's disease. Thus, chronic cerebrovascular insufficiency predisposes to the development of a neurodegenerative process. In addition, cerebral infarction contributes to a more rapid clinical manifestation of an asymptomatic or low-symptom neurodegenerative process [26].

In Alzheimer's disease, amyloid protein is deposited not only in the brain parenchyma, but also in cerebral vessels, which causes amyloid microangiopathy. For this reason, the primary neurodegenerative process is capable of causing or intensifying chronic vascular damage to the brain [25].

The accompanying neurodegenerative process exacerbates and alters vascular cognitive impairment. The prognosis for combined pathology is much more serious: cognitive impairment can progress at a faster pace, and compensation for the underlying vascular disease does not completely prevent further deterioration of the condition. At the same time, the presence of a concomitant neurodegenerative process makes it more reasonable to use drugs recommended for the treatment of Alzheimer's disease in patients with cerebrovascular diseases. In this regard, the identification of an accompanying neurodegenerative process is of great importance for an accurate diagnosis, the choice of an optimal therapeutic strategy, and prognosis [25].

In diagnosing the concomitant neurodegenerative process, a neuropsychological analysis of the quantitative and qualitative features of cognitive impairment plays a key role. At the same time, Alzheimer's comorbidity is evidenced by:

- more severe memory impairment;
- the progressive nature of memory disorders;
- expressed to a greater extent the violation of memory for recent events compared with remote (Ribot's law);
- specific features of mnestic disorders, indicating a primary insufficiency of memorization (not reproduction): a significant difference between immediate and delayed reproduction, impaired recognition in multiple-choice tests, ineffective prompts during reproduction, interweaving of an outsider material during playback (the patient tries to guess the correct answer);

- insufficiency of the nominative function of speech (violated naming of objects) in the absence of post-stroke aphasia.

Undoubtedly, the concomitant neurodegenerative process aggravates the prognosis of cognitive impairment in cerebrovascular diseases. However, in elderly and old people in a similar situation, cognitive impairment can progress quite slowly, in contrast to younger people with "pure" Alzheimer's disease. This is probably due to the fact that vascular diseases of the brain contribute to the clinical manifestation of the early morphological stages of Alzheimer's disease, which are asymptomatic in the absence of vascular damage [26]. The progression of the disease at these stages proceeds at a slower pace, and the possibilities of compensation are still great.

Diagnosis of vascular cognitive impairment

To date, the only method for diagnosing cognitive impairments is recognized as clinical and neuropsychological - a survey of the patient and his immediate family using neuropsychological tests. At the same time, the most reliable and reliable information can be obtained by comparing survey data and data from neuropsychological studies. Often, a single neuropsychological study in isolation from clinical data gives a false-positive result (less often, a false-negative one).

At the same time, no paraclinical research methods, including the study of the latent period of P300 evoked potentials, ultramodern methods of structural and functional neuroimaging, do not provide information about the current state of cognitive functions, although they can provide important information about the causes of cognitive impairment.

For the diagnosis of vascular cognitive impairment, methods should be used, including tests for control functions. Of these tests, the most sensitive [27] are:

- test of connection between numbers and letters, part B;
- test "Symbols and numbers".

In outpatient and inpatient practice, it is advisable to use short test sets followed by an integral assessment of cognitive functions in general, such as the Mini-cog test, the Minimental State Examination (MMSE), the Montreal Cognitive Function Assessment Scale (Montreal Cognitive Assessment, MoCA). In recent years, the MoCA scale has become firmly established in the diagnostic tools of neurologists [7].

It is obvious that the fact of establishing cognitive disorders in neuropsychological studies does not mean automatic recognition of the vascular nature of cognitive impairment, even in patients with a severe vascular history. The diagnosis of "vascular cognitive impairment" seems to be justified only in the presence of one of two signs:

1. a reasonable time sequence between the manifestation of cognitive impairment and a stroke (the first 3-6 months);
2. Specific features of cognitive impairment (predominance of bradyphrenia, reduced concentration and other signs of frontal dysfunction over memory impairment) in combination with neuroimaging signs of microangiopathy (lacunar infarcts, periventricular leukoaraiosis).

These diagnostic criteria with a high degree of probability indicate the presence of a vascular component of cognitive impairment. At the same time, a possible additional component associated with a neurodegenerative process or other diseases is not excluded.

Treatment of vascular cognitive impairment

The role of adequate therapy of the underlying vascular disease and prevention of stroke in the management of patients with vascular cognitive impairment can hardly be overestimated. We

emphasize that only the control of etiological factors can prevent or reduce the rate of development of further vascular damage to the brain, and, consequently, the rate of progression of vascular cognitive impairment.

Of paramount importance is the conduct of antihypertensive, antiplatelet or anticoagulant therapy, according to appropriate indications, monitoring of carbohydrate and lipid metabolism, treatment of cardiac arrhythmias and conduction disorders, methods of vascular surgery. These measures are extremely important for the prevention (primary or secondary) of brain damage. But their direct impact on cognitive functions or the rate of progression of cognitive impairment is not generally recognized, since a small number of studies have been devoted to studying this issue. Along with drug methods, non-drug support for the normal functioning of the patient's cardiovascular system (rational nutrition, overweight, giving up bad habits, rational physical and intellectual stress) is no less important. According to retrospective data, these measures favorably affect, in particular, cognitive functions and the rate of progression of cognitive impairment [21].

Four main groups of drugs are used as specific therapy for vascular cognitive impairment:

1) acetylcholinesterase inhibitors (donepezil, rivastigmine, galantamine) and memantine. Sometimes these drugs are conditionally called neurotransmitters (they help optimize synaptic transmission), or anti-dementia (they are usually used precisely at the stage of dementia). Despite the fact that most clinical studies of neurotransmitters have been conducted in patients with Alzheimer's disease, these drugs demonstrate good clinical efficacy in vascular dementia. There is also a positive experience of using memantine at the stage of moderate cognitive impairment, before the development of dementia [1];

2) vasoactive (vascular) drugs: vinpocetine, pentoxifylline, EGB 761, etc. It is assumed that these drugs help optimize cerebral microcirculation by expanding small-caliber vessels without stealing effect. Used at the non-dementia stage (in case of mild or moderate cognitive impairment);

3) dopamine and noradrenergic drugs (nicergoline, piribedil, dihydroergocriptine). They are used mainly at the non-demented stage. Their mechanism of action is associated both with the activation of the corresponding neurotransmitter systems in the brain, and with the effect on the blood supply to the brain;

4) neurometabolic drugs - the most numerous group of biologically active substances that affect various aspects of cerebral metabolism in order to provide neuroprotection, optimize neuronal plasticity, increase the synthesis and activity of cerebral neurotransmitters.

In recent years, among neurometabolic drugs, doctors and researchers are of particular interest to drugs that reproduce the physiological effects of endogenous neuropeptides. Neuropeptides are a class of biologically active compounds that perform a regulatory function. Neuropeptides act at very low doses and regulate integral functions of the central nervous system such as learning, memory, behavior. Most likely, the nootropic activity of piracetam, the first neurometabolic drug, is due to the fact that, being a mimetic of an endogenous peptide, it is involved in the regulation of memory and learning processes.

Further research led to the synthesis of a new neurometabolic drug with neuropeptide activity - Noopept. This drug is a dipeptide analog of piracetam and terminal fragments of vasopressin, which under experimental conditions many times exceeds the nootropic activity of piracetam and is devoid of the hormonal effects of vasopressin [4].

To date, a wealth of positive experience has been accumulated in the use of Noopept in patients with vascular cognitive impairment. In the study of G.G. Neznamova et al. 40 patients with chronic cerebrovascular insufficiency or the consequences of mild traumatic brain injury received this drug

for a month in two doses - 15 and 30 mg / day. Before treatment, dysmnestic disorders in combination with other cognitive impairments and asthenoneurotic syndrome prevailed in the group of patients with cerebrovascular diseases. During therapy (from the first week of taking the drug), there was a regression of cognitive impairment and positive dynamics of the emotional status of patients. The drug demonstrated a satisfactory safety and tolerability profile and did not cause any clinically significant adverse events. The authors did not find significant differences between the two Noopept dosing regimens [2].

In another study, the effectiveness of Noopept in patients with chronic cerebrovascular disease was compared with that of piracetam. Against the background of the use of each of these drugs, there was a positive trend in the form of regression of cognitive and emotional-affective disorders. However, when using Noopept, these therapeutic effects developed faster and fewer adverse events were noted. The effect was significantly higher against the background of Noopept use, as evidenced by a significant difference between the therapeutic groups on the overall clinical impression scale [3].

A.V. Amelin et al. used Noopept in the treatment of patients with mild cognitive impairment syndrome after ischemic stroke. 60 patients received this drug at a dose of 20 mg/day for two months. There was a significant regression in the severity of violations of higher brain functions on a short scale for assessing mental status. At the same time, differences in the dynamics of cognitive functions compared with placebo reached statistical significance [4].

Thus, the use of neurometabolic drugs against the background of compensation for the underlying vascular disease contributes to a significant regression of vascular cognitive impairment and an increase in the quality of life of patients.

Bibliography

1. Уринов М. Б., Тулаев М. Ж. Cognitive disorders in dyscirculatory encephalopathy and their features //журнал неврологии и нейрохирургических исследований. – 2020. – Т. 1. – №.
2. Эргашов А. Р. Характеристика острой травмы грудопоясничного отдела позвоночника //central asian journal of medical and natural sciences. – 2021. – С. 150-153.
3. Эргашов, А. Р. "Отдаленные Результаты Хирургического Лечения при Острой Травме Грудопоясничного Отдела Позвоночника." Central asian journal of medical and natural sciences 3.2 (2022): 256-260.
4. Мехриддинов, М. К. "Современный Взгляд На Проблемы Этиопатогенеза И Лечение Деструктивных Форм Пневмонии У Детей." Central asian journal of medical and natural sciences 3.2 (2022): 248-255.
5. Mukhsinova L. A., Sharopov S. G. Immunological status in sick children with congenital cleft upper lip and palate //Euro-Asia Conferences. – 2021. – Т. 4. – №. 1. – С. 135-136.
6. Mukhsinova L. A. et al. Cytokine Profile in Patients with Congenital Cleft Upper Lip and Palate //European Journal of Research Development and Sustainability. – Т. 2. – №. 4. – С. 91-93.
7. Yusupov, Sharif Abror Ugli. "Ways to improve the effectiveness of orthodontic treatment in bukhara region to prevent the development of caries." Central Asian Research Journal for Interdisciplinary Studies (CARJIS) 2.3 (2022): 457-464.
8. Ugli, Yusupov Sharif Abror. "The Effectiveness of Rehabilitation Centers on the Psych emotional State of Children of the First Period of Childhood with Congenital Cleft Lip and Palate." Eurasian Medical Research Periodical 7 (2022): 212-214.
9. Мехриддинов, М. К. "Роль Иммунологических Факторов В Патогенезе Развития

Деструктивных Форм Пневмоний У Детей." Central asian journal of medical and natural sciences 3.2 (2022): 234-238

10. Яхно Н.Н., Преображенская И.С., Захаров В.В. и др. Распространенность когнитивных нарушений при неврологических заболеваниях (анализ работы специализированного амбулаторного приема) // Неврология, нейропсихиатрия, психосоматика. 2012. № 2. С. 30-34.
11. Kooten F., Koudstaal P.J. Epidemiology of post-stroke dementia // Haemostasis. 1998. Vol. 28. № 3-4. P. 124-133.
12. Hamroeva D. S. Factors affecting the dental status of the popu lation //Journal For Innovative Development in Pharmaceutical and Technical Science (JIDPTS). – 2021. – Т. 4. – №. 3.
13. Sh, Hamroeva D. "Comparative Analysis Of The Effectiveness Of The Treatment Of Parodontitis In Patients With Obesity." International Journal of Progressive Sciences and Technologies International Journal of Progressive Sciences and Technologies *(IJPSAT) ISSN*: 2509-0119.
14. Loeb C., Gandolfo C., Croce R., Conti M. Dementia associated with lacunar infarction // Stroke. 1992. Vol. 23. № 9. P. 1225-1229.
15. Pasquier F., Leys D. Why are stroke patients prone to develop dementia? // J. Neurol. 1997. Vol. 244. № 3. P. 135142.
16. Pendlebury S.T., Rothwell P.M. Prevalence, incidence, and factors associated with pre-stroke and post-stroke dementia: a systematic review and meta-analysis // Lancet Neurol. 2009. Vol. 8. № 11. P. 1006-1018.
17. Sachdev P.S., Brodaty H., Valenzuela M.J. et al. Clinical determinants of dementia and mild cognitive impairment following ischaemic stroke: the Sydney Stroke Study // Dement. Geriatr. Cogn. Disord. 2006. Vol. 21. № 5-6. P. 275-283.
18. Sundar U., Adwani S. Post-stroke cognitive impairment at 3 months // Ann. Indian Acad. Neurol. 2010. Vol. 13. № 1. P. 42-46.
19. Tamam B., Tapdemir N., Tamam Y The prevalence of dementia three months after stroke and its risk factors // Turk. PsikiyatriDerg. 2008. Vol. 19. № 1. P. 46-56.
20. Xu Q., Lin Y, Geng J.L. et al. The prevalence and risk factors for cognitive impairment following ischemic stroke // ZhonghuaNeiKe Za Zhi. 2008. Vol. 47. № 12. P. 981-984.
21. Вербицкая С.В., Парфенов В.А. Клинический опыт применения мемантина при постинсультной деменции // Неврологический журнал. 2008. Т. 13. № 4. С. 45-47.
22. Парфенов В.А., Вахнина Н.В., Никитина Л.Ю. Когнитивные нарушения после инсульта и их лечение мемантином // Клиническая геронтология. 2005. Т. 11. № 8. С. 49-52.
23. Яхно Н.Н. Когнитивные нарушения в неврологической клинике // Неврологический журнал. 2006. Т. 11. Приложение 1. С. 4-12.