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Modern understanding of the occurrence of cognitive impairments in arterial hypertension and their correction

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Abstract. Hypertension is one of the most common vascular diseases. The brain as target organs in hypertension is damaged more often and earlier. Neurological complications due to hypertension are frequently hyperdiagnosed in Russian neurological practice. Thus, headache, dizziness, impaired recall of recent events, nocturnal sleep disorders, and many other complaints in a hypertensive patient are usually regarded as a manifestation of dyscirculatory encephalopathy. At the same time headaches (tension headache and migraine) in hypertensive patients are predominantly primary; headache associated with dramatic marked elevations in blood pressure is encountered in only a small number of patients. The role of cerebrovascular diseases in the development of dizziness in hypertensive patients is also overestimated. The vast majority of cases, patients with this complaint are in fact identified to have benign paroxysmal postural vertigo, Meniere's disease, vestibular neuronitis, or vestibular migraine. Psychogenic disorders or multisensory insufficiency are generally responsible for non-systemic vertigo in hypertensive patients. Chronic cerebral circulatory insufficiency may cause non-systemic vertigo as a subjective equivalent of postural instability. Cognitive impairments (CIs) are the most common and earliest manifestation of cerebrovascular lesion in hypertension. In most cases, CIs in hypertension were vascular and associated with cerebrovascular lesion due to lacunar infarcts and leukoaraiosis. However, mixed CIs frequently occur when hypertensive patients are also found to have signs of a degenerative disease, most commonly in Alzheimer's disease.

Key words: hypertension; neurological disorders.

Arterial hypertension (AH) is one of the most common vascular diseases with a wide range of dangerous complications. According to epidemiological data, the incidence of hypertension among people over 18 years of age is 15%, and 30–54 years old - 23% [1]. The proportion of patients with hypertension in the practice of a neurologist is extremely high, especially for middle-aged and elderly patients. AH is undoubtedly the most significant risk factor for both acute and chronic cerebrovascular accidents. In this case, the brain often suffers earlier than other target organs of hypertension, such as the myocardium and kidneys. Therefore, an important task of a neurologist is the early diagnosis of vascular lesions of the brain in hypertension to optimize patient management and prevent recurrent acute cerebrovascular accidents (CVA) and the progression of vascular cognitive impairments (CI).

However, in Russian neurological practice, overdiagnosis of neurological complications of hypertension is often observed, when any complaints or objective symptoms in a patient with this disease are associated with real or imaginary vascular

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brain damage. Thus, headache, dizziness, decreased memory for current events, disturbed night sleep and many other complaints of a patient suffering from hypertension are regarded as a manifestation of "discirculatory encephalopathy" without proper clinical analysis of these symptoms. At the same time, these symptoms, of course, can be a manifestation of other pathological conditions, such as primary headache, vestibular disorders, etc. Insufficient diagnosis of concomitant neurological disorders not directly related to hypertension also negatively affects the management of patients and often leads to incomplete or incorrect therapy, chronicity of concomitant neurological disorders and, as a result, to a significant deterioration in the quality of life of patients.

AH can cause CI of varying severity up to vascular dementia. Numerous epidemiological studies indicate the presence of a reliable and strong statistical relationship between hypertension and CI. So, I. Skoog et al. [7, 8], based on 15-year follow-up of patients over 70 years old, came to the conclusion that initially high blood pressure (180/100 or more) significantly correlates with the risk of developing dementia. more than 3700 patients from the South-East region of Asia, a statistical relationship was shown between the level of systolic blood pressure (SBP) in middle age and the risk of developing CI in the future. At the same time, an increase in SBP for every 10 mm Hg. Art. increased the risk of developing CI by 7-16% [9]. The negative effect of hypertension on cognitive function has been demonstrated in a number of other studies [2, 4].

Yu.A. Starchina et al. [3] studied the prevalence and clinical features of CI and emotional-behavioral disorders in patients with hypertension. It has been shown that CIs occur in at least 73.7% of patients with hypertension. At the same time, in patients without a stroke in anamnesis, CI in most cases were mild (46.7%), less often - moderate (MCI, 26.7%). A history of stroke increased the risk of developing more pronounced CI: in patients with hypertension and stroke, MCI (72.7%) prevailed over mild CI (18.2%). At the same time, severe CI (dementia) was observed relatively rarely and only in patients with stroke (9%). The presence and severity of CI in patients with hypertension did not always correspond to complaints of a cognitive nature, which indicates the need for an objective assessment of cognitive functions in patients with hypertension. At the same time, there was a significant correlation between the severity of CI and the level of SBP. Another significant predictor of the development of more pronounced CI was the age of the patients.

Similar results were obtained by O.V. Eremina [5, 6]: cognitive functions in 147 patients (mean age 63.2 ± 10.8 years) with hypertension were assessed depending on the stage of hypertension and other clinical characteristics. The prevalence of mild CI was 68%, moderate - 16.3% and severe - 4.8%. The risk factors for the development of more pronounced CI were the elderly age of patients, stage II and III hypertension, a low level of education and the presence of concomitant dyslipidemia. In addition, the authors noted a significant correlation between the presence of CI and hypertensive left ventricular hypertrophy. These data

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indirectly confirm the assumption that left ventricular hypertrophy can be considered as an indicator of the state of cerebral vessels and, therefore, as a predictor of vascular brain damage in hypertension.

CI in hypertension in most cases are of a vascular nature and are associated with cerebrovascular damage to the brain as a result of lacunar infarctions and leukoaraiosis. However, it is obvious that the presence of hypertension does not protect against other diseases of old age, including Alzheimer's disease (AD). Moreover, according to some data, the risk of asthma in patients with hypertension is higher than among their peers with normal blood pressure. This is explained by the fact that lacunar infarctions and / or leukoaraiosis associated with hypertension can decompensate the asymptomatic stages of AD and accelerate its clinical manifestation. Thus, in some cases of CI in patients with hypertension, they are neurodegenerative in nature. Differential diagnosis of vascular and mixed (vascular-degenerative) CI is of no small importance for the choice of therapeutic tactics and determining the prognosis [9, 12].

Differential diagnosis of vascular and neurodegenerative CI in patients with hypertension is based on the analysis of clinical features, neuroimaging data and follow-up. The vascular nature of CI against the background of AH is indicated by the predominance of attention deficit, control ("frontal") functions of the brain and visual-spatial disorders in the neuropsychological status, which corresponds to the so-called subcortical type of CI.

The governing (regulatory, executive - from the English executive) functions of the brain include:

- goal-setting: the ability to arbitrarily choose and set the goal of the activity. Goal-setting is considered a function of the most anterior parts of the frontal lobe (pole) and the cingulate gyrus. If this function is insufficient, the activity of mental processes, motivation and initiative decrease, emotional indifference develops;

- stability of attention: the ability to build one's cognitive activity and behavior in accordance with the set goal, as well as the ability to inhibit less significant or unacceptable motivations in the existing situation. This component of executive functions is associated with the orbitofrontal cortex. If this factor is insufficient, the patient's behavior becomes impulsive, he is often distracted from the planned activity plan, criticism decreases;

- switchability (intellectual flexibility): the ability to change the paradigm of activity in changed conditions, to move from an already achieved goal to a new one. Switchability is a function of the dorsolateral frontal cortex. If this factor is insufficient, inertia and perseveration develop.

As a rule, in the structure of CIs accompanying AH, one or more of the above signs of insufficiency of executive (frontal) functions are present, and it is these disorders that develop in the first place [11, 12, 14, 17].

Memory in patients with vascular CI against the background of hypertension suffers to a mild or moderate degree. The impairments mostly affect short-term

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memory, while memory for recent and separated events is relatively preserved. An analysis of the neuropsychological features of mnestic disorders suggests that they are based on insufficient reproduction, while memorization and storage of information are not impaired. This is evidenced by the effectiveness of semantic mediation and prompts when testing mnestic function [13, 15]. In the sphere of gnosis and praxis, as already mentioned, violations of spatial functions can be determined. Constructive praxis suffers to a greater extent. However, constructive dyspraxia is more often detected at the stage of vascular dementia and is less typical for lung CI and MCI [17, 18]. Speech with "pure" vascular CI in patients without a history of stroke does not suffer.

The presence of a concomitant neurodegenerative process modifies the picture of CI in hypertension. The most specific feature of concomitant AD is more pronounced memory impairment. The qualitative difference between mnestic disorders in combined vascular-degenerative brain damage from "pure" cerebrovascular pathology is the signs of primary failure to memorize new information - the so-called hippocampal type of memory impairment. Its neuropsychological characteristics are a significant difference between immediate and delayed reproduction; ineffectiveness of semantic mediation of memorization and prompts during reproduction; violation of reproduction in the form of recognition (in tasks with multiple choice); extraneous interweaving during playback. These features of mnestic disorders are determined already in the early stages of the neurodegenerative process [16, 17, 18].

Another specific feature of concomitant AD is the formation of cortical dysphasic disorders. This symptom, in contrast to memory impairments, is not necessary for the diagnosis and in typical cases develops somewhat later. Dysphasic disorders begin with a lack of the nominative function of speech: the patient forgets the names of objects, first low-frequency, and then ordinary. Over time, a complete clinical picture of acoustical-mnestic (according to another classification, transcortical sensory) aphasia may form [19, 20].

Dynamic monitoring of patients is of great importance. "Pure" vascular CIs are characterized by relatively slow progression or may be stationary when adequate blood pressure control is achieved. Progression is usually a stepwise nature: a pronounced deterioration (due to stroke) is replaced by a period of a steady state of varying duration. With the concomitant neurodegenerative process, the progression is smoother and does not depend on the control of hypertension. However, the rate of progression can vary significantly: relatively long periods of stationary status in elderly and senile patients do not completely rule out the diagnosis of concomitant asthma [21, 22].

The most common neurological complication directly related to hypertension is CN. Since hypertension is a strong risk factor for cognitive impairment, it can be assumed that proper blood pressure control helps to reduce the risk of higher cerebral dysfunctions. Numerous observational studies have convincingly shown the positive

effect of antihypertensive therapy in the prevention of dementia [10–14]. At the same time, there was a statistical relationship with the age of initiation of therapy and its duration. The younger the patients were at the beginning of the observation and the longer the observation period itself, the more significantly the risk of developing dementia decreased. At the same time, the risk of developing dementia did not depend on the class of antihypertensive drugs used.

In the Syst-Eur study, it was found that against the background of monotherapy with a prolonged calcium channel blocker nitrendipine or in combination with enalapril and in some cases with hydrochlorothiazide for 2 years of observation, the number of cases of dementia was almost 2 times less than against the background of placebo, which was statistically significant [15]. The PROGRESS study showed a significant decrease in the incidence of dementia associated with recurrent strokes, while there was no difference in the overall incidence of dementia. This study used perindopril alone or in combination with indapamide [16]. In other studies (SHEP, SCOPE, HYVET-Cog), the relationship between antihypertensive therapy and the risk of dementia has not been identified [17–21].

Thus, antihypertensive therapy is clearly indicated for the prevention of stroke and other vascular events. At the same time, timely prescribed long-term sequential treatment can help to reduce the risk of CI progression.

According to some reports, adequate antihypertensive therapy not only helps to curb the development of CI, but can also have a beneficial effect on existing disorders. So, according to Yu.A. Starchinoy et al. [22], a gradual normalization of blood pressure based on the use of the angiotensin-converting enzyme inhibitor cisalapril for 6 months had a beneficial effect on cognitive functions.

Specific therapy of CI against the background of hypertension is based on the generally accepted principles of treatment of CI in general. With MCI and severe CI of both vascular and neurodegenerative etiology, the reversible blocker of NMDA receptors for glutamate akatinol memantine has proven itself well.

According to generally accepted international recommendations, memantine is recommended for Alzheimer's disease with moderate to severe dementia syndrome. However, in our country, the drug is also used for vascular dementia and CI that do not reach the severity of dementia. The efficacy of akatinol memantine in vascular dementia was analyzed in two randomized trials: 9403 / Orgogzo and 9202 / Wilcock (see table) [12, 13]. In both studies, there was a moderate but statistically significant advantage of memantine Akatinol over placebo in terms of cognitive parameters and in the emotional-behavioral sphere.

The largest observational study of the symptomatic effect of akatinol memantine in MCI syndrome in Russia was conducted under the guidance of Academician N.N. Yakhno [14]. 240 patients with CI, not reaching the severity of dementia, of various etiology, were followed up for 6 months. The average age of the patients was 69.2 + 5.7 years. 148 patients received akatinol memantine at a dose of 20 mg / day for 6 months, 92 patients made up the comparison group. In the

comparison group, the use of certain vascular and metabolic drugs was allowed. It was found that against the background of the use of akatinol memantine there was a significant regression of the severity of CI, primarily due to a decrease in the degree of impairment of executive functions, mnestic and visual-spatial disorders, as well as regression of emotional disorders. At the same time, in the comparison group, the positive dynamics of similar indicators was absent or was significantly less pronounced (see figure). The therapeutic effect was observed in patients with both initially more pronounced (22-24 points according to KSHOPS) and less pronounced (25-27 points) disorders. The magnitude of the therapeutic effect did not depend on the etiology of MCI syndrome or the presence of concomitant cardiovascular diseases in patients.

In the study by O.S. Levin et al. [15] 40 patients diagnosed with MCI syndrome, without specifying the etiology, received akatinol memantine for 6 months. The results of neuropsychological testing and assessment of the emotional-behavioral status in these patients were compared with similar results for 20 patients with MCI syndrome, also without specifying the etiology, who received piracetam. It was shown that the proportion of patients with deterioration or absence of positive dynamics of cognitive functions during therapy with akatinol memantine was significantly lower than with piracetam. The general assessment of cognitive functions according to KSHOPS, as well as indicators of auditory-speech memory in both therapeutic groups significantly improved by the 3rd month of observation, but only in the Akatinol memantine group this improvement persisted after 6 months of observation. At the same time, there was an improvement in visual memory, fluency of speech, regression of the severity of depressive disorders and an improvement in the quality of life, but only in the memantine group. The analysis of subgroups showed a greater value of the therapeutic effect in patients with “subcortical” type of CI compared with amnestic type and in patients with a high risk of dementia. Thus, it can be concluded that Akatinol memantine is more effective in CI of vascular etiology.

According to the observations of T.G. Voznesenskaya, therapy with Akatinol memantine promotes regression of both CI and emotional-affective and behavioral disorders in patients with CI of mild to moderate severity [16].

Thus, a detailed analysis of neurological symptoms in patients with hypertension allows in most cases to establish the exact nature of the disorders, which are not always associated with the underlying disease. Determination of the immediate cause of the disorders will contribute to their more differentiated, and, therefore, more effective therapy.

References

1. Kobalava Zh.D., Konradi A.O., Nedogoda S.V. et al. Memorandum of experts of the Russian Society of Cardiology on the recommendations of the European Society of Cardiology / European Society of Arterial Hypertension for the treatment of arterial hypertension 2018 Russian Journal of Cardiology. 2018; (12): 131-42. [in Russian]
2. Rimoldi SF, Scherrer U, Messerli FH. Secondary arterial hypertension: when, who, and how to screen? Eur Heart J 2014;35:1245–1254.
3. Salles GF, Reboldi G, Fagard RH, et al. Prognostic effect of the nocturnal blood pressure fall in hypertensive patients: the Ambulatory Blood pressure Collaboration in patients with Hypertension (ABC-H) meta-analysis. Hypertension 2016;67:693–700.
4. TuckerKL, SheppardJP, StevensR, et al. Self-monitoring of blood pressure in hypertension: a systematic review and individual patient data meta-analysis. PLoS Med 2017;14:e1002389.
5. Parati G, Stergiou G, O'Brien E, et al, European Society of Hypertension Working Group on Blood Pressure Monitoring and Cardiovascular Variability. European Society of Hypertension practice guidelines for ambulatory blood pressure monitoring. J Hypertens 2014;32:1359–1366.
6. Dedov I.I. et al. "Algorithms for specialized medical care for patients with diabetes mellitus." Diabetes mellitus 1S (2019). [in Russian]
7. Cosentino F., Grant P., Aboyans V. et al. 2019 ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD: The Task Force for diabetes, pre-diabetes, and cardiovascular diseases of the European Society of Cardiology (ESC) and the European Association for the Study of Diabetes (EASD). Eur Heart J 2019, published online on 31 August 2019.
8. Ettehad D, Emdin CA, Kiran A, et al. Blood pressure lowering for prevention of cardiovascular disease and death: a systematic review and meta-analysis. Lancet 2016;387:957–967.
9. Моисеев В. С., Мухин Н. А., Смирнов А. В. и соавт. Клинические рекомендации «Сердечно-сосудистый риск и хроническая болезнь почек: стратегии кардионефропротекции» Российский кардиологический журнал 2014, 8 (112): 7–37.
10. Borghi C, Rosei EA, Bardin T, Dawson J, Dominiczak A, Kielstein JT, Manolis AJ, PerezRuiz F, Mancia G. Serum uric acid and the risk of cardiovascular and renal disease. J Hypertens 2015;33:1729–1741.
11. Bacharova L, Schocken D, Estes EH, Strauss D. The role of ECG in the diagnosis of left ventricular hypertrophy. Curr Cardiol Rev 2014;10:257–261.
12. Perrone-Filardi P, Coca A, Galderisi M, et al. Non-invasive cardiovascular imaging for evaluating subclinical target organ damage in hypertensive patients: a consensus paper from the European Association of Cardiovascular Imaging (EACVI), the European Society of Cardiology Council on

Hypertension, and the European Society of Hypertension (ESH). Eur Heart J Cardiovasc Imaging 2017;18:945–960

13. Aboyans V, Ricco JB, Bartelink MEL, et al. 2017 ESC Guidelines on the Diagnosis and Treatment of Peripheral Arterial Diseases, in collaboration with the European Society for Vascular Surgery (ESVS): Document covering atherosclerotic disease of extracranial carotid and vertebral, mesenteric, renal, upper and lower extremity arteries. Endorsed by: the European Stroke Organization (ESO)The Task Force for the Diagnosis and Treatment of Peripheral Arterial Diseases of the European Society of Cardiology (ESC) and of the European Society for Vascular Surgery (ESVS). Eur Heart J 2017;39:763–816.

14. Abdullaeva U.K. Predicting the risk of atrophic transformation in chronic gastritis using serum pepsinogen // World journal of pharmaceutical research, Faculty of Pharmacy Medical University, Bulgaria, Vol. 8, Iss. 13, 2019, P. 219-228.

15. Abdullaeva U.K., Sobirova G.N., Karimov M.M., Aslonova I.J. The prevalence and possibilities of prevention of noncardial gastric cancer in the Bukhara region // American journal of medicine and medical sciences, 2020, 10(9), P. 679-681.

16. Sobirova G.N., Abdullaeva U.K., Nosirova M.S., Aslonova I.J. Evaluation of the gastrointestinal mucosa by the OLGA system in chronic atrophic gastritis // Journal of critical reviews, Kuala Lumpur, Malaysia, Vol. 7, Iss. 2, 2020, P. 409-413.

17. Karimov M.M., Sobirova G.N., Abdullaeva U.K., Aslonova I.Zh., Tulyaganova F.M. Possibilities of serological diagnosis of atrophic processes of the gastric mucosa // European Journal of Molecular & Clinical Medicine Vol. 7, Iss. 11, 2020, P. 2955-2960.

18. Karimov M.M., Sobirova G.N., Abdullaeva U.K. Chronic gastritis and carcinogenesis issues // Herald of Pancreatic Club, 45 (4). P. 65-70. (in Russian)

19. Abdullaeva U.K. Predicting the risk of atrophic transformation in chronic gastritis using serum pepsinogen // World journal of pharmaceutical research, Faculty of Pharmacy Medical University, Bulgaria, 8 (13) P. 219-228.

20. Sobirova G.N., Abdullaeva U.K. Immunopatogenesis of chronic gastritis and its role in carcinogenesis // Journal of Biomedicine and Practice, 1 (4). P. 40-44.

21. Karimov M.M., Sobirova G.N., Abdullaeva U.K., Aslonova I.Zh., Tulyaganova F.M. Possibilities of Serological Diagnosis of Atrophic Processes of the Gastric Mucosa // Annals of the Romanian Society for Cell Biology, , Vol. 25, Issue 1, 2021, Pages. 6168 – 6174.

22. Abdullaeva U.K., Shadjanova N.S. Using the OLGA system in chronic atrophic gastritis // New day in medicine, 2020, №2, P. 9-12.