THE SIGNIFICANCE OF COGNITIVE DYSFUNCTION IN PATIENTS WITH ARTERIAL HYPERTENSION

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Annotation. *The review considers the etiology, pathogenesis and prevalence of various degrees of cognitive impairment in patients with arterial hypertension. The importance and value of balanced antihypertensive therapy in the prevention of moderate cognitive impairment and vascular dementia caused by arterial hypertension in young and elderly patients is emphasized.*
Key words: *arterial hypertension, cognitive dysfunction, etiology, pathogenesis.*

ЗНАЧЕНИЕ КОГНИТИВНОЙ ДИСФУНКЦИИ У БОЛЬНЫХ АРТЕРИАЛЬНОЙ ГИПЕРТОНИЕЙ

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Аннотация. *В обзоре рассматриваются этиология, патогенез и распространенность различной степени когнитивных нарушений у больных артериальной гипертонией. Подчеркивается важность и ценность сбалансированной антигипертензивной терапии в профилактике умеренных когнитивных нарушений и сосудистой деменции, обусловленных артериальной гипертензией у пациентов молодого и пожилого возраста.*
Ключевые слова: *артериальная гипертензия, когнитивная дисфункция, этиология, патогенез.*

ARTERIAL GIPERTENZIYAGA CHALINGAN BEMORLARDA KOGNITIV DISFUNKTSIYANING AHAMIYATI

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Annotatsiya. *Mazkur sharhda arterial gipertenziya kasalligi bilan og'rigan bemorlarda turli darajadagi kognitiv buzilishlarning etiologiyasi, patogenezi va tarqalishi masalalari ko'rib chiqiladi. Yosh va keksa bemorlarda arterial gipertenziyadan kelib chiqqan o'rtacha kognitiv buzilish va qon tomir demansning oldini olishda muvozanatli antigipertenziv terapiyaning muhumligi va ahamiyati ta'kidlangan.*
Kalit so'zlar: *arterial gipertenziya, kognitiv disfunktsiya, etiologiya, patogenez.*

The problem of cognitive impairment in patients with arterial hypertension (AH) is one of the topical problems in therapy, cardiology, neurology, and in the work of general practitioners. Such close attention, first of all, is caused by the current trend of population aging, because it is in elderly and senile people cognitive impairment due to AH is the most common. AH is currently considered as the greatest non-communicable pandemic in the history of mankind, affecting almost half of the adult population.

The incidence of AH is 40% in men and 41% in women. Awareness of patients about the presence of AH among men is 35%, and among women - 60%. Less than 25% of male patients with AH and less than 50% of female patients with AH receive drug therapy [11,20]. AH is a high independent risk factor for the development of acute cerebral circulatory disorders (ACBD), hypertensive cerebral crises, acute hypertensive encephalopathy, transient ischemic attacks, hypertensive dyscirculatory encephalopathy, myocardial infarction, acute coronary insufficiency, nephropathy, Parkinson's syndrome. Currently, it is considered that more than 1 million patients suffering from AH and various cerebral pathologies developed against this background suffer from cognitive impairment of varying severity [1, 13].

The situation is complicated by the fact that, along with extremely high prevalence of AH, the Russian population is characterized by extremely unsatisfactory awareness of patients about the presence of the disease, insufficient coverage of drug therapy for these patients and catastrophically low compliance,

which causes low efficiency of hypotensive therapy and the growth of cerebrovascular complications [13, 19, 20]. On the one hand, the relevance of the problem of cognitive disorders in patients with AH in recent years is beyond doubt and is due to the fact that timely detection and proper treatment of these disorders improves their quality of life, allows to slow down, and in some cases prevent, the development of vascular and mixed dementia of potentially able-bodied population, which is extremely important in the current demographic situation in our country. On the other hand, it is necessary to raise awareness of outpatient physicians in the field of cerebral complications of AH, including the most frequent, but rare and late diagnosed complication, such as cognitive disorders [1, 20].

Cognitive functions are understood as the most complex functions of the brain, by means of which the process of rational cognition of the world is realized and purposeful interaction with it is ensured [8]. This process includes four main interacting components: perception, information processing and analysis, memorization and storage, information exchange, and the construction and implementation of an action program [10].

Each of the above stages of cognitive activity is associated with a certain function: perception of information - gnosis; processing and analysis of information - the so-called "executive" functions, which include arbitrary attention, communication, identification of similarities and differences; memorization and storage of information - memory; exchange of information, construction and implementation of a program of actions (praxis). It is currently accepted that cognitive disorders are disorders of one or more cognitive functions (memory, praxis, gnosis, speech, regulation of voluntary activity) as a result of any disease, including AH [3].

Cognitive impairment can be divided into mild (preservation of the ability to live independently), moderate (some degree of care is required) and severe with the development of vascular or mixed dementia (the patient is completely helpless in everyday life) [7].

In the pathogenesis of mild cognitive impairment in old age, the natural weakening of attention, short-term memory, and dysregulatory disorders associated with aging play an important role. Both clinical experience and data from experimental and psychological studies convincingly demonstrate that memory, attention, verbal-logical, psychomotor and other cognitive functions often deteriorate with age, even in the absence of clinically delineated brain disease [9].

In 1994, experts from the International Association proposed using the term "age-related cognitive dysfunction" to refer to mild cognitive impairment of a predominantly age-related nature. In practice, most older adults have several chronic cardiovascular, other somatic and neurological diseases. Many of these can adversely affect cognitive function. It is rather difficult to clearly distinguish between the contribution of age itself and the contribution of age-associated diseases to the formation of cognitive insufficiency in the elderly, which has a multifactorial etiology, and requires clarification during a comprehensive clinical examination [9].

In recent years, much attention in the world literature has been paid to the problem of moderate cognitive impairment (MCI) in old age. This term is commonly understood as disorders of memory and other higher brain functions that are beyond the age norm but do not cause social maladaptation [3, 9].

The term "mild cognitive impairment" (MCI) was first proposed in 1997 by R. Petersen to describe the pre-dementia stages of Alzheimer's disease [49, 50]. The first diagnostic criteria for this condition reflected exactly the pre-dementia stage of Alzheimer's disease: the diagnosis was based on the presence of subjective and objective memory impairment with preservation of cognitive functions in general [51, 55]. Sometimes, the absence of severe cerebrovascular disorders and focal neurological symptoms was also suggested as additional diagnostic criteria for moderate cognitive disorders. However, it is now proven that moderate cognitive impairment, like dementia, is a polyetiologic syndrome that can be caused by the same multiple brain diseases that lead to the development of dementia. The term is used to describe cognitive impairment intermediate between age-related cognitive changes and dementia [2, 22, 24, 27-29, 31, 32].

ICD-10 suggests the following criteria for the diagnosis of moderate cognitive disorders: the presence of a decrease in memory, attention, and learning ability; subjective complaints of increased fatigue during mental work; absence of association of cognitive disorders with mental confusion, absence of dementia, and organic nature of cognitive disorders [12].

Cognitive disorders in moderate cognitive disorders against the background of cardiovascular pathology, including AH, are progressive in most cases. In 55-65% of cases within 5 years there is a transformation of moderate cognitive disorders into clinically delineated dementia of predominantly Alzheimer type [4,6]. This fact determines the need for early diagnosis of moderate cognitive disorders in patients with AH, allowing timely implementation of preventive measures aimed at preventing or delaying the onset of social disadaptation of the able-bodied population [5].

In domestic neurological practice, patients with moderate cognitive disorders on the background of AH are often diagnosed with dyscirculatory hypertensive encephalopathy. This occurs especially often in the presence of concomitant cardiovascular diseases [4, 8]. It is assumed that the decline in memory and other cognitive functions in patients with cerebrovascular insufficiency is a direct result of chronic cerebral ischemia. It is now established that hypertension, atherosclerosis of the main arteries of the head and other vascular pathology plays a

role in the formation of neurodegenerative changes in brain tissue [15].

Summarizing the above, moderate cognitive disorders can be defined as a polyetiologic (multifactorial) decline in one or more cognitive domains beyond the age-related norm, but not leading to a loss of independence and autonomy of the patient in everyday life [14].

The prevalence of moderate cognitive impairment syndrome in AH patients requires further study. A survey of more than 60 leading world experts on this problem showed that the prevalence of moderate cognitive disorders in the age group over 60 years does not exceed 30%. The data of wide population epidemiologic studies agree with this [25, 30, 35, 58]. Thus, according to the Canadian Study of Health and Aging (Canadian Study of Health and Aging, 1997), cognitive impairment that does not reach the degree of dementia is noted in 14.9% of the elderly [27, 41, 62, 72]. A German study of the elderly (Leipzing Longitudinal Study of the Aged) reported figures of 5.1% [29]. The risk of developing a moderate cognitive impairment syndrome at the age of over 65 years within one year is 5% and 19% during 4 years of follow-up [6,8,21,23,26]. The above epidemiologic data emphasize the importance of clinical diagnosis of RBM syndrome in AH patients.

The clinical picture of moderate cognitive impairment syndrome is determined by the nosologic form underlying the cognitive impairment. As the concept and research on RBM has evolved, it has become apparent that there are three main clinical variants. Amnestic variant (memory impairment for current events predominates in the clinical picture, later on, as a rule, the unfolding picture of dementia of the Alzheimer's or vascular Alzheimer's type develops. Moderate cognitive disorders with multiple cognitive deficiency (characterized by the presence of combined lesions of several cognitive functions, this type of moderate cognitive disorders can be observed in the initial stages of AH, as well as in Alzheimer's disease, fronto-temporal degeneration, etc.). RBM with impairment of one of the cognitive functions with preserved memory, variants of this syndrome with predominance of speech or praxis impairment are possible; this type of moderate cognitive impairment syndrome can be observed in the early stages of neurodegenerative diseases, for example, in primary progressive aphasia, dementia with Levi's corpuscles [44, 45, 50, 52].

Thus, when diagnosing CHD in the practice of a therapist, in the structure of hypertensive dyscirculatory encephalopathy, knowledge of other causes of dementia and differential diagnosis is required, which is not done at the level of polyclinic health care in the vast majority of cases.

In those cases when memory and other cognitive disorders in patients with AH are so pronounced that they prevent the realization of professional and social activities, it is customary to speak of vascular dementia. Vascular dementia (dementia) is an acquired as a result of an organic brain disease or somatic disease (e.g., AH) stable disorders of memory and other higher brain functions, which have a significant impact on the patient's behavior and daily (professional, social and domestic) activity. At the stage of dementia, the patient completely or partially loses his or her independence and autonomy, often requiring extraneous care. This is the most severe clinical syndrome of cognitive impairment [3, 4, 7, 42].

According to the recommendations of the latest revision of the International Classification of Diseases (ICD-10, 1995) [12], the diagnosis of vascular dementia is legitimate in cases when the patient develops a steady, compared to the previous level, decline in mnestic and other cognitive abilities. This decline in AH patients is based on secondary brain damage, cognitive impairment is determined against the background of clear consciousness, and, as a rule, is combined with changes in the emotional sphere or in his behavior [10].

Defining vascular dementia. For general practitioners, cardiologists, and general practitioners, vascular dementia is of most interest. Vascular dementia is interpreted in ICD 10 (1995) as the result of cerebral infarction due to vascular disease, including AH, but this position is currently under review (e.g., Binswanger's disease). The onset of the disease is usually late in life. According to these criteria, the following is necessary for diagnosis: the presence of dementia, the cognitive defect should be heterogeneous - in some areas the impairment may be significantly pronounced, others may be preserved.

In addition, the detection of focal neurological symptoms in the form of at least one of the following - central hemiparesis, unilateral increase in deep reflexes, pathological foot reflexes, pseudobulbar palsy. There are also anamnestic, clinical or paraclinical signs of a pronounced cerebral disease that is etiologically associated with dementia (presence of stroke in the history, signs of cerebral infarction) [5].

Several types of vascular dementia are distinguished: with acute onset, multi-infarct, subcortical vascular dementia (Binswanger's disease), mixed cortical and subcortical vascular dementia, unspecified, others. In patients with AH, it is possible to develop all of the above types of vascular dementia. Dementia with acute onset occurs within the 1st month (not later than 3 months) after being a massive hemorrhage [5, 16].

- Multi-infarct vascular dementia is predominantly cortical; the onset is more gradual (within 3-6 months) after a series of small ischemic episodes, lacunar strokes with scanty symptomatology in the acute period, which are most typical for AH, especially when there are irregularities in the regularity of hypotensive medications, there may be periods of clinical improvement between ischemic episodes.
- Subcortical vascular dementia includes cases characterized by a history of arterial hypertension and ischemic destructive foci in the deep layers

of the white matter of the cerebral hemispheres. The cerebral cortex is usually preserved, and this contrasts with the clinical picture of Alzheimer's disease.

• Mixed cortical and subcortical vascular dementia is suspected based on clinical presentation, findings including autopsy, brain MRI, or both [34, 53].

• Vascular dementia is the second most common cause of dementia in Western Europe and the United States. It is diagnosed in about half of patients hospitalized for dementia. In the countries of the former USSR and Japan, vascular dementia is more common than Alzheimer's disease [38-40]. The average age of patients with vascular dementia is slightly less than that of patients with Alzheimer's disease, and the duration of the disease from the moment of diagnosis to the onset of death among them is about 5-7 years (for comparison, in Alzheimer's disease - from 6 to 8 years) [5].

Arterial hypertension in combination with hyperlipidemia is known as a significant risk factor for the development of atherosclerosis. It is now established that they are many times greater than the risk of developing and Alzheimer's disease [27,38-40]. Some authors believe that AH may be a secondary pathology in relation to Alzheimer's disease: due to the fact that the deposition of amyloid in vessels in this disease reduces cerebral blood flow at the level of stem vasomotor structures, and to maintain it at a normal level, the systemic blood pressure increases.

D. Bennet et al. [26] consider Binswanger's disease a relatively rare type of vascular dementia. According to the proposed criteria, the diagnosis of Binswanger's disease requires the presence of:

1) dementia;

2) vascular risk factors or signs of systemic vascular disease: vascular lesions of the brain (focal neurological symptoms); “subcortical neurological disorders (parkinsonian walking disorder, senile or ‘magnetic’ gait; paratonia; urinary incontinence in the presence of spastic bladder);

3) bilateral leukoareosis (in the form of periventricular thinning of the white matter of the brain) according to CT/MRI or bilateral multiple or diffuse areas in the white matter of the cerebral hemispheres.

It is emphasized that the patient must not have multiple or bilateral cortical foci on CT and MRI and severe dementia. Pathomorphological examination reveals marked demyelization, lacunae in subcortical sections, and infarcts may be detected [28]. The predominant lesion of myelin of the white matter of the cerebral hemispheres is confirmed by the results of pathomorphologic study. [28].

In recent years, the problem of high blood pressure as a risk factor for cognitive disorders and the development of vascular dementia has attracted increasing interest [2, 13]. This is due to the high prevalence of AH among the elderly [13]. Disturbing physiological processes of autoregulation of cerebral blood circulation and adaptation of higher nervous activity, AH significantly affects not only the duration but also the quality of life of patients [1, 13].

Long-term epidemiologic studies have shown the association of AH with cognitive impairment, and that balanced antihypertensive therapy can reduce the risk of vascular dementia. The opinion that increased blood pressure is a predisposing factor in the development of vascular dementia and cognitive impairment was first expressed by Skoog et al. [53, 58] based on the results of a 15-year follow-up of patients over 70 years old. In this study it was found that in patients with an initially high level of BP (178/101 mm Hg.) after 79 years of age, vascular dementia occurred more often than in those with lower blood pressure (164/92 mm Hg.). The relationship between high blood pressure, vascular dementia and moderate cognitive impairment in elderly patients has been established in large epidemiologic studies Framingham [32], EVA [59], Gothenburg [56], Honolulu-Asia Aging Study [43].

Thus, the Honolulu-Asia Aging Study, which included 3735 participants aged 45 to 50 years, showed an association between blood pressure levels in middle-aged patients, and cognitive function in later life over three decades. High systolic blood pressure in midlife was directly correlated with the risk of cognitive dysfunction in old age. An increase in systolic blood pressure for every 10 mmHg increase in risk of moderate cognitive impairment by 7% and severe cognitive impairment by 9%. In further analysis, it was found that the risk of vascular dementia was higher in patients who did not receive antihypertensive therapy and therapy for cognitive impairment, including neurotrophic, nootropic drugs and other drugs with high affinity for vascular dementia (NMDA-receptor antagonists, anticholinesterase drugs, etc.) [9].

The prevalence of vascular dementia increases exponentially with age. Every 5.3 years, the number of patients doubles. Despite the relevance of the problem under consideration, the data on the prevalence of vascular dementia in patients with AH are approximate. The ongoing studies are fragmentary, and in the Russian Federation have a local character. The figures reported in the literature are obtained mainly in studies performed in hospitals where patients with severe disease are hospitalized. Verification of the diagnosis of vascular dementia in these cases was often based on autopsy data, and less often on lifetime neuroimaging methods (brain MRI) [20].

It should be noted that it is difficult to generalize the accumulated data due to the heterogeneity of tests, scales and questionnaires used for the diagnosis of vascular dementia, the lack of clear inclusion and exclusion criteria, and the heterogeneity of the age group of the observed patients. Thus, at present the data of previously conducted studies do not fully reflect the true prevalence of vascular dementia in AH patients. There are no clear algorithms for prevention and treatment of this serious, disabling complication in patients of working age.

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