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CAUSES OF COGNITIVE IMPAIRMENT AND THEIR MANIFESTATIONS IN PATIENTS WITH ARTERIAL HYPERTENSION

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Ключевые слова: *когнитивные нарушения при артериальной гипертензии, диагностика когнитивных расстройств, нейропсихологические исследования*

Abstract. *Causes of cognitive impairments development and their manifestations in patients with arterial hypertension. Krotova V.Yu., Khomazyuk T.A. The article considers risk factors for the development of cognitive disorders, the most powerful of which is age. The role of the cardiovascular system diseases in the formation of cognitive impairments, in particular, the development of changes in the cognitive sphere in arterial hypertension, is reflected. The main causes of the appearance and clinical variants of the manifestation of cognitive impairment in patients with arterial hypertension are highlighted. Attention is paid to morpho-functional changes in the brain, large and small cerebral vessels in the increased blood pressure and their relationship to cognitive impairments. The indications to the study of the cognitive sphere and the variants of diagnosis of cognitive impairments in patients with arterial hypertension are reflected.*

Реферат. *Причини формування когнітивних порушень та їх прояви у хворих на артеріальну гіпертензію. Кротова В.Ю., Хомазюк Т.А. У статті розглянуті фактори ризику розвитку когнітивних порушень, найбільш сильним серед яких визнаний вік. Відображено роль захворювань серцево-судинної системи у формуванні когнітивних порушень, зокрема розвиток змін когнітивної сфери при артеріальній гіпертензії. Висвітлено основні причини появи і клінічні варіанти прояву когнітивних порушень у пацієнтів з артеріальною гіпертензією. Придільено увагу морфо-функціональним змінам у головному мозку, у великих і малих церебральних судинах при підвищенні артеріального тиску і їх взаємозв'язок з когнітивними порушеннями. Відображено показання до дослідження когнітивної сфери й варіанти діагностики когнітивних порушень у пацієнтів з артеріальною гіпертензією.*

Generally accepted and the most strong and independent risk factor for cognitive impairment (CI) is age because the brain undergoes a series of regular changes that make it more vulnerable to various pathological effects. Thus, with age, the mass of the brain decreases as well as, the number of synapses, the activity of dopaminergic, noradrenergic, acetylcholinergic and other neurotransmitter systems changes. These involutive changes ultimately reduce neuronal flexibility. [14, 15]. A known disorder of cognitive function is Alzheimer's (AD) disease, which is a genetically determined disease. AD beginning to 60 years is characterized by autosomal dominant type of transmission and high penetrance of pathological genes. [20, 37]. In addition to age and heredity, an important risk factor for cognitive impairment is cardiovascular disease, especially arterial hypertension (AH). In AH the risk of developing vascular dementia is higher by 62% at the age of 30-50 years [3, 26].

According to the European Congress on Hypertension (ESH – Barcelona, 2018), more than 1 billion people in the world are prone to steady rise in blood pressure (BP), (Mancia, J Hypertens 2018). In Europe AH is observed in 44% of the adult population, in the USA and Canada–28% [24]. The dynamics of statistical indicators of the health of the population of Ukraine testifies to the unceasing increase in the prevalence of AH. According to the official data of the Center for Medical Statistics of the Ministry of Health in Ukraine, more than 12 million patients with AH have been registered in Ukraine, accounting for about one third of the adult population (30% in urban areas and 36% in rural areas). The specific gravity of AH in the structure of the prevalence and morbidity of diseases of the circulatory system is the highest for all age groups: adults – 46.8% and 41.8% respectively; able-bodied 55,2% and 46,0%. The analysis of the overall mortality rate in Ukraine shows that mortality from

cardiovascular diseases (CVD) is 61.6% among all causes of mortality. According to WHO data, 17.5 million patients die from CVD, but one of the most common circulatory diseases is AH, in which the risk of cerebrovascular disease increases 3-fold [19, 33]. The attention of the international medical community to AH as a factor in lesion of many organs and systems and one of the leading causes of mortality in the able-bodied population has been tracked since the beginning of the past century after the research conducted in Europe. Epidemiological studies of Systolic Hypertension in Europe trials, PROGRESS, LIFE, SCOPE, and MOSES have convincingly shown that AH is a significant risk factor for the development and progression of cognitive impairment [21, 27, 28, 32, 34, 36].

According to large population studies conducted in different regions of the world independently of each other, it was concluded that the presence of AH in the middle age is associated with an increased risk of developing memory impairments in the elderly and senile age [35, 38]. Possible mechanisms by which AH provokes the onset or clinical manifestation of AD, is currently being clarified. Most likely decompensation of the subclinically occurring degenerative process as a result of lacunar infarcts and/or progression of leukoencephalopathy [18, 22, 29, 30] is a decisive factor. Recently, it has been proven that type 2 diabetes also significantly increases the risk of cognitive impairments. According to the LADIS study (European study on the relationship between leukoencephalopathy and disability study), there is a statistical association between diabetes mellitus and a characteristic marker of the neurodegenerative process - atrophy of the medial parts of the temporal parts of the brain [6, 31]. Hyperlipidemia and abdominal obesity in the middle age also increase the risk of developing cognitive impairment as aging. Expectedly that the maximum risk is observed in the combination of AH, hyperlipidemia, abdominal obesity and type 2 diabetes, which is often observed in patients with a so-called "metabolic syndrome". The periventricular zone of white substance is considered as a zone of terminal blood supply, which determines its specific sensitivity to both elevated blood pressure levels and hypotension.

The primary lesion of the subcortical basal ganglia and deep sections of the white substance of the cerebral hemispheres is caused by anatomical and physiological features of the cerebral circulation. These structures are located in the so-called watershed area between the carotid and vertebro-basilar basins, that is why they are the most typical localization of "muted" infarcts and leukoencephalopathy as a result of microangiopathy of penetrating cerebral

arteries with long-term uncontrolled AH. Damage to the deep sections of the white substance of the brain and basal ganglia involves a functional disruption of the prefrontal subcortical association (separation phenomenon), which plays a leading role in the formation of the main clinical syndromes: cognitive, emotional and motor disorders [23].

The proven risk factors for cognitive impairment in the elderly include cranio-cerebral trauma and episodes of history of depression, female sex, deficiency of B group vitamins and folic acid, low intellectual and physical activity in young and middle years of life [2, 16, 17]. There is a direct correlation between the level of blood pressure at the age of 50 years and the state of thinking at the age 70 years: the better the control of blood pressure, the better the cognitive function. Thus, AH is today considered as a risk factor for dementia of any etiology.

Risk factors for cognitive impairments in AH:

- uncontrolled AH,
- hypertensive crises (violation of the blood-brain barrier),
- high variability of blood pressure,
- high nightly arterial hypertension ("nightpeaker"),
- excessive reduction of blood pressure at night time ("overdipper") and/or in the afternoon [11, 12, 28, 35].

Risk factors for the development of leukoencephalopathy and hypertensive encephalopathy:

1. Uncontrolled hypertension, including the so-called "soft" AH.
2. Hypertensive crises (breakdown of the upper border of autoregulation, violation of the blood-brain barrier).
3. High variability of blood pressure.
4. High night hypertension.
5. Excessive reduction of blood pressure.
6. High pulse pressure.
7. Episodes of orthostatic hypotension.
8. Age (> 60 years) [1, 9, 10].

Cognitive impairments are classified according to severity. Light, moderate, and heavy CI are distinguished [4]. If due to CI a partial or complete dependence from outside help develops, it is a case of severe CI (dementia). The obvious question is: when and who to evaluate cognitive functions? This should be done in middle-aged patients when there are complaints of memory loss or decreased concentration of attention; if relatives indicate to a cognitive decline in recent years; when there are problems to present anamnesis or to correctly follow the doctor's recommendations; in case when the

patient, in response to a question from the doctor, redirects the question to the accompanying relative.

Patients with AH have lower results in all neuropsychological tests:

- reaction time,
- spatial and visual memory,
- direct and delayed playback of memorized words,
- rate of the reaction of choice,
- analysis of information,
- solving problems,
- revealing similarities and differences,
- generalization, activity, motivation, programming action,
- state arbitrary attention [28].

For diagnostics of CI in clinical trials, in clinical practice and scientific research, neuropsychological research methods are most often used. The most popular and easy-to-interpret techniques are the Mini-Mental State Examination (MMSE) [25], Frontal Assessment Battery (FAB) [8], the clock drawing test, and the Global Deterioration Scale Rating [5].

The implementation of complex neuropsychological tests depends on dynamic factors such as concentration of attention, the mood of the patient, his motivation to achieve maximum results. Of great importance are the level of education and premorbid mnemonic-intellectual abilities [15].

For practical purposes, timely diagnosis of CI is important, since it is precisely in the early stages of brain damage that one can expect the greatest success of therapeutic measures. Clinical manifestations of light and moderate CI depend on the cause of the

violations. In the early stages of Alzheimer's disease, in the clinical picture memory impairments dominate. The most specific symptoms are the inability to remember the names of recent acquaintances or to retell the newly read, difficulty in selecting the right word in the conversation. In light CI associated with the predominant lesion to subcortical basal ganglia and the most frequent variants of vascular cerebral insufficiency, the "clinical subcortical-frontal" CI appears in the foreground of the plan view as a violation of the planning and switching activity, reducing the reaction rate and mental performance, impulsive behavior. Such disorders are usually accompanied by symptoms of depression and neurological disorders [7].

It is not clear finally by how much is the effect of AH on CF in younger patients is expressed. However, there is evidence that even in adolescence, a higher level of AS is associated with the decrease in mathematical and creative abilities. At present, AH is considered as a factor accelerating the realisation of the genetic predisposition to the degenerative process in the brain (*Lande M., et al., 2013*).

Thus, it should be emphasized that to detect cognitive impairment in patients with cardiovascular diseases including those with arterial hypertension, especially at early, pre-dementia stages, identifying the cause of their development is important for primary care physicians, since this impacts the effectiveness of treatment, duration and quality of their life.

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ЗМІНИ ПАРАМЕТРІВ ФУНКЦІЇ ЗОВНІШНЬОГО ДИХАННЯ У ХВОРИХ З ТЕРМІНАЛЬНОЮ СТАДІЄЮ ХРОНІЧНОЇ ХВОРОБИ НИРОК, ЯКІ ЗНАХОДЯТЬСЯ НА ЗАМІСНІЙ ТЕРАПІЇ

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Ключові слова: *функція зовнішнього дихання, термінальна стадія хронічної хвороби нирок, трансплантація нирки*

Ключевые слова: *функция внешнего дыхания, терминальная стадия хронической болезни почек, трансплантация почки*

Key words: *function of external respiration, end-stage of chronic kidney disease, kidney transplantation*

Реферат. *Изменения параметров функции внешнего дыхания у больных с терминальной стадией хронической болезни почек, которые находятся на заместительной терапии. Курята А.В., Штепа О.А., Галушак О.В. Целью нашей работы было проанализировать изменения показателей функции внешнего дыхания (ФВД) у больных с терминальной стадией болезни почек в условиях проведения заместительной терапии и сравнить с результатами у больных после трансплантации почек. В первую группу вошли 40 больных с терминальной стадией хронической болезни почек, которые находятся на гемодиализе. Во вторую группу – 19 больных после трансплантации почки. Была определена достоверная разница ($p < 0,05$) у больных первой и второй групп между показателями ФЖЕЛ (90 [75-110]% и 98 [91-108]%), ОФВ₁ (79 [71-93]% и 96 [84-104]%), ПОС (61 [40-87]% и 82 [64-94]%), СОС₂₅₋₇₅ (52,5 [39-71]% и 80 [66-112]%). Показатели обеих групп достоверно отличались относительно показателей ФВД группы сравнения: ФЖЕЛ (107,5 [105,5-124]%), ОФВ₁ (100,5 [96-105,5]%), ПОС (99,5 [95-102,5]%), СОС₂₅₋₇₅ (98,5 [97,5-101,5]%). У больных первой группы*