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FEATURES OF COGNITIVE DISORDERS IN PATIENTS WITH ARTERIAL HYPERTENSION OF LOW CARDIOVASCULAR RISK

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Ключевые слова: *артериальная гипертензия, когнитивные расстройства, сердечно-сосудистый риск*

Abstract. Features of cognitive disorders in patients with arterial hypertension of low cardiovascular risk. Krotova V.Yu. *By the WHO data, Ukraine is country number 1 in Europe and number 2 in the world according to the cardiovascular mortality rate. In the structure of the prevalence of cardiovascular diseases in Ukraine, the percentage of persons of working age with arterial hypertension is 36.7%. The improvement of the prognosis of patients with arterial hypertension depends not only on long-term effective control of blood pressure, but the diagnosis and initiation of therapy at the initial stage of the development of the disease, when the target organs have not yet undergone hypertensive damage is also an important condition. The article presents the results of neuropsychological examination of 509 outpatients with a controlled second stage arterial hypertension, with an integrated assessment of cognitive functions using the Mini-Mental State Examination (MMSE) and Montreal Cognitive Assessment (MCA) methods. It has been established that even in patients with controlled arterial hypertension stage II with a low cardiovascular risk, by SCORE scale cognitive disorders were revealed in 32,2%. The peculiarities of the development of cognitive disorders in arterial hypertension in connection with the history and course of the disease are analyzed. The majority of patients with hypertension have an increased level of anxiety, especially personality, and this is not due to the presence or absence of cognitive disorders. In patients with hypertension and cognitive disorders, on the basis of testing data by the SF-36 scale, there was a significant ($p<0.001$) decrease in quality of life on all scales as compared with healthy ones on average by 24.5-66.0 points.*

Реферат. Особенности когнитивных нарушений у больных артериальной гипертензией невысокого сердечно-сосудистого риска. Кротова В.Ю. *По данным ВООЗ, Украина является страной № 1 в Европе и страной № 2 в мире по рейтингу смертности от сердечно-сосудистых заболеваний (ССЗ). В структуре распространенности ССЗ в Украине процент лиц трудоспособного возраста при артериальной гипертензии – 36,7%. Улучшение прогноза больных с артериальной гипертензией (АГ) зависит не только от эффективного контроля артериального давления (АД), важным условием является также диагностика и инициация терапии на начальном этапе развития заболевания, когда еще не произошло гипертензивное поражение органов-мишеней. В статье приведены результаты нейропсихологического обследования 509 амбулаторных работающих больных с контролируемой АГ II стадии и интегральной оценкой когнитивных функций по методикам Mini-Mental State Examination (MMSE) и Montreal Cognitive Assessment (MoCA). Установлено, что даже у больных с контролируемой АГ II стадии и невысоким сердечно-сосудистым риском по шкале SCORE у 32,2% выявляются недементные когнитивные нарушения. Проанализированы особенности развития когнитивных расстройств при артериальной гипертензии во взаимосвязи с анамнезом и особенностями течения заболевания. У большинства больных АГ выявили повышенный уровень тревоги, особенно личностной, что не было связано с наличием или отсутствием когнитивных нарушений (КН). У больных с АГ и КН на основании данных тестирования по шкале SF-36 регистрировали достоверное ($p<0,001$) снижение показателей качества жизни (КЖ) по всем шкалам по сравнению со здоровыми в среднем на 24,5-66,0 баллов.*

According to the European Society of Cardiologists and European Society of Hypertension (ESC/ESH – Munich, Barcelona, 2018), more than 1 billion people in the world are prone to steady rise in blood pressure (BP). According to the recent WHO data, Ukraine ranks 1st in Europe and 2nd in the world by number of deaths from cardio-vascular diseases (CVD) [14]. The improvement of the prognosis of patients with arterial hypertension (AH) depends not only on long-term effective control of blood pressure, but diagnosis and initiation of therapy at the initial stage of the disease development, when hypertension of the target organs has not yet occurred is an important condition as well [3]. Epidemiological studies in the international multicenter trials Framingham, EVA Gothenburg, Honolulu-Asia Aging Study, Systolic Hypertension in Europetrials, PROGRESS, LIFE, SCOPE, MOSES, ONTARGET, TRANSCEND have convincingly shown that AH is a significant risk factor for the development and progression of cognitive disorder (CD), the presence of which, in turn, worsens the quality of life (QL) of patients with hypertension and reduces their social adaptation [8]. The updated European document on hypertension treatment (ESC/ESH, 2018) emphasizes compulsory early diagnosis and monitoring of CD as a marker for brain damage associated with hypertension. Cognitive disorder is found in 73% of patients, both middle aged and elderly, with AH duration of more than 5 years [2, 11].

A retrospective analysis of the medical documentation of 509 able-bodied patients with a controlled AH stage II in real medical practice showed absence of any information about the CD during the dispensary follow-up of the disease. The medical generalization of cognitive disorders was hidden, and in the conclusions they were considered as "dyscirculatory encephalopathy". A purposeful drug correction of the CD was not envisaged at all. It has been found that primary care physicians do not have formal regulatory documents, as a rule they are not familiar with and/or have experience in both diagnosis of CD and planning of primary, secondary prevention and treatment.

The purpose of the study is to determine the state of the cognitive sphere, the profile of cognitive impairment and the relationship with quality of life in patients with controlled arterial hypertension, stage II.

MATERIALS AND METHODS OF RESEARCH

To identify general patterns and peculiarities of the development of CD in patients with controlled AH stage II (target levels BP <140 and 90 mm Hg) [2] a comparative analysis in 3 groups was used. The main clinical group was made up of 157 patients with a controlled AH stage II with a duration of more than 5 years, with CD revealed by means of commonly accepted neuropsychological tests (MMSE, MoCA). There were 70 (44.6%) men, and 87 (55.4%) women (Fig. a). Most of the patients examined were in the age group from 50 to 59 years old – 66 (42,0%), from 40 to 49 years old – 44 (28,0%), from 60 to 70 years – 40 (25,5%), age group from 34 to 39 years old made up 4.5% (n=7) (Fig. b). The average age was 52.3±0.68 (SD=8.55) years. The duration of hypertension in the examined patients varied from 5 to 23 years, the median was 10.0 (9.0-13.0) years. Regarding the educational level of the patients included in the study: most of them, 108 (68.79%) had higher education, 42.7% – secondary special education, and only 7 patients (4.46%) had a secondary vocational education. The study was conducted in compliance with the Helsinki Declaration on Human Rights in Research in Medicine [16].

The comparison group included 28 patients with a controlled AH stage II but without CD, statistically comparable by the main characteristics (age, sex, AH duration, office level, BMI, lipid profile) with patients in the main group. The criteria for exclusion from the study were: an ischemic and / or hemorrhagic stroke in history, a history of craniocerebral trauma, history of alcohol and/or substance abuse, oncological diseases, surgical intervention on the brain in the history, symptomatic AH, uncontrolled or resistant hypertension, depression syndrome, dementia syndrome, diabetes mellitus, ischemic heart disease (HF III-IV FC, MI in anamnesis), heart failure III-IV FC by NYHA, intolerance to nootropic and anticholinesterase agents or contraindications for their administration, refusal of the patient to participate or to continue participation in the study, other states, which, to the opinion of the researcher, questioned the patient's participation in the study. The third group consisted of 28 practically healthy women and men without AH and CD corresponding to the cohort of the studied patients with hypertension by sex and age (p>0.05). The obtained data were processed using the methods of medical statistics (descriptive statistics taking into account the distribution law (Shapiro-Wilk test); parametric and nonparametric criteria: Student (t, T), Wilcoxon (W), Mann-Whitney test (U), Bonferonni adjustment with multiple comparison, Pearson Xi-squared criterion (χ^2), Fischer's exact test, Spirman correlation analysis, ROC-analysis, logistic regression method).

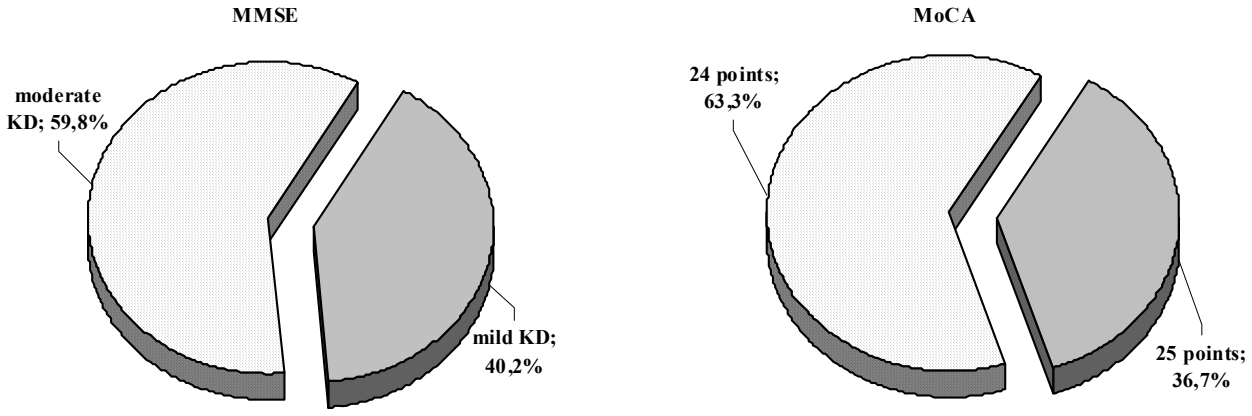
RESULTS AND DISCUSSION

The calculation of total cardiovascular risk (CVR) by the SCORE scale in the study subjects showed that all patients with AH, as well as healthy individuals, had a certain risk of developing fatal cardiovascular events during 10 afteryears. No risk was reevaled (0%) in any case, this is explained by the age of the study subjects, the participation in the study of both male and female subjects, and the detected fact of smoking in 47% of the surveyed.

The vast majority of patients with hypertension had a low risk of CV events during 10 after years (<5%), including 80.9% of patients with CD and 78.6% of patients without CD (p>0.05 among groups). High risk of fatal events (5-9% by the SCORE scale) was 19.1% in the main group and 21.4% in comparison group respectively. Among healthy individuals, no high risk was observed – $p_{1-3}<0.01$ and $p_{2-3}<0.05$. Thus, the obtained data testify to the absence of significant differences relatively CVR by the SCORE scale between the studied groups of AH patients (p>0.05) and a higher incidence of high risk compared to healthy subjects (p<0.05).

In an in-depth neuropsychological study among patients with a controlled AH stage II, test batteries were used: MMSE (Mini-Mental State Examination) and Montreal Cognitive Assessment (MoCA) scales for the integral assessment of CF [15]. Of 157 patients included in the study, by MMSE method (n=97) mild non-demental CD (27-26 points) were revealed in 39 (40.2%) patients and moderate CD (25-24 points) – in 58 (59.8%). The mean score of severity of cognitive functions (CF) in the group of patients with hypertension was 25.10±0.11, which was 12.6% less than that of practically healthy subjects (28.71±0.21 points) in p<0.001. The integral score of CF in testing patients with hypertension (n=60) by the MoCA test was also low (24.37±0.06 points) and corresponded to the criteria of cognitive deficiency (CD) (less than 26 points).

In the course of CF study by FAB method [15], in 97 patients of the main group (AH with CD), in none of the cases diagnostically low rates - less than 12 points were obtained, which testified to pronounced frontal dysfunction. Most patients had normal points of frontal function (16-18 points) – 61 (62.9%). Other 36 (37.1%) patients received 15 points by this mehtod, which indicated that only a mild degree of frontal dysfunction was present.



a b

Distribution of patients with hypertension in terms of severity of CD, determined by MMSE (a) and MoCA (b) methods

Investigation of the level of attention in AH patients by the method of F.Ye. Rybakov [15] using the technique of counting balls in the sectors made it possible to investigate the degree of concentration of the excitatory process in the visual and motor analyzers. All AH patients with detected CD had disturbances in the concentration of the excitatory process in the visual and motor analyzers. Thus, only 2 patients (1.3%) fulfilled the task without errors up to the 5th sector (norm), 28 (17.8%) patients managed with the calculations up to the 4th sector, 65 (41.4%) - up to the 3d sector, 56 (35.7%) - up to the 2nd sector, 6 (3.8%) more patients aged 55 to 65 years could not perform the task without errors. Thus, the median value of the concentration of attention in AH patients before treatment was 3 (2-3).

A more in-depth study of the level of attention and sensorimotor reactions rate was carried out according to the method of Schulte Table [15]. The obtained data indicated a decrease in attention and sensorimotor reactions rate due to an increase in the timing of performing tasks in the five tables and the presence of errors in performing tasks, especially expressed in patients with AH and CD. Such patients were characterized by rapid fatigability, unevenness in performing task, the refusal of further exercise due to fatigue and inability to concentrate. The average time spent doing the task in patients of the main group throughout the study exceeded the data of patients in the comparison group by 1.3-1.6 times ($p<0.001$), and in practically healthy individuals – by 1.4-1.7 times ($p<0.001$). According to the results of the test by Schulte Table, the indicators of work efficiency, adaptability and mental stability were calculated and it was established that in the presence of CD in patients with hypertension, the performance indicators were significantly higher, and psychological stability – lower than that of patients in the comparison group and healthy individuals (from $p<0.05$ to $p<0.001$).

During investigation of arbitrary verbal memory by the method of A.R. Luria, [15] a significant decrease in the volume of direct reproduction, long-term memory and memory efficacy in all examined patients with hypertension with CD, as compared to patients with hypertension without CD and with healthy subjects ($p <0.001$) was revealed. Thus, the average number of words reproduced after the first presentation by patients in the main group (3.80±0.08) was 1.6 times less than in the comparison group (6.22±0.26; $p<0.001$), and 2.2 times less relative to practically healthy subjects (8.29±0.45; $p<0.001$). The volume of delayed reproduction (long-term memory) in patients with hypertension and CD was also less by 2 and 2.2 times than in groups without CP ($p<0.001$).

Thus, based on the findings of in-depth neuropsychological testing, it was concluded that in patients with AH stage II, CD not related to dementia are found in 32.22% of cases. Their characteristics at different levels of higher brain functions corresponded to all spheres of cognitive activity of a man, but the processes of neurodynamic nature (ability to focus, rate of psychomotor reactions) and verbal memory suffer mostly.

Reliable correlations between the state of CF, estimated by different neuropsychological methods and age of patients, duration of the disease, vegetative index (according to Wein questionnaire) were established. Thus, with an increase in the age of the subjects, the assessment of frontal function by FAB technique (rs= -0.23; p<0.05), the degree of concentration of attention by F.Ye. Rybakov (rs= -0.20; p<0.05), visual constructive skills by MoCA test (rs= -0.22; p<0.05) worsened. The long course of hypertension (more than 5 years) correlated with a decrease in the adaptability indicator by Schulte technique (rs= -0.17; p<0.05); the total score of CD by MoCA test (rs= -0.19; p<0.05) and its subscales: attention (rs= -0.29; p<0.01) and abstraction (rs= -0.24; p<0.05).

The presence of CD, even in controlled AH stage II reliably was associated with more frequent complaints of heavy headedness and headache – 78.3% vs. 60.7% in patients with hypertension without CD (rs=+0.15; OR=2.34 (95% CI 1.01-5.47); p<0.05), weakness, irritability and increased fatigue – 73.2% vs. 25.0% (rs=+0.37; OR=8.21 (95% CI 3.26-20.73) p<0.001), memory impairment due to reduced productivity of attention processes and memory retention in preserved long-term memory – 62.4% vs. 28.6% (r=+0.25; OR=4.15 (95% CI 1.72-10.02); p<0.001), sleep disurder – 76.4% vs 39.3% (rs=+0.29; OR=5.01 (95% CI 2.16-11.65), p<0.001).

The obtained data coincide with the known that CD are often accompanied by symptoms of anxiety, depression and neurotic disorders [1, 4, 7, 9]. As noted above, more than 70% of patients with controlled AH and CD complained of increased irritability and sleep disorders; one third of patients (36.3%) noted a decline in interest in the world around. Therefore, an important task was to study levels of anxiety using the hospital scale HADS, as well as indicators of personal and reactive anxiety by Spielberger-Khanin technique [15]. Study subjects of all groups did not have an existent depression, according to the HADS test, the number of scores received was lower than 7. At the same time every third patient with hypertension, regardless of CD presence (61-33.0%), had clinically expressed anxiety (11 points and higher by the HADS anxiety scale). The average anxiety level in the group of patients with hypertension and CD was 9.32±0.25 points, in the comparison group - 8.96±0.43 points (p>0.05). A borderline with normal anxiety level in practically healthy persons was also found to be 7.50±0.30 points, however, it was significantly lower than the corresponding indices in patients with hypertension (p<0.001 and p<0.05). Consequently, increased anxiety correlates with the presence of hypertension (rs=+0.30; p<0.001) and practically does not depend on the state of CF in such patients (rs=+0,09; p>0.05).

Studies on the features of anxiety by Spielberger-Khanin's technique revealed increased levels of reactive and personality anxiety in most of the study subjects. The majority of patients with hypertension with CD (64 individuals – 66.0%) had a high level of personal anxiety, while in one third of patients (32.0%) the level of anxiety was classified as moderate and in only 2 patients the indices did not exceed the norm (up to 30 points). Similar tendencies were noted in the comparison group: 53.6% of patients with hypertension without a CD had a high level of personal anxiety, 39.3% – moderate, in 2 cases - low (p>0.05, in comparison with the main group). The severity of reactive anxiety met the criteria of high level in almost half of AH patients (49.5% and 46.4%) and only in 17.8% of practically healthy subjects (p<0.01 and p<0.05).

Thus, the data obtained also allow us to conclude that in the majority of patients with hypertension an increased anxiety level, especially personality was revealed, and this was not associated with the presence or absence of CD.

At the same time, the severity of anxiety in hypertension patients significantly correlated with the state of the autonomic nervous system by Wayne questionnaire, and with certain characteristics of cognitive activity, so with an increased level of anxiety, estimated by HADS procedure it correlated with a long course of hypertension (rs=+0.15; p<0.05). High vegetative index directly correlated with all the investigated indicators of anxiety: for levels of anxiety by HADS – rs=+0.26; p<0.001; for personal and reactive anxiety – rs=+0.28; p<0.001 and rs=+0.31; p<0.001. A high degree of personal anxiety adversely affected the increase in time for the tasks performed by Schulte Table (rs=+0.24; p<0.05), the general indicator of work efficiency (rs=+0.16; p<0.05) and mental stability (rs= -0.21; p<0.05).

It should be noted that the obtained data on the relationship between the course of hypertension in middle aged patients and the state of CF are consistent with the results of other studies [6, 13, 12], which emphasizes the relevance of the problem of timely diagnosis and correction of CD in hypertension.

The analysis of the data showed that in patients with hypertension and CD there was a significant (p<0.001) decrease in the mean indicators of QL by all scales compared with healthy people, including the scale of role emotional functioning – by 66.0 scores (s.), physical functioning – by 55.0 s., role

physical functioning – by 50.0 s., pain sensation – by 41.5 s., mental and general health – by 39.0 s. and 35.0 s., vital force – by 32.5 s., social functioning – by 24.5 s. The subjective scorings of QL of patients in the comparison group (hypertension without CD) are also significantly differ (from $p<0.01$ to $p<0.001$) from practically healthy people by almost all scales (difference from 12.5 s. by the scale of vital force to 50,0 s. by role emotional functioning), except general and mental health ($p>0.05$) and social functioning ($p>0,05$). At the same time, they are significantly above the score in patients with hypertension and CD – from 15.0 s. by the scale of pain ($p<0.05$) to 34.0 s. by the score of mental health ($p<0.001$), except role physical functioning ($p>0.05$).

According to the results of the correlation analysis, the direct correlation between the deterioration of practically all components of QL and CF disturbances assessed by different methods was also confirmed. Therewith, the closest correlations were established between the MoCA scale and assessment of physical condition ($rs= + 0.65$; $p<0.001$), mental health ($rs= + 0.60$; $p<0.001$), restrict vital ($rs= + 0.33$; $p<0.001$) and social activity ($rs= + 0.35$; $p<0.001$). The reverse correlation was established between a high level of personal anxiety and a subjective assessment by a person of his/her psycho-emotional state ($rs= -0,30$; $p<0.001$) and life energy ($rs= -0.21$; $p<0.05$). Thus, the data obtained coincide with the known ones as for development and progression of cognitive and psycho-emotional disorders which deteriorate QL of patients with hypertension and reduce their social adaptation [5, 6, 10, 12]. From the above one can draw a conclusion that CD significantly affect and reduce not only medical but also social components of QL even in patients with controlled hypertension and low CVR.

CONCLUSIONS

1. In working patients with controlled AH stage II non-dementional cognitive impairment was detected in 32.22% of cases. Their characteristics at different levels of higher cerebral functions corresponded to all spheres of cognitive activity of a man, but processes of neurodynamic nature (ability to focus, rate of psychomotor reactions) and verbal memory suffered most of all.
2. In the majority of patients with AH stage II an increased level of anxiety especially personal was revealed, and this is not due to the presence or absence of CD.
3. In patients with controlled AH stage II with non-dementional cognitive impairment, there was a significant decrease in the mean values of QL by all scales in comparison with healthy subjects (difference from 24.5 to 66.0 points; $p<0.001$) and in patients without cognitive impairment (difference from 15.0 to 34.0 points; $p<0.05$, except for the role physical functioning), which indicated a significant impact of cognitive disorders not only on medical but also on the social components of QL, even in patients with target blood pressure levels and low CVR.
4. According to the results of correlation analysis, a reliable direct correlation between the deterioration of practically all components of quality of life and disorders of cognitive functions assessed by different neuropsychological techniques has been confirmed. Therewith, the closest correlations were established between the results of cognitive disorders by MoCA scale and the assessment of physical ($rs=+0.65$; $p<0.001$), mental health ($rs=+0.60$, $p<0.001$), restrict vital ($rs=+0.33$; $p<0.001$) and social activity ($rs=+0.35$; $p<0.001$). The reverse probable moderate correlation was established between a high level of personal anxiety and a subjective assessment by a person of his/her psycho-emotional state ($rs= -0,30$; $p<0,001$) and life energy ($rs= -0.21$; $p<0.05$). The quality of life of patients with hypertension without CD is also significantly different (from $p<0.01$ to $p<0.001$) from practically healthy subjects by almost all scales except general and mental health ($p>0.05$) and social functioning ($p>0.05$), but they were significantly higher than scores in patients with AH and cognitive impairment.

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