

CHANGES OF COGNITIVE FUNCTION IN PATIENTS WITH HYPERTENSION WITH CONCOMITANT DIABETES MELLITUS TYPE 2

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Relevance. Till now there is no clear clinical trial understanding of the relationship between hypertension (AH) and the patient's cognitive function.

Objective: investigation of changes in cognitive function in patients with hypertension with concomitant type 2 diabetes mellitus (DM2).

Materials and methods. 215 people were examined: Group I (n = 131) – stage II hypertensive disease (HD); Group II (n = 46) – HD, combined with diabetes mellitus2; Group III, control (n = 38) – without a diagnosis of HD and diabetes mellitus2. All examined blood pressure (BP), echocardiogram. Clinical complaints, anamnestic data, and neuropsychiatric testing data were used to diagnose moderate cognitive impairment (MCI). Used modified diagnostic criteria J. Touchon, R. Petersen. To assess cognitive function used: Short scale of assessment of mental state (Mini-Mental State Examination - MMSE); Frontal Assessment Battery (FAB); clock drawing test; test for literal and categorical associations; Schulte tables; the Global Deterioration Scale (GDS) and the Clinical Dementia Rating (CDR).

Result. In patients with HD, the most significant risk factors for moderate cognitive impairment are hypercholesterolemia and overweight (with OR 1.8), obesity (OR 1.6), the presence of concomitant diabetes mellitus2, which, especially in overweight, significantly impairs cognitive function (OR 2.56). Deterioration of cognitive function correlates with the duration of HD, cholesterol levels. Concomitant diabetes mellitus2 in patients with HD creates a statistically significant additional negative effect on the results of cognitive function. In patients with HD with a distorted daily blood pressure profile, the neurodynamic component of cognitive function is first of all affected - conceptualization, repetition, reaction of choice. The relationship between cognitive function and daily monitoring of blood pressure often have a U-shaped relationship, where the maximum indicators of cognitive function are at the level of the optimal recommended blood pressure figures (130-139 mm Hg for SBP, and 75-85 mm Hg for DBP, and the daily index within 10%).

Conclusions. There is a dependence of changes in cognitive function on the presence of risk factors and signs of subclinical damage to target organs. The nonlinear U-shaped character of the relationship between the average daily, average night and average daily blood pressure and the results of screening tests and scales for assessing cognitive function is shown.

Key words: arterial hypertension, cognitive functions, type 2 diabetes mellitus

Relevance. Hypertension (AH) is an urgent problem among the working age population and the most important risk factor for acute cerebrovascular disorders, as well as a harbinger of Alzheimer's disease, vascular dementia and other cognitive disorders [1]. The relationship between cognitive impairment, including dementia of various etiologies, and blood pressure (BP) and the need for adequate antihypertensive therapy to prevent them is being investigated. To date, there is no clinical trial based clear understanding of the relationship between blood pressure and cognitive function [2, 3, 4]. While most long-term studies have shown elevated blood pressure before occurrence of Alzheimer's disease or vascular dementia and other cognitive impairment, most crossover and short-term studies have shown an association between low blood pressure and dementia or no association with blood pressure. and cognitive impairment. There

are no data on the effect of antihypertensive therapy on cognitive function, and studies on this issue are few and contradictory [5].

Thus, the identification of general patterns of formation of cognitive disorders in patients with hypertension and assessment of the possibility of their correction on the background of antihypertensive therapy is an urgent interdisciplinary medical problem.

Objective: investigation of changes in cognitive function in patients with hypertension with concomitant type 2 diabetes mellitus (DM2).

MATERIALS AND METHODS

A total of 215 people were examined. Of these – 177 patients with hypertension (HD) and 38 people without HD. Patients with HD were divided into 2 groups: Group I (n = 131) – HD stage II; Group II (n = 46) – HD,

combined with diabetes mellitus². The duration of HD in groups I and II ranged from 6 months to 37 years. Group III (or control group) (n = 38) included patients with mild somatic pathology without a diagnosis of HD and diabetes mellitus² (according to the results of clinical, laboratory and instrumental examinations), comparable in age, sex, level of education with groups I and II.

The mean age of patients was 50.4 ± 11.7 years.

According to the purpose of the study, patients were further divided into subgroups:

In group I (stage II HD), 20 patients (15.3%) had grade 1 HD, and 111 patients (84.7%) had grade 2 HD;

In group II (stage II HD + diabetes 2) 6 patients (13%) had 1 degree of HD, and 40 patients (87%) – 2 degree of HD;

Within 24 hours, all patients underwent blood pressure monitoring, echocardiographic examination of the heart, for the diagnosis of moderate cognitive impairment (MCI) used clinical complaints, anamnestic data and neuropsychiatric testing data. Syndromic diagnosis establishes the fact of reduced cognitive abilities in comparison with the individual norm with an assessment of the severity of cognitive impairment. The starting point in the syndromic diagnosis of cognitive impairment in most cases are complaints of memory loss or mental retardation [6].

When diagnosing «MCI syndrome» used modified diagnostic criteria J. Touchon, R. Petersen, 2004 [7, 8].

Commonly used for clinical trials and validated tests and scales were used to assess cognitive function, namely: The Mini-Mental State Examination (MMSE) proposed by M.F. Folstein, S.E. Folstein, P.R. Hugh, 1975; Frontal Assessment Battery (FAB), proposed by B. Dubois, 1999; clock drawing test; test for literal and categorical associations; Schulte tables; the Global Deterioration Scale (GDS) and the Clinical Dementia Rating (CDR).

RESULTS AND DISCUSSION

Patients were interviewed for complaints of memory, attention, orientation, memory and thinking speed impairment. Patients were asked to self-assess these indicators of cognitive function on a five-point scale from 1 to 5 points, where 1 point – a significant deterioration, and 5 points – the absence of any complaints. According to the results of data processing, in the group of patients with HD without diabetes mellitus on all complaints is dominated by 4 points, followed by the frequency of presentation – 5 points and 3 points. At the same time, in the group of patients with HD with concomitant diabetes mellitus, the predominant indicator is 3 points, followed by the frequency of presentation – 4 and 2 points for the vast majority of indicators.

It was found that in patients with HD the most common complaints were of memory impairment (22.4% of patients rated the function on 3 points, 44.7% – 4 points), 27.6% of patients did not complain of memory impairment at all, thus, complaints of memory impairment, regardless of severity, were found in 72.4% of patients.

In second place were the difficulty of mentioning and orientation impairment (19.7% of respondents on both indicators rated the condition at 3 points), in third place in the frequency of presentation were complaints of decreased speed of thinking (17.1% – 3 points, 39.5% – 4 points), there were no complaints of impaired thinking (5 points) in 88% of patients (Fig. 1).

In the second group of patients – patients with HD and concomitant diabetes mellitus 2 – the frequency of complaints was as follows (Fig. 2).

The lowest score was obtained for the deterioration of the function of thinking speed, 20% of patients rated the function at 2 points, 42.8% – at 3 points, only 17.1% had no complaints (5 points). Complaints of memory impairment were rated 3.1% of patients, 42.8% of patients rated the speed of thinking at 3 points, and only 14.3% of patients did not complain of memory impairment. The least affected functions in patients of the second group were the difficulty of mentioning and impaired orientation – 42.8% on both indicators received 3 points.

In the control group, patients had no complaints of memory impairment, speed of thinking, orientation, attention and difficulty remembering, a small proportion of patients had a score of 4 points.

Among the examined patients in the first study group, the criteria of the syndrome of moderate cognitive impairment were found in 23 patients (17.56%), in the second group of patients with HD and concomitant diabetes mellitus – in 26 patients (56.52%), at the same time in the group control under these criteria fell 1 person, which is 2.63%. The obtained data are comparable with the literature sources of persons of the appropriate age category and the presence of relevant risk factors.

Thus, cognitive function in general in patients with HD is statistically significantly reduced compared with the control group, which is representative of the main parameters. Also, a comparison of groups I and II revealed statistically significantly worse results in group II for most screening tests and scales, except for the sample for literal and categorical associations.

Consider the influence of different risk factors on the cognitive function of patients with HD and in patients with HD and concomitant diabetes mellitus² (Table 1). Risk factors whose effect on cognitive function we studied include, according to the recommendations of the European Society of Cardiology: obesity (BMI ≥ 30 kg / m²), overweight (BMI ≥ 25 kg / m²), smoking, hypercholesterolemia (more than 4.9 mmol / l), left ventricular hypertrophy (LV) (for men IMMLV > 115 g / m², for women IMMLV > 95 g / m²). To analyze the risk and chance of moderate cognitive impairment (MCI) in the presence of various risk factors, we use the method of bipolar tables.

Notes: SMCI – syndrome of moderate cognitive impairment, HD- hypertension, CD2 – type 2 diabetes, LV – left ventricle

Among all risk factors in the examined patients, LV hypertrophy was most common in both men and

women – 81% and 80%, respectively. In second place in terms of frequency among risk factors was overweight – 78%, hypercholesterolemia – 71%.

Smoking and obesity among patients in the study population were observed in 34% and 35%, respectively (Fig. 3).

In addition, type 2 diabetes, as a recognized risk factor, creates an additional negative impact on cognitive function in combination with HD. There is a cumulative effect, which leads to significantly worse indicators of cognitive function testing compared with patients with HD without diabetes, the results of which are also significantly

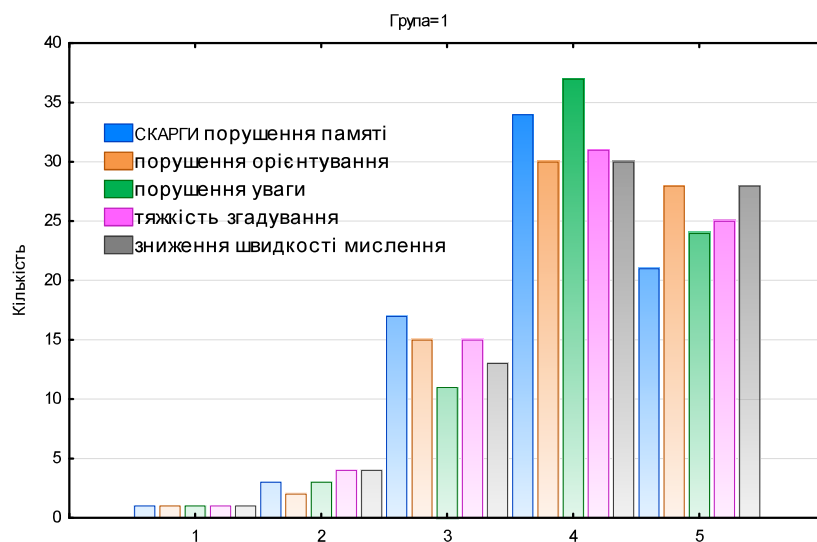


Fig. 1. Frequency of complaints of patients with cognitive impairment in group I (HD)

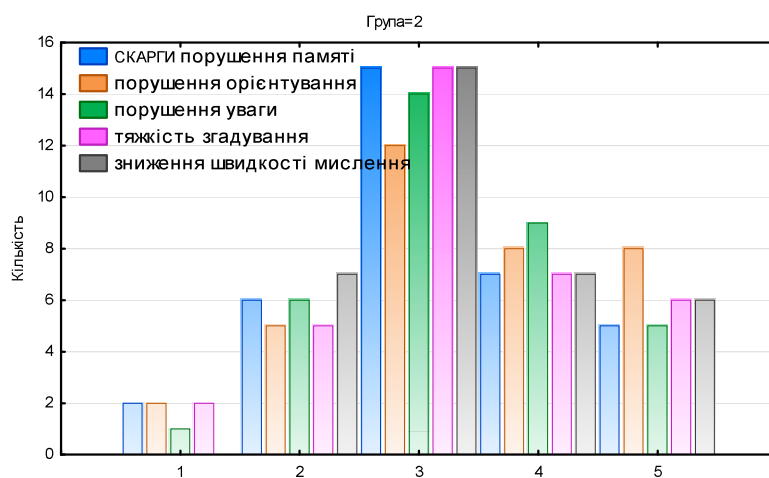


Fig. 2. Frequency of complaints of patients with cognitive impairment in group II (HD + CD2)

Table 1

Distribution of risk factors for the development of moderate cognitive impairment in patients with hypertension

Risk factor and its presence		group 1 (HD), n=131		group 2 (HD+DM2), n=46	
		SMCI	No SMCI	SMCI	No SMCI
Smoking	yes	4	48	3	5
	no	19	60	23	15
Obesity & overweight (BMI≥25kg / m2)	yes	16	84	23	15
	no	7	24	3	5
Obesity (BMI≥30kg / m2)	yes	10	34	17	1
	no	13	74	9	19
Hypercholesterolemia	yes	21	76	9	10
	no	4	30	5	8
LV hypertrophy (male)	yes	18	55	6	14
	no	1	19	1	1
LV hypertrophy (female)	yes	7	15	4	2
	no	4	3	0	0

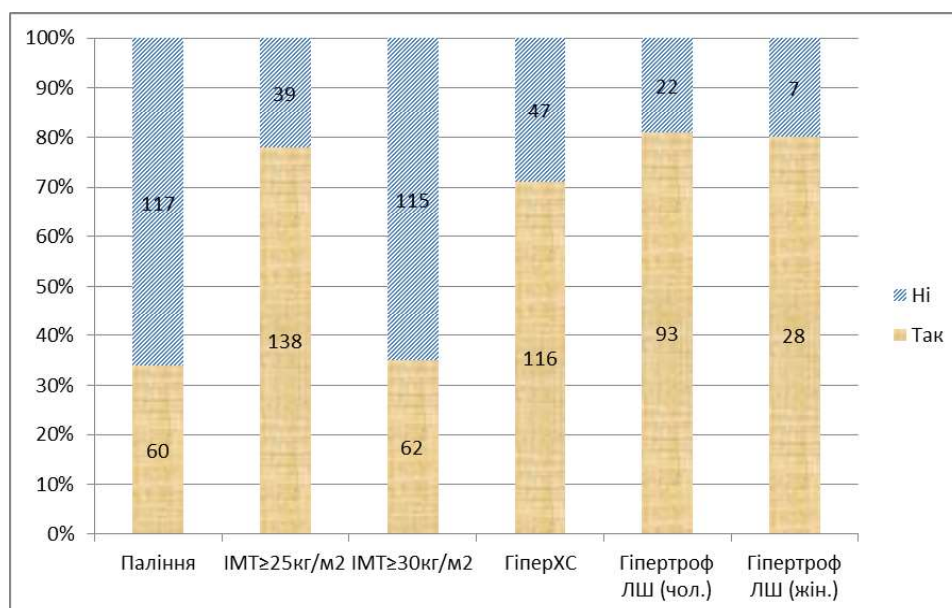


Fig. 3. Distribution of study patients depending on the presence of risk factors

lower when comparing the mean values (or mode and median) compared with the control group.

Among 131 patients of the first group, 50 people had a normal level of blood pressure at night at 10-20%, which is 38.3% of the total number of patients, 2 patients had a daily profile of the type of over-dipper with a daily index of more than 20% (1, 7%). 68 patients had an insufficient level of nocturnal blood pressure lowering – a daily profile of the non-dipper type (51.7% of the total). And 11 (8.3%) patients had a night picker profile – an increase in night blood pressure above the daytime, daily index less than 0. The distribution of patients by groups is shown in Figures 2-5. That is, the vast majority of patients have a daily profile with insufficient nocturnal decrease of blood pressure.

Statistically significant groups differ from each other in the MMSE test (Kruskal-Wallis test: $H = 19.38415$, $N = 91$, $p = 0.0002$); when multiple comparison of MMSE test results among subgroups with different profiles of daily blood pressure was found that in the group night picker ($p = 0.059$), non-dipper ($p = 0.0007$) and normal dipper ($p = 0.005$) the results are different from the control group (normotonics), herewith a statistically significant difference between the groups night picker, non-dipper and normal dipper is absent (Fig. 4).

The analysis of the polynomial scatter plot showed that in patients with HD the relationship between cognitive function and daily monitoring is not linear, and therefore is not detected in routine comparative statistical processing between groups.

Thus, a U-shaped relationship was found between the average daily SBP and the MMSE test result (Fig. 5).

Analyzing the diagram, we can conclude that the best range of blood pressure, in which the maximum values

are observed when testing cognitive function, are in the range of 130-140 mm Hg systolic blood pressure. The average daily SBP below 120 mm Hg is associated with a decrease in MMSE scores. A similar, but steeper, «tail» of the curve found at SBP above 140 mm Hg. – with the growth of the average daily, the effectiveness of MMSE decreases extremely rapidly.

A similar effect observed when analyzing the results of the MMSE scale and the average daily DBP. Optimal for satisfactory cognitive function is the average daily DBP at the level of 75-85 mm Hg, when the indicators of cognitive function are maximum in the studied category of patients (Fig. 6, fig. 7)

Probably, the basis of these disorders and phenomena is a violation of hemodynamics and trophism of the brain, especially at night, accompanied by a decrease in cerebral blood flow [9].

CONCLUSIONS

1. In patients with HD, the most significant risk factors for moderate cognitive impairment are hypercholesterolemia and overweight (with OR 1.8), obesity (OR 1.6), the presence of concomitant type 2 diabetes, which, especially in conditions of overweight, significantly impairs cognitive function (OR 2,56).

2. Cognitive function in patients with HD is statistically significantly lower according to the results of neuropsychological tests and scales compared to the representative control group. Deterioration of cognitive function correlates with the duration of HD, cholesterol levels.

3. Concomitant type 2 diabetes mellitus in patients with HD creates a statistically significant additional negative effect on the results of cognitive function both in comparison with the comparable control group and in

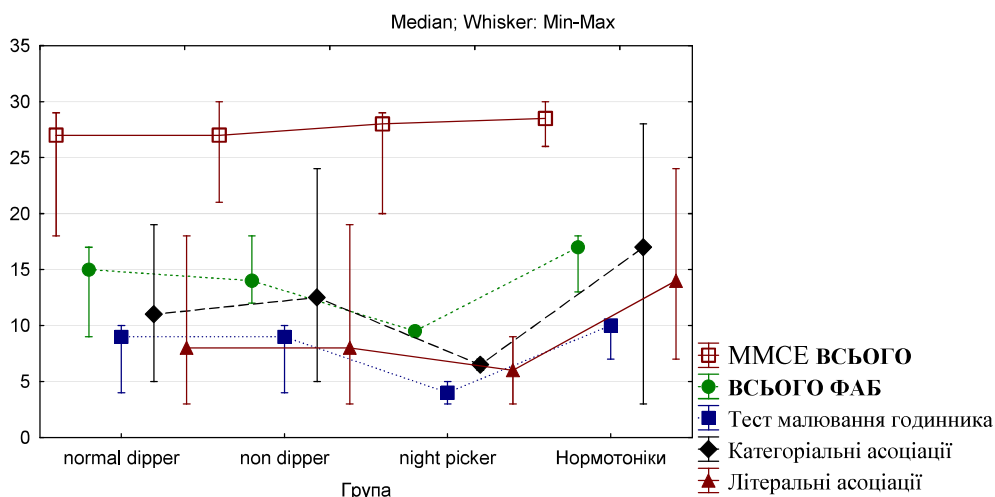


Fig. 4. Median and minimum-maximum values of tests and scales in groups of patients by type of daily profile

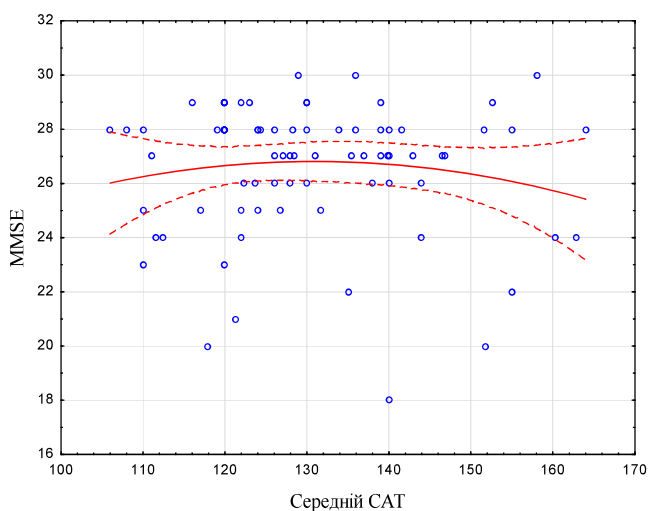


Fig. 5. Diagram of scattering of average daily CAT and scores based on the MMSE scale

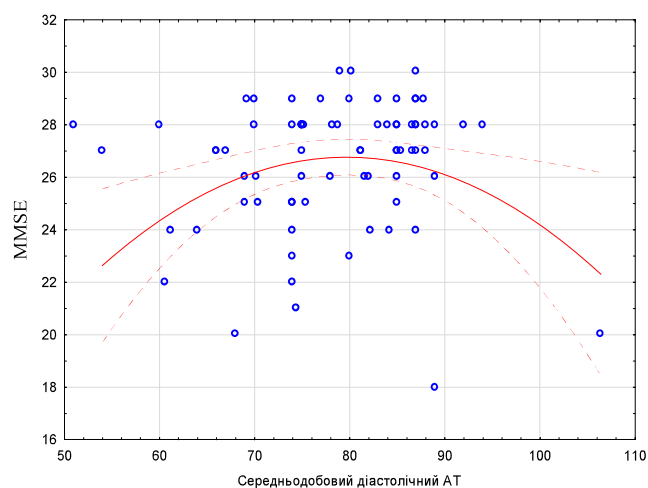


Fig. 6. Diagram of scattering of average daily DBP and scores according to the MMSE scale

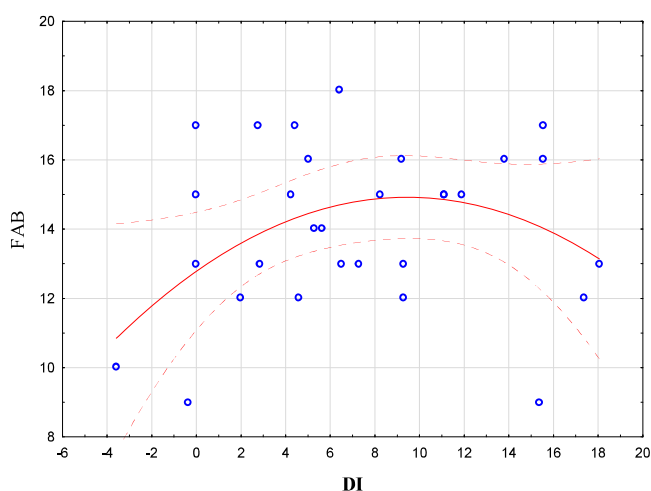


Fig. 7. Diagram of scattering of the daily index of blood pressure at night and scores on the FAB scale

comparison with the group of patients with HD without concomitant type 2 diabetes. Cognitive impairment in both subjects groups is mediated through neurodynamic subdomains and with signs of damage to the deep ganglia of the cerebral cortex.

4. In patients with HD with a distorted daily blood pressure profile, the neurodynamic component of cognitive function is first of all affected – conceptualization, repetition, reaction of choice. In addition, the relationship between cognitive function and daily monitoring of blood pressure often have a U-shaped relationship, where the maximum indicators of cognitive function are at the level of the optimal recommended blood pressure, which is 130-139 mm Hg for SBP, and 75- 85 mm Hg for DBP and daily index within 10%.

5. In patients with HD there is a U-shaped relationship between the mean values of average daily SBP and DBP, daily index and the results of screening tests and scales

for the diagnosis of cognitive impairment, with the maximum cognitive result in patients with HD observed at average SBP values in the range of 130-139 mm Hg and DBP 75-85 mm Hg at the level of night blood pressure decrease by 8-10%.

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ЗМІНИ КОГНІТИВНОЇ ФУНКЦІЇ У ХВОРИХ НА ГІПЕРТЕНЗІЮ З СУПУТНІМ ЦУКРОВИМ ДІАБЕТОМ ТИПУ 2

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Актуальність. До сьогодні не існує чітко доведеного клінічними дослідженнями розуміння взаємозв'язку рівня артеріальної гіпертензії (АГ) та стану когнітивної функції пацієнта.

Ціль: дослідити зміни когнітивної функції у хворих на гіпертензію з супутнім цукровим діабетом типу 2 (ЦД2).

Матеріали та методи. Обстежено 215 осіб: I група (n=131) – гіпертензивна хвороба (ГХ) II стадії; II група (n=46) – ГХ, поєднана з ЦД2; III група, контролю (n=38) – без встановленого діагнозу ГХ та ЦД2. Усім досліджували артеріальний тиск (АТ), ехокардіограму. Для діагностики синдрому помірних когнітивних порушень (ПКП) використовували клінічні скарги, анамнестичні дані та дані нейропсихічного тестування. Користувалися модифікованими діагностичними критеріями J. Touchon, R. Petersen. Для оцінки когнітивної функції використані: Коротка шкала оцінки психічного стану (Mini-Mental State Examination – MMSE); Батарея лобної дисфункції (Frontal Assessment Battery – FAB); тест малювання годинника; тест на літеральні та категоріальні асоціації; таблиці Шульте; шкала глобального погіршення (Global Deterioration Scale – GDS) і клінічна рейтингова шкала деменції (Clinical Dementia Rating – CDR).

Результат. У хворих на ГХ найбільш значущими факторами ризику помірних когнітивних порушень встановлено гіперхолестеринемію та надмірну масу тіла (з OR 1.8), ожиріння (OR 1,6), наявність супутнього ЦД2, який особливо за умов надмірної маси тіла, значно погіршує когнітивні функції (OR 2,56). Погіршення результатів когнітивних функцій корелює з тривалістю ГХ, рівнем холестерину. Супутній ЦД2 у пацієнтів із ГХ створює статистично значимий додатковий негативний вплив на результати когнітивної функції. У пацієнтів із ГХ зі спотвореним добовим профілем АТ в першу чергу вражається нейроди-

намічна складова когнітивної функції – концептуалізація, повторення, реакція вибору. Взаємозв'язок когнітивної функції та показників добового моніторингу АТ найчастіше мають U-подібну залежність, де максимальні показники когнітивної функції знаходяться на рівні оптимальних рекомендованих цифр артеріального тиску (130-139 мм.рт.ст для САТ, та 75-85 мм.рт.ст. для ДАТ, та добовий індекс в межах 10%).

Висновки. Існує залежність змін когнітивної функції від наявності факторів ризику та ознак субклінічного ураження органів-мішеней. Показаний нелінійний U-подібний характер залежності між середньодобовим, середньонічним та середньоденним АТ та результатами скринінгових тестів та шкал для оцінки когнітивної функції.

Ключові слова: артеріальна гіпертензія, когнітивні функції, цукровий діабет 2 типу

ИЗМЕНЕНИЯ КОГНИТИВНОЙ ФУНКЦИИ У БОЛЬНЫХ С ГИПЕРТОНИЧЕСКОЙ БОЛЕЗНЬЮ С СОПУТСТВУЮЩИМ САХАРНЫМ ДИАБЕТОМ 2 ТИПА

Нетяженко В.З., Мальчевская Т.И., Пленова О.Н., Потаскалова В.С., Таранчук В.В.

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Актуальность. До сих пор не существует четко доказанного клиническими исследованиями понимания взаимосвязи уровня артериальной гипертензии (АГ) и состояния когнитивной функции пациента.

Цель: исследовать изменения когнитивной функции у больных с гипертонической болезнью с сопутствующим сахарным диабетом 2 типа (СД2).

Материалы и методы. Обследовано 215 человек: I группа (n=131) – гипертоническая болезнь (ГБ) II стадии; II группа (n=46) – ГБ, с сопутствующим СД2; III группа, контроль (n = 38) – без установленного диагноза ГБ и СД2. Всем исследовали артериальное давление (АД), эхокардиограмму. Для диагностики синдрома умеренных когнитивных нарушений (УКН) использовали клинические жалобы, анамнестические данные и данные нейропсихического тестирования. Пользовались модифицированными диагностическими критериями J. Touchon, R. Petersen. Для оценки когнитивной функции использованы: Краткая шкала оценки психического состояния (Mini-Mental State Examination – MMSE); Батарея лобной дисфункции (Frontal Assessment Battery – FAB); тест рисования часов; тест на литеральные и категориальные ассоциации; таблицы Шульце; шкала глобального ухудшения (Global Deterioration Scale – GDS) и клиническая рейтинговая шкала деменции (Clinical Dementia Rating - CDR).

Результат. У больных ГБ наиболее значимыми факторами риска умеренных когнитивных нарушений установлено гиперхолестеринемию и избыточную массу тела (с OR 1,8), ожирение (OR 1,6), наличие сопутствующего СД2, который, особенно в условиях избыточной массы тела, значительно ухудшает когнитивные функции (OR 2,56). Ухудшение результатов когнитивных функций коррелирует с продолжительностью ГБ, уровнем холестерина. Сопутствующий СД2 у пациентов с ГБ создает статистически значимое дополнительное негативное влияние на результаты когнитивной функции. У пациентов с ГБ с искаженным суточным профилем АД в первую очередь поражается нейродинамическая составляющая когнитивной функции – концептуализация, повторение, реакция выбора. Взаимосвязь показателей когнитивной функции и показателей суточного мониторинга АД чаще всего имеют U-образную зависимость, где максимальные показатели когнитивной функции находятся на уровне оптимальных рекомендованных цифр артериального давления (130-139 мм.рт.ст САД и 75-85 мм.рт.ст. для ДАД, и суточный индекс в пределах 10%).

Выводы. Существует зависимость изменений когнитивной функции от наличия факторов риска и признаков субклинического поражения органов-мишеней. Показан нелінійний U-образний характер залежності між середнесуточним, середньонічним і середньоденним АД і результатами скринінгових тестів і шкал для оцінки когнітивної функції.

Ключевые слова: артериальная гипертензия, когнитивные функции, сахарный диабет 2 типа.