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Effect of Nitrendipine and Amlodipine on Cognitive Functions of Patients with Arterial Hypertension

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Abstract

Background: Arterial hypertension (AH) is one of the main factors causing a high risk of cardiovascular complications and mortality. The existence of a relationship between high blood pressure (BP) and the risk of developing central nervous system pathology, primarily stroke, and cognitive impairment, has been shown. The purpose of this study was a comparative assessment of the effect of 12-month antihypertensive therapy (AHT) with the inclusion of nitrendipine (NIT) or amlodipine (AML) on cognitive functions (CF) in hypertensive patients.

Methods and Results: The study included 111 patients of both genders aged 30-75 years with AH Grades 1-3 (ESC/ESH, 2018). All patients underwent the following examinations: assessment of traditional risk factors, physical examination, clinical and biochemical laboratory methods, 12-lead ECG, echocardiography, pulse contour analysis, and 24-hour ambulatory blood pressure monitoring, neuropsychological tests (Mini-Cog test, Montreal Cognitive Assessment (MoCA) test, Hospital Anxiety and Depression Scale (HADS), and self-assessment questionnaire for memory, attention, thinking, ability to cope with one's affairs, and ability to make decisions). After the screening stage, all patients were discontinued from previous therapy and assigned to the 2 regimes of AHT. Group 1 included 58 AH patients who received NIT as monotherapy or as part of combination AHT; Group 2 included 53 patients who received AML as monotherapy or as part of combination AHT. Correlation analysis between the parameters of diurnal blood pressure profile and the MoCA test revealed a weak but statistically significant negative correlation between the total MoCA score and the average 24-h systolic BP (r_s=-0.33, *P*=0.015). In addition, there was a weak but statistically significant negative correlation between the total MoCA score and the daytime systolic BP variability and daytime diastolic BP variability (r_s=-0.40 and r_s=-0.35, respectively, *P*=0.000 in both cases). A weak but statistically significant negative correlation was found between the total Mini-Cog score and pulse wave velocity and central pulse pressure (r_s=-0.24, *P*=0.01 and rs=-0.27, *P*=0.007, respectively). Analysis of the office BP indicators showed high antihypertensive efficacy of 12-month therapy in both groups, regardless of the therapy regimens.

A comparative analysis of the effect of AHT with the inclusion of NIT or AML on CF in AH patients showed the advantages of combined AHT with the inclusion of NIT. Amlodipine treatment did not significantly affect any test score. Thus, in Group 1, after 12 months of therapy, there was an increase in the total Mini-Cog score from 3.8±1.08 points to 4.55±0.75 points (*P*<0.001), while in Group 2, there was a non-significant decrease in this score from 4.26±0.98 points to 3.92±0.95 points (*P*>0.05). There was also an increase in the total MoCA score in Group 1 from 23.3±2.8 points to 25.08±2.6 points (*P*<0.001), while in Group 2, there was a non-significant decrease in this score from 24.06±2.73 points to 23.07±2.7 points (*P*>0.05). It should be noted that only in Group 1 did we find a significant improvement in CF, such as abstraction, delayed recall, memory, and attention, as well as a significant improvement in work-coping and decision-making. In Group 1, the HADS Depression score decreased from 4.6±3.7 points to 3.32±2.95 points (*P*<0.05), HADS Anxiety score decreased from 7.01±5.37 points to 4.95±3.75 points (*P*<0.02). At the same time, in Group 2, in contrast, the HADS Depression score and the HADS Anxiety score did not significantly change.

Conclusion: A weak but statistically significant negative correlation was found between the total MoCA score and the daytime SBP/DBP variability in AH patients. A weak but statistically significant negative correlation was found between the total Mini-Cog score and pulse wave velocity and central pulse pressure. A pronounced antihypertensive efficacy of 12-month combination therapy was noted, with the inclusion of both NIT and AML. The NIT-based treatment contributed to a significant increase in the total Mini-Cog score and the total MoCA score and a substantial improvement in CF. Abstraction, delayed recall, memory, attention, work-coping, and decision-making significantly improved, compared to AML-based treatment. The presented data allow a differentiated approach to tactics for treating AH patients with severe cognitive impairment.(**International Journal of Biomedicine. 2023;13(2):217-223.**)

Keywords: arterial hypertension • cognitive impairment • amlodipine • nitrendipine

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Abbreviations

AH, arterial hypertension; **AHM**, antihypertensive medication; **AHT**, antihypertensive therapy; **ACEI**, angiotensin-converting enzyme inhibitor; **ARB**, angiotensin receptor blocker; **AP**, augmentation pressure; **AIx**, augmentation index; **BP**, blood pressure; **BMI**, body mass index; **CCBs**, calcium channel blockers; **CF**, cognitive functions; **CIMT**, carotid intima-media thickness; **DBP**, diastolic BP; **DBPP**, diurnal blood pressure profile; **HADS**, Hospital Anxiety and Depression Scale; **LVH**, left ventricular hypertrophy; **MoCA**, Montreal Cognitive Assessment; **PPc**, central pulse pressure; **PP**, pulse pressure; **PWV**, pulse wave velocity; **SBP**, systolic BP; **TD**, thiazide diuretic.

Introduction

Arterial hypertension (AH) is one of the main factors causing a high risk of cardiovascular complications and mortality. Overall, according to ESH/ESC data (2018), the prevalence of hypertension is in the range of 30%-45% of the general population, with a sharp increase with age. In people over 65, AH is detected in 30%-50% of cases. According to ESH/ESC (2018), 76% of patients with hypertension are at risk of dying within 10 years.[1] The existence of a relationship between high blood pressure (BP) and the risk of developing central nervous system pathology, primarily stroke, and cognitive impairment, has been shown.[2] Cerebral complications of hypertension occur the earliest, dominate, and make the greatest contribution to the structure of mortality associated with hypertension.

Numerous studies have found a relationship between taking antihypertensive medication (AHM) and the state of cognitive function, which confirms the positive effect of antihypertensive therapy (AHT) on slowing the progression of cognitive impairment.[3-6]

An analysis of data from a number of published studies has demonstrated the relationship between treatment with calcium channel blockers (CCBs) and less cognitive impairment in patients, compared with the use of other antihypertensive medications (AHMs).[6-8] However, when analyzing the results of most observational studies, the type of CCB prescribed was not taken into account, although some of the studies show the benefits of dihydropyridine derivatives.[9] Animal studies have demonstrated that dihydropyridine CCBs can influence the production and clearance of amyloid in the brain (the pathological substrate of Alzheimer's disease). Another possible mechanism for the effect of CCB therapy on cognitive function is the protection of neurons from the influx of excess calcium ions, which can trigger apoptosis.[6,10,11] In a number of experimental studies, the above positive effects were observed with the use of nitrendipine, nicardipine, lercanidipine, nimodipine, and some other rarely used CCBs.[10-12]

A special place among the drugs of this class is occupied by nitrendipine, which, to a greater extent than other CCBs (nilvadipine, nimodipine, nicardipine and lercanidipine), has the ability to block the formation of beta-amyloid, and also increases its clearance, unlike felodipine and amlodipine.[13] The clinical efficacy of nitrendipine has been demonstrated in randomized placebo-controlled trials Syst-Eur and Syst-China.[14,15]

It is well known that the most commonly prescribed and most studied dihydropyridine CCB is amlodipine. Its high antihypertensive and organ-protective efficacy has long been known. However, nitrendipine is a CCB with neuroprotective activity. The purpose of this study was a comparative assessment of the effect of 12-month AHT with the inclusion of nitrendipine (NIT) or amlodipine (AML) on cognitive functions (CF) in hypertensive patients.

Materials and Methods

The study included 111 patients of both genders aged 30-75 years with AH Grades 1-3 (ESC/ESH, 2018), who were on outpatient treatment at the Republican Specialized Scientific and Practical Medical Center for Cardiology. Exclusion criteria were symptomatic hypertension, valvular heart disease, acute coronary syndrome, chronic heart failure (NYHA FC>III), cardiac arrhythmia, history of stroke and myocardial infarction, diabetes, occlusive peripheral arterial disease, renal impairment, severe co-morbidities, orthostatic hypotension.

Office BP was measured using a mercury sphygmomanometer, according to Korotkov's method. BP was measured 3 times, and the means of these measurements were used in the analyses. The 24-hour ABPM was performed using a BR-102 plus (SCHILLER, Switzerland).

The pulse contour analysis was carried out using the SphygmoCor device (AtCor Medical, Australia), which obtains peripheral arterial pressure waveforms by applying an arterial applanation tonometer to the wrist. Such indicators as the central SBP (SBPc), central DBP (DBPc), central PP (PPc), augmentation pressure (AP), augmentation index (AIx), and pulse wave velocity (PWV) were analyzed.

CF were assessed using neuropsychological tests: Mini-Cog test (drawing a clock, reproducing words), Montreal Cognitive Assessment (MoCA) test, and self-assessment questionnaire for memory, attention, thinking, ability to cope with one's affairs, and ability to make decisions. The Hospital Anxiety and Depression Scale (HADS) was used to assess levels of anxiety and depression.

After the screening stage, all patients were discontinued from previous therapy and assigned to the 2 regimes of AHT. Group 1 included 58 AH patients who received NIT (Nitresan, Pro.Med.CS, Czech Republic) as monotherapy or as part of combination AHT; Group 2 included 53 patients who received AML (Normodipin, "Gedeon Richter", Hungary) as monotherapy or as part of combination AHT.

The average daily dose of NIT and AML was 13.6±7.05mg and 6.13±2.11mg, respectively.

In Group 1, 37.9% of patients received monotherapy, 43.1% - dual therapy (NIT+TD or NIT+ACEI/ARB), and 18.9% - triple therapy (NIT+ACEI/ARB+TD).

In Group 2, 32.0% of patients received monotherapy, 43.4% - dual therapy (AML+TD or AML+ACEI/ARB), and

22.4% - triple therapy (AML+ACEI/ARB+TD) (Table 1). Dosing of AHM, taking into account the maximum doses, was titrated at 2-week intervals to achieve a target blood pressure. The effectiveness of the prescribed therapy was evaluated after 12 months of treatment.

The effectiveness of therapy was assessed by achieving the target BP level according to 2018 ESH/ESH Guidelines for the management of AH. The primary target level for SBP and DBP was <140 mmHg and <90 mmHg, respectively.

Table 1.

Characteristics of antihypertensive therapy

Therapy	Group 1 n=58	Group 2 n=53
Monotherapy	22 (37.9%)	17 (32.0%)
Dual therapy	25 (43.10%)	23 (43.4%)
ССВ + TD БКК+ ACEI/ARB	15 (25.9%) 10 (17.2%)	14 (26.4%) 9 (16.9%)
Triple therapy		
ACEI/ARB +CCB + TD	11 (18.9 %)	13 (22.4%)
BB	40 (69.0%)	38 (71.7%)

Statistical analysis was performed using the statistical software «Statistica» (v10.0, StatSoft, USA). Baseline characteristics were summarized as frequencies and percentages for categorical variables and as mean± standard deviation (SD) for continuous variables. The Mann-Whitney U Test was used to compare the differences between the two independent groups (for nonparametric data). The Wilcoxon criterion was used to compare the differences between the paired samples. Group comparisons with respect to categorical variables were performed using chi-square test. Spearman's rank correlation coefficient (r_s) was calculated to measure the strength and direction of the relationship between two variables. A probability value of $P<0.05$ was considered statistically significant.

The study protocol was reviewed and approved by the Ethics Committee of the Republican Specialized Centre of Cardiology. All participants provided written informed consent.

Results

In Groups 1 and 2, the average age of the patients was 58.6±11.6 years and 53.7±12.6 years, respectively, and the average duration of AH was 11.2±7.07 years and 8.12±5.84 years, respectively (Table 2).

Correlation analysis between the parameters of DBPP and the MoCA test revealed a weak but statistically significant negative correlation between the total MoCA score and the average 24-h SBP (r_s=-0.33, P=0.015) (Table 3). In addition, there was a weak but statistically significant negative correlation between the total MoCA score and the daytime SBP variability and daytime DBP variability (r_s=-0.40 and r_s=-0.35, respectively, P=0.000 in both cases). A weak but statistically significant negative correlation was found between the total Mini-Cog score and PWV and PPc (r_s=-0.24, P=0.01 and r_s=-0.27, P=0.007, respectively) (Table 4).

Table 2.

Clinical characteristics of AH patients in the study groups

Parameter	Group 1 n=58	Group 2 n=53	*P*
Age, yrs	58.6±11.6	53.7±12.6	0.06
AH duration, yrs	11.2±7.07	8.12±5.84	0.01
SBP, mmHg	157.8±16.1	161.7±16.2	0.1
DBP, mmHg	95.9±8.85	98.2±7.68	0.09
BPmean, mmHg	116.5±10.1	119.3±9.36	0.8
BMI, kg/m^2	30.6±4.85	30.9±4.78	0.2
BMI >30 kg/m^2, %	28 (48.2%)	30 (56.6%)	0.378
BMI >25<30 kg/m^2, %	19 (32.7%)	19 (35.8%)	0.7321
LVH, %	49 (84.4%)	41 (77.3%)	0.343
PE/PA< 1.0, %	43 (74.0%)	35 (66.0%)	0.360
PWV >10 m/sec, %	35 (60.0%)	29 (54.7%)	0.574
CIMT ≥0.9 mm, %	36 (62.0%)	27 (50.9%)	0.241
Dyslipidemia, %	41(70.6%)	30 (56.6%)	0.127

Table 3.

Correlation analysis between the parameters of DBPP and the MoCA test.

	r_s	*P*
Average 24-h SBP and MoCA total score	-0.33	0.015
Daytime SBP variability and MoCA total score	-0.40	0.000
Daytime DBP variability and MoCA total score	-0.35	0.000

Table 4.

Correlation analysis between the total Mini-Cog score and PWV and PPc.

	r_s	*P*
PWV and Mini-Cog total score	-0.24	0.01
cPP and Mini-Cog total score	-0.27	0.007

Analysis of the office BP indicators showed high antihypertensive efficacy of 12-month therapy in both groups, regardless of the therapy regimens (Table 5): SBP, DBP, and BPmean significantly decreased.

Table 5.

Antihypertensive efficacy of 12-month therapy in the study groups

Parameter		Group 1 n=58	Group 2 n=53	*P*
SBP, mmHg		157.7±16.1 125.1±10.7*	161.1±16.2 125.5±11.5*	0.1
DBP, mmHg		95.9±8.85 79.5±5.94*	98.2±7.68 78.7±7.69*	0.09
BPmean, mmHg		116.5±10.1 94.7±7.12*	119.3±9.36 94.4±8.17*	0.8
Δ% SBP		-20.26±7.09	-21.7±8.97	0.4
Δ% DBP		-16.53±8.73	-19.1±9.29	0.2
Δ% BPmean		-18.35±6.99	-20.4±8.01	0.5
Achieving the target level of BP	SBP DBP SBP&DBP	49(84.4%) 50(86.2%) 48(82.7%)	45(84.9%) 44(83.0%) 43(81.1%)	0.942 0.642 0.828

*The numerator represents the results before treatment and the denominator - after treatment. P-value - between Groups 1 and 2 before treatment. * - P<0.001 before treatment and after 12-month therapy within the group.*

In general, in both groups, against the background of therapy, a positive dynamic of the DBPP indicators was noted; however, the advantages of therapy with the inclusion of AML were revealed. In Group 2, the nighttime SBP load decreased more significantly (from 73.4±28.7% to 42.5±30.7%, $P<0.05$), as well as the nighttime DBP load (from 59.4±32.7% to 27.6±31.7%, $P<0.02$) vs. Group 1 (from 64.83±36.6% to 48.5±35.9%, $P<0.05$, and from 51.4±38.6% to 30.5±36.6%, respectively) (Table 6).

The effectiveness of both therapy regimens was found for parameters of central hemodynamics (SBPc, PPc) and arterial stiffness, with the advantages of therapy with the inclusion of NIT (Table 7). In particular, the indicators of AP and PWV decreased significantly only in Group 1.

A comparative analysis of the effect of AHT with the inclusion of NIT or AML on CF in AH patients showed the advantages of combined AHT with the inclusion of NIT. AML treatment did not significantly affect any test score (Table 8). Thus, in Group 1, after 12 months of therapy, there was an increase in the total Mini-Cog score from 3.8±1.08 points to 4.55±0.75 points ($P<0.001$), while in Group 2, there was a non-significant decrease in this score from 4.26±0.98 points to 3.92±0.95 points ($P>0.05$). There was also an increase in the total MoCA score in Group 1 from 23.3±2.8 points to 25.08±2.6 points ($P<0.001$), while in Group 2, there was a non-significant decrease in this score from 24.06±2.73 points to 23.07±2.7 points ($P>0.05$). It should be noted that only in Group 1 did we find a significant improvement in CF, such as abstraction, delayed recall, memory, and attention, as well as a significant improvement in work-coping and decision-making. In Group 1, the HADS Depression score decreased from 4.6±3.7 points to 3.32±2.95 points ($P<0.05$), HADS Anxiety score decreased from 7.01±5.37 points to 4.95±3.75 points ($P<0.02$)(Table 8). At the same time, in Group 2, in contrast, the HADS Depression score and the HADS Anxiety score did not significantly change.

Table 6.

Dynamics of ABPM indicators against the background of 12-month therapy in the study groups.

Parameter	Group 1 n=58	Group 2 n=53	Mann-Whitney U Test	
			U	*P*
Average 24-h SBP, mmHg	144.5±23.3 125.6±12.4*	144.08±19.9 123.7±8.01*	484	0.11
Average 24-h DBP, mmHg	88.5±16.2 76.3±8.11*	88.5±13.5 75.2±7.85*	482	0.88
Average daytime SBP, mmHg	147.18±22.9 125.9±11.7	145.9±20.42 125.05±8.97	2158	0.9
Average daytime DBP, mmHg	90.3±14.96 77.5±9.7*	89.8±13.5 76.07±8.6*	543	0.6
Average nighttime SBP, mmHg	137.7±24.5 120.5±14.47*	136.1±17.8 118.5±9.62*	532	0.7
Average nighttime DBP, mmHg	81.7±15.2 72.04±10.75º	82.5±12.09 70.1±8.69*	514	0.5
Daytime SBP variability, mmHg	15.8±5.62 14.05±3.54	13.6±4.43 12.9±2.35	1564	0.9
Daytime DBP variability, mmHg	14.1±6.2 11.3±2.65	15.3±4.93 12.2±4.43	1534	0.2
Nighttime SBP variability, mmHg	15.9±19.3 11.5±3.92	14.7±5.13 11.6±4.81	2000	0.2
Nighttime DBP variability, mmHg	11.7±11.3 9.2±3.02	12.27±4.8 9.6±3.43	2196	0.4
Daytime SBP load, %	48.02±36.6 24.3±27.4	51.6±34.9 18.02±19.3	2245	0.6
Daytime DBP load, %	43.97±35.3 23.7±29.05	46.2±31.3 18.3±23.1	2213	0.7
Nighttime SBP load	64.83±36.6 48.5±35.9	73.4±28.7 42.5±30.7^	674	0.6
Nighttime DBP load, %	51.4±38.6 30.5±36.6	59.4±32.7 27.6±31.7º	707	0.7

*The numerator represents the results before treatment and the denominator - after treatment. P-value - between Groups 1 and 2 before treatment. * - P<0.001, º - P<0.02, and ^ - P<0.05 before treatment and after 12-month therapy within the group.*

Table 7.

Dynamics of parameters of central hemodynamics and vascular stiffness against the background of 12-month therapy

Parameter	Group 1 n=58	Group 2 n=53	Mann-Whitney U Test	
			U	*P*
SBPc, mmHg	156.2±21.8 142.8±18.7º	155.1±26.5 138.9±18.5*	1438	0.7
DBPc, mmHg	79.8±15.01 81.9±9.47	82.8±17.6 82.4±10.1	1252	0.4
PPc, mmHg	75.1±18.8 59.9±14.9*	71.1±20.01 61.09±14.83º	1155	0.1
AP, mmHg	18.6±7.94 16.05±6.6*	14.8±7.54 14.6±5.7	1114	0.06
AI, %	32.5±10.3 32.2±8.09*	29.02±11.8 31.8±9.47*	4951	0.5
PWV, m/sec	11.3±2.67 9.85±2.41^	10.6±2.65 9.17±2.05	4229	0.8

*The numerator represents the results before treatment and the denominator - after treatment. P-value - between Groups 1 and 2 before treatment. ^- P<0.001, º- P<0.02, and *- P<0.05 before treatment and after 12-month therapy within the group.*

Table 8.

Dynamics of cognitive functions against the background of 12-month therapy in the study groups.

Parameter	Group 1 n=58	Group 2 n=53	Mann-Whitney U Test	
			U	*P*
Mini-Cog test				
Total score	3.8 ± 1.08 4.55±0.75*	4.26±0.98 3.92±0.95	1162	0.02
Word recall	2.17±0.86 2.72±0.58*	2.52±0.63 2.33±0.61	1186	0.06
Clock draw	1.67±0.63 1.82±0.42	1.73±0.59 1.66±0.55	1436	0.5
HADS Anxiety score	7.01±5.37 4.95±3.75º	5.88±3.39 5.96±2.57	1469	0.6
HADS Depression score	4.6±3.7 3.32±2.95^	4.73±3.29 5.88±2.47	1473	0.7
MoCA test				
Total score	23.3±2.8 25.08±2.6*	24.06±2.73 23.07±2.7	1197	0.04
Visuospatial abilities	3.67±1.26 4.08±0.97^	4.13±1.01 3.84±1.06	1216	0.05
Naming	2.72±0.45 2.87±0.37	2.96±0.3 2.81±0.48	1400	0.1
Attention	4.84±1.18 5.27±1.12*	5.32±0.75 5.03±1.03	1197	0.04
Language	2.20±0.61 1.98±0.54	1.83±0.91 1.75±0.64	11293	0.04
Abstraction	1.3±0.68 1.82±0.5*	1.67±0.56 1.67±0.51	1078	0.006
Delayed recall	2.8±1.22 3.29±1.02^	2.86±1.24 2.64±1.22	1533	0.9
Orientation	5.89±0.3 5.87±0.32	5.88±0.31 5.77±0.5	1522	0.9
Self-assessment questionnaire				
Memory	7.04±2.36 8.24±1.24*	7.26±1.77 6.89±1.73	1509	0.5
Attention	8.75±1.72 9.34±1.17^	8.26±1.89 7.85±1.57	1518	0.2
Thinking	9.09±1.58 9.36±0.38	9.08±1.31 8.26±1.38	1684	0.9
Work-coping	8.03±1.18 9.41±1.17*	8.72±1.8 8.2±1.63	1788	0.9
Decision-making	7.84±2.3 9.02±1.36*	8.4±2.19 7.97±1.71	1551	0.03

*The numerator represents the results before treatment and the denominator - after treatment. P-value - between Groups 1 and 2 before treatment. * - P<0.001, º - P<0.02, ^ - P<0.05 before treatment and after 12-month therapy within the group.*

Discussion

To date, numerous studies have shown that parameters of the circadian rhythm of BP are more closely correlated with target organ damage than with BP measured by the traditional method, and, in addition, the assessment of DBPP provides additional information on indicators such as the increased variability and impaired BP circadian rhythm, and the increased rate of morning rise in BP.[16-18] In particular, "non-dipper" AH patients with insufficient nighttime BP reduction and increased BP variability in the morning and early morning hours are at high risk for developing cerebrovascular and cardiovascular complications, as well as LVH.[19] It is important to note that BP variability is an independent predictor of the development of dementia and its subtypes. In particular, in a study by Jung Eun Yoo et al.[20] a relationship was noted between higher BP variability and the incidence of dementia. Our study showed a negative correlation between the total MoCA score and the average 24-h SBP, Daytime SBP variability, and Daytime DBP variability, consistent with the literature data.

PPc and PWV are known to be independent predictors of cardiovascular disease, including stroke,[21-24] and are considered markers of preclinical cardiovascular disease.[25] Both high and low PP predict the onset of Alzheimer's disease.[26] In addition, higher PP has been associated with lower levels of cognition among people without dementia.[27] In cross-sectional studies, PWV has been found to be higher in patients with vascular dementia, Alzheimer's disease, or mild cognitive impairment than in people with normal cognitive function.[28] Higher PWV has also been associated with lower levels of cognition when screened with the Mini-Mental State Examination (MMSE) test.[29,30] The data obtained in the presented study are consonant with the literature data. In particular, a negative correlation was found between the PWV and CPP index and the total Mini-Cog score.

It is well known that AHM should not only have a prolonged antihypertensive effect during the day, helping to improve DBPP with regression of target organ damage, but also have a positive effect on impaired CF. Modern classes of AHM have approximately the same antihypertensive efficacy; however, not all classes of AHM can improve CF in AH patients. It should be noted that CCBs have a fairly convincing evidence base in improving the prognosis of AH patients (ASCOT, TOMHS, PREVENT, ALLHAT). A unique feature of CCBs is their ability to penetrate the blood-brain barrier and reduce the metabolism of monoamine mediators, which become deficient in degenerative dementia. This property underlies their preventive action against cognitive impairment in AH patients. One of the new representatives of the CCB class is NIT, which belongs to the group of dihydropyridine derivatives and has a convincing evidence base.[13-15] The randomized, double-blind, placebo-controlled, multicenter the Systolic Hypertension in Europe (Syst-Eur) trial[15] examined the effect of NIT on preventing cardiovascular complications in patients over 60 years with isolated systolic hypertension, as well as on quality of life and the incidence of post-stroke dementia. There was a 27% reduction in cardiovascular mortality, a 56% reduction in myocardial infarction, a 42%

reduction in strokes, and a 31% reduction in the combined rate of all fatal and non-fatal cardiovascular endpoints. At the same time, NIT had a pronounced cerebroprotective effect, reducing the risk of developing dementia by 55%. In the Syst-China study, an NIT-based regimen significantly reduced the risk of stroke by 38%, all-cause mortality by 39%, cardiovascular mortality by 39%, stroke mortality by 58%, and all cardiovascular events by 37%.[31]

Our clinical experience with using NIT in combination with other AHM has shown its high efficiency, comparable with the therapy regimen based on AML, in organ protection in AH patients with a high risk of CVD. However, in the NIT-based group, compared with the AML-based group, a significant improvement in CF was demonstrated by the end of 12 months of therapy. It should be noted that the NIT-based treatment contributed to a significant increase in the total Mini-Cog score, in contrast to the decrease in this indicator under AML-based therapy. We also noted an increase in the total MoCA score during the NIT-based therapy, in contrast to AML-based therapy, which did not significantly affect this score.

It should be noted that only in Group 1 was there a significant improvement in CF, such as abstraction, delayed recall, memory, and attention, as well as a significant improvement in work-coping and decision-making. Testing on the HADS scale showed that the severity of anxiety and depression significantly decreased in Group 1; on the contrary, an increase in depression was noted in Group 2. The presented data allow a differentiated approach to tactics for treating AH patients with severe cognitive impairment.

Conclusions:

A weak but statistically significant negative correlation was found between the total MoCA score and the daytime SBP/DBP variability in AH patients.

A weak but statistically significant negative correlation was found between the total Mini-Cog score and PWV and PPc.

A pronounced antihypertensive efficacy of 12-month combination therapy was noted, with the inclusion of both NIT and AML.

The NIT-based treatment contributed to a significant increase in the total Mini-Cog score and the total MoCA score and a substantial improvement in CF. Abstraction, delayed recall, memory, attention, work-coping, and decision-making significantly improved, compared to AML-based treatment.

Competing Interests

The authors declare that they have no competing interests.

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