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CORRECTION OF THE NEUROTRANSMITTER POOL AS A NEW APPROACH IN THE TREATMENT OF PATIENTS WITH MULTIFOCAL ATHEROSCLEROSIS

T. MOTSAK[1]✉, V. LYZOGUB[1], O. KUPCHYNSKA[1,2], Y. BIELIKOVA[1]

[1]Bogomolets National Medical University, Kyiv, Ukraine;
[2]SI "National Scientific Center "Institute of Cardiology, Clinical and Regenerative Medicine named after Academician M.D. Strazhesko" National Academy of Medical Sciences of Ukraine, Kyiv, Ukraine;
✉e-mail: tetianamihalovna@gmail.com

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Multifocal atherosclerosis (MAS) is associated with the development of ischemia in many organs and a significant deterioration in the prognosis for patients. An important role in this disease is played by the imbalance of neurotransmitters and increased content of matrix metalloproteinases (MMP) caused by ischemia. The aim of the study was to develop approaches to drug optimization of blood levels of dopamine, histamine and MMP in patients with multifocal atherosclerosis. The study included: 66 men with MAS aged 67.2 ± 2.9 years, who were divided into two groups: group 1 – patients with ischemic stroke, group 2 – patients with myocardial infarction, common to patients in both groups were atherosclerotic encephalopathy, ischemic heart disease and intermittent claudication syndrome; the control group consisted of 18 practically healthy men aged 63.4 ± 5.1 years. In addition to the basic treatment, patients received cilostazol (50 mg twice a day), GABA – aminalon (250 mg twice a day), atenolol (25 mg once a day) and catechins – Green T-Max (1 capsule per day) for 16 weeks. The examination included: determination of volumetric blood flow (FV) in the coronary, cerebral and femoral vascular territories, walking distance, daily ECG monitoring, estimation of dopamine and histamine levels in serum and MMP-2,-9 level in blood plasma by ELISA. Cognitive function was determined using the Montreal scale. Significantly lower FV in the studied vascular areas and extremely high histamine and dopamine levels were found in both MAS groups compared with the control group. The levels of MMP-2 and MMP-9 in both groups notably exceeded the indices in control group. After additional treatment with the studied medications, the drop in excessively high levels of histamine, dopamine, MMP-2 and MMP-9l was observed, the clinical condition, FV, cognitive functions and walking distance in patients of both MAS groups were improved. Thus, the use of the combination of cilostazol, aminalon, atenolol and catechins, in addition to standard therapy, allowed us to optimize the levels of neurotransmitters dopamine and histamine, which may reduce the risk of recurrent cardiovascular events in patients with MAS.

K e y w o r d s: multifocal atherosclerosis, dopamine, histamine, metalloproteinases-2, -9.

Multifocal atherosclerosis (MAS) is characterized by injury to two or more vascular territories and is associated with a high risk of developing cardiovascular events (CVE) and a worsening prognosis of patients [1-3]. An important role in this process is played by the destabilization of atherosclerotic plaques (AP), which is closely associated with an increase in the content of matrix metalloproteinases (MMPs) in the blood, in particular MMP-2 and MMP-9. It is known that excessive amounts of MMP-2 and MMP-9 increase the risk of thrombosis, the development of CVE, in particular, MI and ischemic stroke (IS) [4-6], the concentration of MMP-9 in the blood is independently associated with an increase in the thickness of the intima-media complex and the instability of AP in the carotid artery [6, 8], positively correlates with the size of the necrotic core of AP in the coronary arteries of patients with myocardial infarction (MI) [7], and is associated with a high risk of mortality.

Ischemia of vital organs, such as the heart and brain, causes an imbalance of neurotransmitters, in particular dopamine and histamine. Dopamine receptors are expressed by vascular and myocardial

smooth muscle cells, which affects vascular tone, myocardial contractility, kidney function, and the functioning of the cardiovascular system in general [9-11]. Dopamine activates the processes of restoration of brain structure and function after IS [12-14]. However, excessive intake of dopamine from the gastrointestinal tract can lead to increased synthesis of adrenaline and noradrenaline, which provokes hemodynamic disturbances [15-17].

Mast cells, which are abundant in coronary vessels and myocardium, capture and release histamine when activated, which can cause coronary vasoconstriction and lead to the development of MI [19]. Elevated histamine levels in the blood are positively associated with the activation of inflammation, atherosclerosis severity, myocardial ischemia, and the development of CVE [18]. It is histamine, by activating MMP, that contributes to the destabilization of AP and vascular remodeling. [20-22]. According to K Wang et al., against the background of histamine deficiency, a decrease in the manifestations of atherosclerosis and inflammatory reactions is observed, which confirms the role of histamine in the progression of the disease [23]. Inhibition of excessive histamine levels in patients with a history of stroke prevents the activation of post-stroke neuroinflammation, reduces neurological symptoms, and improves cognitive functions [24].

We have previously conducted a number of studies of the dynamics of serotonin, dopamine, and MMP in patients with MAS under the influence of a number of drugs added to basic therapy. At the first stage, the effects of cilostazol were studied, at the second stage, aminalone, and at the third stage, atenolol [25-28]. In this study, we focused on determining the dynamics of dopamine and histamine in patients with MAS under the influence of complex therapy based on the addition of cilostazol, aminalone, atenolol and a histidine decarboxylase blocker, catechins, to basic therapy. As it is known, cilostazol is recommended for the treatment of patients with intermittent claudication syndrome (ICS) (recommendation 1A) and for the prevention of IS [2, 29, 30]. Atenolol, a selective beta1-adrenergic blocker that does not cross the blood-brain barrier (BBB), acts on D2 dopamine receptors, exerting cardioprotective effects, and blocks the active sites of MMP-2 and MMP-9 [9, 39, 40]. Gamma-aminobutyric acid (GABA) is a non-proteinogenic amino acid, the main inhibitory neurotransmitter in the central nervous system, which may prevent neurodegeneration [41, 42].

Despite the large number of studies on the prevention of CVE, the development of this issue requires further attention. At the same time, it is important to focus on studying the relationship between neurotransmitters and atherosclerotic changes, which opens a new approach to the therapy of this category of patients, given the negative impact of MAS on the prognosis of patients, insufficient effectiveness of secondary prevention of CVE.

This research aimed to develop approaches to drug optimization of blood levels of dopamine, histamine and MMP in patients with multifocal atherosclerosis.

Material and Methods

The study included 66 male patients with a mean age (67.2 ± 2.9) years with MAS. Patients were divided into 2 groups: in Group-1 (n = 34), all patients had suffered an ischemic stroke (IS) no less than 12 months before inclusion in the study, patients in Group-2 (n = 32) had a myocardial infarction (MI) at least a year before inclusion in the study. Common to both groups were the presence of intermittent claudication syndrome (ICS) stage I-II according to the Fontaine-Pokrovsky classification, atherosclerotic encephalopathy (AE), hemodynamically significant AB in the carotid arteries, ischemic heart disease (IHD) and left ventricular ejection fraction (LVEF) over 45%. Patients who had an MI had coronary angiography data. The control group consisted of 18 practically healthy men, comparable in age to the patients of the MAS groups, with a mean age (63.4 ± 5.1) years. All patients were informed about the nature of the study and signed informed consent before inclusion in the study.

Exclusion criteria: acute ischemic stroke or transient ischemic attack (TIA) less than 1 year before inclusion in the study, hemorrhagic stroke, life-threatening cardiac arrhythmias (ventricular arrhythmias, QT interval prolongation), cardiac or aortic aneurysm, heart failure Class III and higher (according to NYHA classification), uncontrolled hypertension, LVEF < 45%, any history of bleeding, severe liver and/or kidney dysfunction, oncological diseases.

A general clinical examination was performed on all patients. Additionally, the ankle-brachial index (ABI) was determined using the standard method, and the painless walking distance (PWD) and maximum walking distance (MWD) were measured. Using Doppler (on the HITACHI, ALOKA,

AriettaS70 device), we determined the velocity and volume (volumetric blood flow velocity – FV) indicators of blood flow in the arteries of the vascular territories: cerebral - *a. carotis interna* (aACI), femoral - *a. femoralis communis* (aFC) and *a. tibialis posterior* (aTP). Using the Holter ECG monitoring method (HM ECG) (on the Cardio Sense K device KHAI-MEDIKA), we determined the number and duration of painful (PEMI) and painless episodes of myocardial ischemia (PLEMI). Enzyme-linked immunosorbent assay (ELISA) was used to determine the levels of neurotransmitters (dopamine and histamine) in blood serum (a set of reagents for enzyme-linked immunosorbent assay of antibodies to endogenous bioregulators in blood serum, LLC "LABTIME LTD", Kyiv, Ukraine; ELISA analyzer (Humareader, Germany), as well as the levels of MMP-2 and MMP-9 in blood plasma [43]. Cognitive function was determined using the Montreal Cognitive Assessment Scale (MoCA) [44].

Patients in both groups of MAS received basic therapy according to existing recommendations [2, 29, 30]. Dual antiplatelet therapy (acetylsalicylic acid (ASA) + clopidogrel/cilostazol) and statins were mandatory; other drugs: angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin-II receptor blockers (ARBs), calcium antagonists, β-adrenoceptor blockers, nitrates, diuretics – were prescribed depending on symptoms. After the basic examination, patients were additionally prescribed cilostazol (50 mg twice a day), GABA – aminalon (250 mg twice a day), atenolol (25 mg once a day) and histidine decarboxylase inhibitor catechins – Green T-Max (1 capsule per day). After 16 weeks, a comprehensive examination was repeated. The control group patients were examined once. This study complied with the ethical principles of the Declaration of Helsinki of the World Medical Association of Physicians (revision 2008), ethical and moral requirements according to the Order of the Ministry of Health of Ukraine No. 281 dated 01.11.2000, including anonymity, confidentiality and benevolence.

Statistical analysis of data was performed using the IBM SPSS program, version 23, EZR on R commander version 1.61, 2022. Differences were considered significant at $P < 0.05$.

Results

The clinical picture of patients with MAS was due to the defeat of three vascular territories – coronary, cerebral and femoral. Clinically, this was manifested by the presence of signs of stable angina pectoris of the II-III functional class, atherosclerotic encephalopathy and ICS. Clinical symptoms of ICS were confirmed by the presence of AP in the vessels of the femoral area, a decrease in ABI and indicators of volumetric blood flow in aFC and ATP, compared with the data of the control group (Table 1). In patients of Group-1, the ABI ranged within (0.66 ± 0.02), Group-2 – (0.72 ± 0.03), while in the control group, it was (1.02 ± 0.04).

During dopplerography, we detected hemodynamically significant AP in the arteries of the vascular territories – cerebral (aCI), femoral (aFC and aTP) and coronary (according to coronary angiography). As can be seen in Fig. 1, the FV indicators in patients of Group-1: in aCI were 31.4% lower, and in aFC 56.7% lower, compared with the control group data, and in Group-2 – by 26.2 and 53.3%, respectively ($P < 0.001$ in all cases). The most significant changes were recorded in aTP: in Group-1, the FV level was 3.2 times lower, and in Group-2, it was 2.9 times lower, compared with the control group data, which is clinically reflected in patients of both groups of ICS.

The severity and dynamics of MAS, in particular, the development of acute circulatory disorders, largely depend on the stability of AP. The decisive role in the process of AP destabilization is played by MMPs, in particular MMP-2 and MMP-9, the increased level of which is considered a reliable predictor of the risk of acute coronary and cerebrovascular events. As can be seen from Table 3, the levels of MMP-2 in Group-1 exceeded their values in the control group by 58.9%, in Group-2– by 58.0%, and MMP-9 – by 62.4 and 61.5%, respectively ($P < 0.01$ in all cases). The data obtained by us coincide with the literature data on the worsening of the course of the disease and an increase in the risk of developing repeated CVE, especially in patients with previous IS, with increased levels of MMPs [4, 25-27].

Pathologically high levels of neurotransmitters histamine and dopamine are associated with the development of ischemia of vital organs (Table 2). Histamine levels in Group-1 were higher than in the control group by 2.8 times, and in Group-2 – by 2.74 times ($P <0.001$ in both cases), and dopamine levels by 78.2 and 58.7%, respectively ($P < 0.01$ in both cases). The data we obtained are comparable with the literature data on the pathological effect of excessively high levels of histamine and dopamine on the deterioration of CVE [9, 18, 31].

Table 1. Clinical characteristics of patients in both groups and basic therapy before the appointment of additional drugs

Measurements	Control group, $n = 18$	Group-1, $n = 34$	Group-2, $n = 32$
Age, years	63.4 ± 5.1	67.2 ± 2.9	66.1 ± 3.1
Men	18 (100%)	34 (100%)	32 (100%)
ICS	0	34 (100%)	32 (100%)
Smoking	0	27 (79.4%)	29 (90.6%)
Ischemic stroke in anamnesis	0	34 (100%)	0
Atherosclerotic encephalopathy	0	34 (100 %)	27 (84.4%)
MI in anamnesis	0	0	32 (100%)
Angina pectoris HF II Class	0	25 (73.5%)	28 (87.5%)
Hypertension	0	15 (44,1%)	12 (37.5%)
AP in carotid arteries	0	34 (100%)	32 (100%)
AP in coronary arteries	0	34 (100%)	32 (100%)
AP in femoral arteries	0	34 (100%)	32 (100%)
Basic treatment:			
ASA	0	34 (100%)	32 (100%)
Clopidogrel	0	25 (73.5%)	27 (84.4%)
Statins	0	34 (100%)	32 (100%)
Beta-blockers	0	28 (82.4 %)	32 (100%)
Nitrates (episodically)	0	11 (32.4%)	21 (65.6%)
ACEIs/ARBs	0	27 (79.4%)	29 (90.6%)
Diuretics	0	29 (85.3%)	28 (87.5%)

Note. ASA – acetylsalicylic acid; ACEI – angiotensin-converting enzyme inhibitors; ARB – angiotensin-II receptor blockers; AP – atherosclerotic plague; ICS – intermittent claudication syndrome; HF – heart failure

Table 2. Histamine, dopamine, and MMP levels in patients of both groups and their dynamics under the influence of treatment (Me (Q1; Q3))

Measurements	Control group, $n = 18$	Group-1, $n = 34$		Group-2, $n = 32$	
		before treatment	after treatment	before treatment	after treatment
MMP-2, CU/mg protein	0.112 (0.108; 0.189)	0.178 (0.139; 0.192)**	0.132 (0.121; 0.161)$^{\#\#}$	0.177 (0.148; 0.188)**	0.135 (0.129; 0.163)$^{\#\#}$
MMP-9, CU/mg protein	0.109 (0.105; 0.181)	0.177 (0.169; 0.188)**	0.161 (0.148; 0.187)	0.176 (0.168; 0.220)**	0.156 (0.147; 0.178)$^{\#}$
Histamine, CU	0.54 (0.20; 0.73)	1.52 (0.89; 1.85)***	1.26 (0.83; 1.63)$^{\#}$	1.48 (0.88; 1.61)***	1.21 (0.77; 1.52)$^{\#}$
Dopamine, CU	0.92 (0.75; 1.52)	1.64 (1.15; 1.92)**	1.50 (1.12; 1.88)	1.46 (1.11; 1.83)**	1.37 (1.04; 1.48)

Note. MMP – metallomatrix proteinases. Significance of the difference compared to control group: *$P < 0.05$; **$P < 0.01$; ***$P < 0.001$. Significance of the dynamics of indicators under the influence of treatment: $^{\#}P < 0.05$; $^{\#\#}P < 0.01$; $^{\#\#\#}P < 0.001$

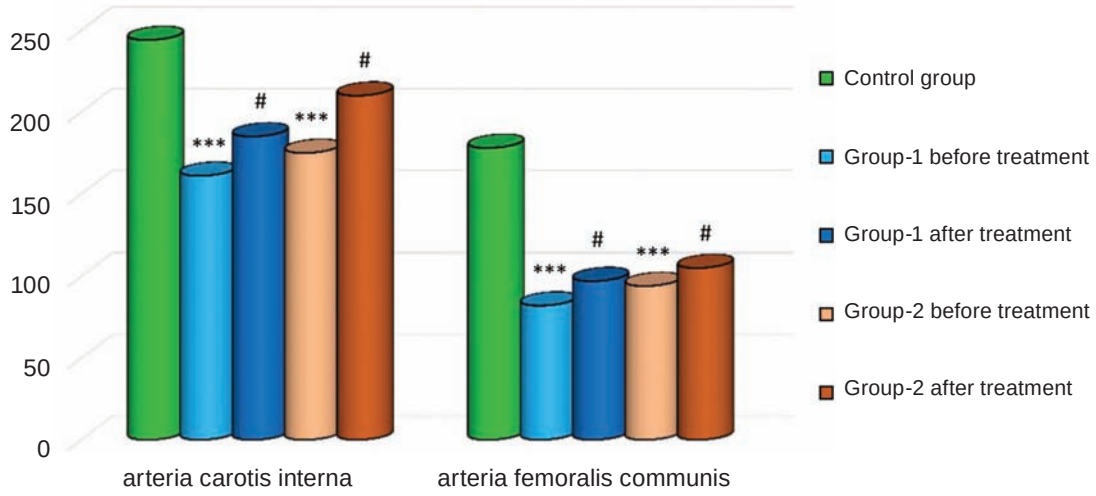

*Fig. 1. Dynamics of volumetric blood flow (FV, ml/min) in a.carotis interna and a.femoralis communis under the influence of treatment and compared with the control group. The significance of the differences in the indicator compared to the control group: *P < 0.05; **P < 0.01; ***P < 0.001. The significance of the dynamics of the indicators under the influence of treatment: #P < 0.05; ##P < 0.01; ###P < 0.001*

After the treatment with the addition of cilostazol, aminalone, atenolol, and catechins, we recorded positive clinical dynamics in patients of both groups of MAS. Patients had reduced pain in the lower extremities, numbness and tingling were bothersome, and walking distance increased. In Group-1, PWD increased by 64.7%, in Group-2 – by 66.8%, while MWD increased by 41.4 and 43.6% ($P < 0.01$ in all cases), respectively. According to the HM ECG data, the treatment contributed to a decrease ($P < 0.01$) in the number of PEIM and PLEIM in patients of both groups: in Group 1 by 16.2 and 16.5%, and in Group-2 by 17.3 and 17.6%, respectively.

Volumetric blood flow indicators significantly improved in both groups of patients (see graph 1). In patients of Group-1, the level of FV in aCI increased by 17.8%, in aFC – by 16.8%, and in Group-2 – by 18.9 and 17.6%, respectively ($P < 0.05$ in all cases). The improvement of blood supply against the background of the addition of cilostazol affected not only the increase in walking distance, but also the increase in FV in aTP in patients of both groups: in Group-1 this indicator improved by 47.5, and in Group-2 - by 50.8% ($P < 0.01$ in both cases). A statistically significant increase in FV indicators, especially in the arteries of the lower extremities, an increase in walking distances indicates a positive effect of cilostazol on the clinical manifestations and course of ICS. [2].

After the comprehensive treatment of patients with MAS, MMP levels significantly decreased, in particular, MMP-2 levels decreased by 25.8% in Group-1 and by 23.7% in Group-2 ($P < 0.01$ in both cases). MMP-9 levels significantly decreased only in Group-2 by 11.4% ($P < 0.05$); in patients of Group-1, a significant decrease was not observed, but this is a positive point for patients with a history of IS.

Levels of histamine significantly decreased due to the use of catechins: in Group-1 – by 17.1%, and in Group-2 – by 18.2% ($P < 0.05$ in both cases), compared with the data before treatment. As for the levels of dopamine, they had a clear tendency to decrease, which may also have a positive effect on regenerative processes in the brain in patients with MAS.

In Group-1, significant memory improvement against the background of complex treatment was found in 64.7% of patients (22/34), in Group-2 – in 75.0% (24/32) of patients, attention improvement – in 70.6% (24/34) and 78.1% (25/32), respectively (Fig. 2).

Discussion

Based on the results of our previous studies, we have proposed a new approach to treating patients with MAS that is based on correcting neurotransmitter disorders [25-27]. We have shown that pathologically high levels of serotonin in the blood can be reduced under the action of citostazol, which was accompanied by an increase in volumetric blood flow in the cerebral and femoral arterial basins, as well as an improvement in cognitive functions, a decrease

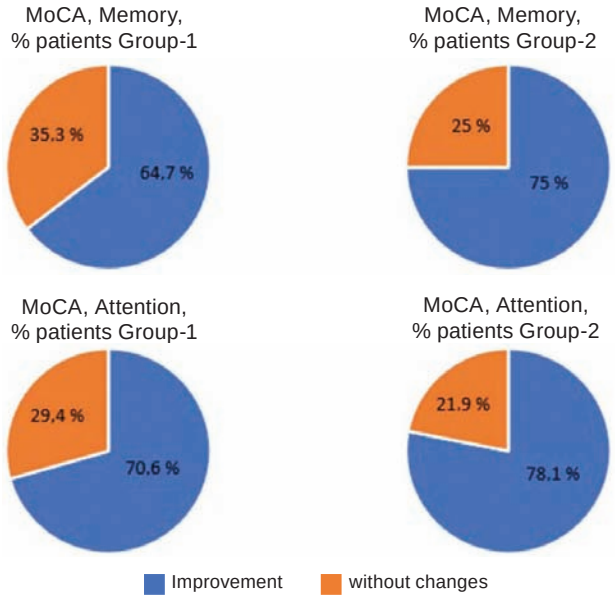

Fig. 2. Improvement in cognitive function, according to the Montreal Cognitive Assessment (MoCA) scale, in patients of both groups under the influence of treatment

in the number of PEIM and PlEIM, levels of MMP-2 and MMP-9 [25-27].

In this study, the characteristics of the levels of dopamine and histamine in the blood of two groups of patients with MAS, with clinical, hemodynamic and morpho-functional manifestations of atherosclerosis – atherosclerotic plaques in three vascular territories – cerebral, coronary and femoral. The groups differed in that in Group-1, all patients had suffered from IS, and in Group-2, all patients had suffered from MI in anamnesis; common to patients in both groups were atherosclerotic encephalopathy, ischemic heart disease and intermittent claudication syndrome. Our studies showed significantly lower FV values in all three studied vascular areas. Low FV values were comparable to the imbalance of the main neurotransmitters involved in the atherosclerotic process. We first detected extremely high levels of histamine and dopamine, which were significantly higher than in the control group, which worsened the course of the disease in this category of patients.

In patients of both groups, a significant increase in the level of histamine was observed, in patients of Group-1 by 2.81 times, and in Group-2 group by 2.74 times ($P < 0.001$ in both cases) compared to the control group. It is known that high levels of histamine cause histamine intoxication, which, according to the literature, can lead to a decrease in vascular resistance and hypotension and, in critical conditions even, to cardiac arrest [32]. According to the literature, increased histamine levels are associated with AP formation, ischemic changes in the myocardium and increased vascular wall permeability [33-38]. According to our data, the imbalance of neurotransmitters, in particular high levels of dopamine and histamine, also plays a certain role in increasing the level of MMP-2 and MMP-9, which in turn contributes to an increased risk of AP destabilization [4, 20-22]. The data obtained by us indicate a high probability of cardiovascular complications in patients with MAS.

Increased dopamine levels were recorded in 29/34 patients in Group-1 and in 25/32 in Group-2. At the same time, on average, the increase in dopamine levels in Group-1 was 78.2% ($P < 0.01$) higher, and in Group-2 by 58.7% ($P < 0.01$), compared with the CG. The obtained data confirm the positive effect of dopamine on the regenerative properties of the brain after stroke [9, 39]; however, excessively high numbers have negative consequences for the CVE. Therefore, it was important for us to block the effect of excessively high dopamine levels on the cardiovascular system while at the same time preserving their positive properties for brain recovery, particularly in patients after IS. To optimize the level of dopamine, we used a selective beta1-adrenoblocker atenolol, which does not penetrate the blood-brain barrier and acts on D2-dopamine receptors, while exhibiting a cardioprotective effect, which was very important to us [9, 39]. After the treatment, we obtained a decrease in dopamine levels in both groups; however, it was not significant. In addition, At has a structural formula that exhibits the properties of blocking the active centers of MMP-2 and MMP-9 [9, 39].

As a result of the treatment we performed, we observed positive dynamics of the clinical symptoms of ICS, which was manifested in a decrease in paresthesia and numbness of the lower extremities, patients could walk a greater distance without stopping. These data were confirmed by a significant ($P < 0.01$) increase in walking distance in both groups of patients, mainly due to the addition of cilostazol to increase walking distance (recommendation 1A) [14-16] peripheral arterial blood supply improved in both cases), compared to the data before treatment. Volumetric blood flow indicators in aCI and aFC also significantly ($P < 0.05$) improved af-

ter the treatment. No side effects were recorded with complex treatment. Only with Cilostazol monotherapy – an increase in heart rate is possible. However, the addition of Atenolol and Aminalon completely blocked this side effect. Against the background of the applied treatment, heart rate levels did not significantly change in patients in both groups.

We eliminated the excessively high levels of histamine that were recorded in patients with MAS by using a blocker of histidine decarboxylase, which is the main enzyme in the conversion of histidine into histamine, catechin. After the treatment, we found a significant decrease in histamine levels in both groups of patients: in Group-1 by 17.1% and in Group-2 by 18.2% ($P < 0.05$ in both cases). The data we obtained confirm the positive effect of low histamine levels on the atherosclerotic process and a decrease in MMP activity [20-23]. As for the latter, owing to the combination therapy (which included cilostazol, aminalone, catechin), a significant ($P < 0.05$) decrease in MMP levels in patients of both groups was found. According to the literature, a decrease in the activity of MMP-2 and MMP-9 contributes to an increase in the stability of AP and a decrease in the risk of repeated CVE [5, 7, 45].

Thus, in our opinion, to improve the quality of secondary prevention of CVE in patients with MAS, it is advisable to add cilostazol, aminalone, catechin and atenolol to standard therapy. Any beta-blocker should be replaced with atenolol, which does not penetrate the BBB, acts on D2-dopamine receptors and beta-1 adrenoreceptors, has unique properties of blocking the active centers of MMP-2 and MMP-9, which play a key role in the destabilization of AP. Adding cilostazol to the treatment regimen has not only antiaggregatory properties and effects on peripheral arteries but also affects coronary, cerebral and mesenteric blood flow. It is known that 3 out of 5 patients with asymptomatic peripheral artery disease die from severe CVE [46]. We have proven the effectiveness of cilostazol in patients with MAS [25-27]. According to the 2024 guidelines [2], cilostazol is recognized as the main drug (evidence level 1A) for patients with PAD. Regarding histamine, we consider it advisable to block the conversion of histidine to histamine using a histidine decarboxylase blocker, thus reducing its level in the blood plasma. The use of a combination of cilostazol, aminalone, atenolol and catechin allowed to reduce pathologically high levels of MMP-2 and MMP-9 and optimize the levels of neurotransmitters dopamine and histamine, which may reduce the risk of repeated CVE in this category of patients.

At the moment, we continue the study for long-term observation of the stability of the effects of the drug combination and the dynamics of neurotransmitters. The work presented demonstrates studies conducted on a small cohort of patients, data are provided only on 2 neurotransmitters (histamine, dopamine). Currently, the research is ongoing, we continue our research on serotonin, angiotensin, beta-endorphin, which will be presented in subsequent publications after the completion of the study.

Conflict of interest. The authors have completed the Unified Conflicts of Interest form at http://ukrbiochemjournal.org/wp-content/uploads/2018/12/coi_disclosure.pdf and declare no conflict of interest.

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КОРЕКЦІЯ НЕЙРОМЕДІАТОРНОГО ПУЛУ – НОВИЙ ПІДХІД У ЛІКУВАННІ ПАЦІЄНТІВ ІЗ МУЛЬТИФОКАЛЬНИМ АТЕРОСКЛЕРОЗОМ

Т. М. Моцак[1]✉, В. Г. Лизогуб[1], О. Г. Купчинська[1,2], Ю. О. Бєлікова[1]

[1]Національний медичний університет імені О. О. Богомольця, Київ, Україна;
[2]ДУ «ННЦ «Інститут кардіології, клінічної та регенеративної медицини імені академіка М. Д. Стражеска» НАМН України, Київ;
✉e-mail: tetianamihalovna@gmail.com

Мультифокальний атеросклероз (МАС) асоціюється з розвитком ішемії багатьох органів та суттєвим погіршенням прогнозу для пацієнтів. Важливу роль у патогенезі цієї хвороби відіграє дисбаланс нейромедіаторів і підвищений вміст матриксних металопротеїназ (ММП), спричинений ішемією. Метою дослідження було розробити підходи до медикаментозної оптимізації рівнів дофаміну, гістаміну та ММП у крові пацієнтів з мультифокальним атеросклерозом.У

дослідження були включені: 66 чоловіків із МАС віком 67,2 ± 2,9 років, яких поділили на дві групи:група 1 – пацієнти з перенесеним ішемічним інсультом, група 2 – пацієнти з перенесеним інфарктом міокарда, загальним для хворих обох груп були атеросклеротична енцефалопатія, ішемічна хвороба серця та синдром переміжної кульгавості; контрольна група склала 18 практично здорових чоловіків віком 63,4 ± 5,1 років. Окрім базової терапії, пацієнти додатково отримували цилостазол (50 мг двічі на добу), гамма-аміномасляну кислоту – аміналон (250 мг двічі на добу), атенолол (25 мг один раз на добу) та катехіни – Green T-Max (1 капсула на добу) протягом 16 тижнів. Обстеження включало: визначення об'ємного кровотоку (ОК) у коронарному, мозковому та стегновому судинних руслах, дистанції ходьби, добовий моніторинг ЕКГ, оцінку рівнів дофаміну та гістаміну у сироватці крові, а також рівнів ММП-2 і ММП-9 у плазмі методом ІФА. Когнітивні функції оцінювали за Монреальською шкалою. У обох групах МАС зафіксовано достовірно нижчі показники ОК у досліджуваних судинних ділянках і суттєво підвищені рівні гістаміну та дофаміну у порівнянні з контрольною групою. Рівні ММП-2 і ММП-9 також значно перевищували показники контрольної групи. Після додаткового лікування досліджуваними препаратами спостерігалося зниження надмірно високих рівнів гістаміну, дофаміну, ММП-2 і ММП-9, а також покращення клінічного стану, показників ОК, когнітивних функцій та дистанції ходьби в обох групах з МАС. Таким чином, застосування комбінації цилостазолу, аміналону, атенололу і катехінів на додаток до стандартної терапії дозволяє оптимізувати рівні нейромедіаторів дофаміну та гістаміну, що може знизити ризик повторних серцево-судинних подій у пацієнтів з МАС.

Ключові слова: мультифокальний атеросклероз, дофамін, гістамін, металопротеїнази-2, -9.

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