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EVALUATION OF THE COMPARATIVE EFFICACY OF THE CONTROL OF ARTERIAL HYPERTENSION AND IMPROVEMENT OF THE QUALITY OF LIFE OF PATIENTS WITH ARTERIAL HYPERTENSION AFTER CORONAVIRUS INFECTION USING VARIOUS REGIMENS OF THREE-COMPONENT ANTIHYPERTENSIVE THERAPY

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Abstract

In patients who have undergone coronavirus infection, decompensation of the course of chronic cardiovascular diseases, including arterial hypertension, is often observed, which is due to a number of their common pathogenetic mechanisms.

To evaluate the comparative effectiveness of controlling arterial hypertension and improving the quality of life who underwent a new coronavirus infection.

Totally 62 patients with arterial hypertension who had previously undergone coronavirus infection were examined. The criterion for inclusion in the study was a decrease in blood pressure control on the background of previously effective two-component therapy. Depending on the heart rate at rest, the patients were divided into two groups. In both groups, triple antihypertensive therapy was used as a second step. In the first group - a combination of perindopril 5 mg, indapamide 2.5 mg, amlodipine 5 mg. The second group included patients with a heart rate of more than 80 beats per minute, perindopril 5 mg, bisoprolol 5 mg, amlodipine 5 mg. The antihypertensive efficacy of the studied drug combinations was analyzed according to the data of 24-hour blood pressure monitoring. During the treatment of arterial hypertension, the dynamics of quality-of-life indicators was analyzed.

A study of 24-hour monitoring and blood pressure variability in both groups of patients with coronavirus infection demonstrated the lack of effective blood pressure control. The use of the analyzed variants of three-component therapy made it possible to achieve the target level of blood pressure in 89.6% and 93.9% of cases, respectively. In both study groups, the achievement of office blood pressure control was accompanied by a statistically significant decrease in all its daily parameters.

On the background of antihypertensive therapy in both groups of the study, there was a significant and reliable ($p<0.05$) increase in all parameters for assessing the quality of life, which reflects the effectiveness of the treatment of arterial hypertension in patients who have had a coronavirus infection in increasing satisfaction with their lives and improving social functioning.

Therapy with the use of perindopril, bisoprolol, amlodipine was accompanied by the achievement of significantly ($p<0.05$) higher rates of mental and physical health components.

Keywords: *arterial hypertension, coronavirus infection, quality of life, triple antihypertensive therapy.*

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Introduction

Arterial hypertension is one of the leading modifiable risk factors for cardiovascular, cerebrovascular, and renal diseases [*Williams B. et al., 2018*]. The prevalence of this disease is one of the highest, increases with age and reaches more than 60 % in patients of older age groups [*Boytsov S. A. et al., 2014*]. Intensive control of hypertension with the achievement of individual target levels of blood pressure (BP) can significantly reduce the incidence of adverse cardiovascular events, terminal renal failure, which generally affects the reduction of cardiovascular and overall mortality [*Ettehad D. et al., 2016; Lewington S. et al.,2002*].

Currently, one of the factors reducing the effectiveness of hypertension control has become the developing new coronavirus infection, as well as the formation of post-Covid syndrome. In patients who have undergone a new coronavirus infection, decompensation of the course of chronic cardiovascular diseases, including arterial hypertension, is largely due to a number of their common pathogenetic mechanisms [*Shlyakhto E. V. et al., 2020; Fang L. et al., 2020*]. The development of COVID-19 is accompanied by systemic damage to the vascular bed with the formation of severe endothelial dysfunction, accompanied by coagulopathy and an increased risk of thromboembolic complications [*Korostovtseva L.S. et al., 2020; Teplova N.V., Grishin D.V., 2020; Shatunova P.O. et al., 2020*]. Dysregulation of the renin-angiotensin-aldosterone system, caused by the influence of the virus, leads to a change in vascular tone, the development of proliferation and inflammation in the vascular endothelium [*Fisun A.Ya. et al., 2020; Zhou P., 2020*].

Decompensation of the course of hypertension in patients with a history of coronavirus infection is in most cases characterized by the absence of hypertension control against the background of the use of previously effective antihypertensive therapy, which requires a change in the treatment strategy [*Shlyakhto E. V. et al., 2020; Korostovtseva L.S. et al., 2020*]. In addition, one of the characteristic manifestations of the post-COVID syndrome is an increase in heart rate and the development of various cardiac arrhythmias [*Podzolkov V.I. et al., 2021*]. A heart rate of more than 80 beats per minute in patients with hypertension is currently considered as an independent, prognostically unfavorable risk factor that requires correction [*Williams B. et al., 2018*].

According to the current clinical guidelines, most patients with hypertension use combination therapy using two antihypertensive drugs as the first step of antihypertensive therapy. In case of its ineffectiveness, a triple antihypertensive therapy is recommended as the second step in the treatment of hypertension. At the same time, the main combination for most patients is the use of a renin-angiotensin-aldosterone system blocker, a diuretic, and a calcium channel blocker. Beta-blockers, remaining one of the main classes of antihypertensive drugs, are used in special clinical situations, one of which is tachycardic heart rhythm disturbances [*Williams B. et al., 2018*]. Data from comparative studies of the effectiveness of various options for triple therapy in patients with hypertension who have had a coronavirus infection are currently insufficient. In this connection, it is relevant to evaluate the effectiveness of hypertension control in patients of this category using standard triple therapy and triple therapy with a renin-angiotensin-aldosterone system blocker, a beta-blocker, and a calcium channel blocker in the category of patients with an initial increased heart rate.

The main criteria for the effectiveness of the treatment of hypertension are not only the achievement of an individual target level of blood pressure, but also an increase in the patient's quality of life, which contributes to optimal adherence to therapy [*Balanova Yu.A. et al.,2016*]. Currently, the assessment of the quality of life is becoming one of the most studied areas of a comprehensive assessment of a patient's health, which allows, in addition to objective medical data, to get an idea of the subjective perception of the patient's own health. The patient's quality of life reflects the satisfaction of his needs and adaptation in the physical, psychological and social spheres. Evaluation of the dynamics of the quality of life against

To overcome it is possible, due to the uniting the knowledge and will of all doctors in the world

the background of ongoing therapy for chronic diseases, including hypertension, allows a comprehensive analysis of not only the effectiveness of treatment, but also the tolerability of therapy, to some extent assess the prognosis of the disease [*Potemina T.E. et al., 2018*]. A wide range of symptoms accompanying the development of post-COVID syndrome significantly impairs the quality of life of patients, and therefore it is relevant to assess the dynamics during the treatment of the quality of life of patients with hypertension who have undergone coronavirus infection [*Amirov N.B. et al., 2021*].

Objective: to evaluate the comparative effectiveness of controlling arterial hypertension and improving the quality of life of patients with arterial hypertension who underwent a new coronavirus infection using various options for three-component antihypertensive therapy.

MATERIALS AND METHODS.

We examined 62 patients with arterial hypertension (mean age 59.3 ± 0.9, men – 28 and women – 34) who had previously had a new coronavirus infection in terms of 1 to 12 weeks. All patients included in the study, prior to the development of coronavirus infection, received dual therapy for hypertension using a renin-angiotensin system blocker and a calcium channel blocker, which allowed effective control of hypertension. The criterion for inclusion in the study was a decrease in blood pressure control against the background of previously effective therapy. Depending on the heart rate at rest, the patients were divided into 2 groups (comparable by sex and age). The first group included 29 patients with an initial heart rate of 80 or less, the second group included 33 patients with an initial heart rate of more than 80 beats per minute.

Taking into account the ineffectiveness of two-component antihypertensive therapy in patients of both groups, in accordance with the current Clinical guidelines, three-component antihypertensive therapy was used as a second step. In the first group – a combination of perindopril 5 mg, indapamide 2.5 mg, amlodipine 5 mg. In the second group - perindopril 5 mg, bisoprolol 5 mg, amlodipine 5 mg.

The observation was carried out for 8 weeks. During 3 visits (2, 4, 8 weeks), the dynamics of blood pressure and heart rate (HR), tolerability of the treatment was assessed. Complaints, anamnesis and clinical examination data, the appearance of adverse events during treatment were analyzed. All patients underwent 24-hour blood pressure monitoring with an ABPM-04 Holter device for monitoring blood pressure and electrocardiography (Labtech, Hungary). We analyzed the average values of systolic and diastolic blood pressure, indicators of “pressure load”, systolic blood pressure variability, diastolic blood pressure, pulse blood pressure per day, in the daytime and at night, and also calculated the rate of morning increase in systolic and diastolic blood pressure.

The quality of life of all patients was also assessed before the appointment of treatment and after 8 weeks of therapy using the internationally certified questionnaire Medical Outcomes Study Form (SF-36). The SF-36 questionnaire includes 36 questions that characterize two components of health – physical and psychological. The components are assessed using 8 health scales: physical performance, social activity, the degree of limitation of physical performance and social activity, mental health, energy and fatigue, pain, general health assessment.

Statistical data processing was carried out using variation statistics using the Statistica 10 package. The methods of descriptive statistics were used, the correspondence of the type of distribution of the attribute to the law of normal distribution was determined. Comparison of groups by indicators was carried out using non-parametric analysis based on the Mann-Whitney and Wilcoxon criteria.

RESULTS AND ITS DISCUSSION.

In all patients at the time of inclusion in the study, office blood pressure exceeded the level of 150/100 mm Hg. and averaged blood pressure in the group had composed 163.2/102.4 mm Hg. The study of 24-hour blood pressure monitoring and blood pressure variability in both groups of patients with coronavirus infection demonstrated the lack of effective blood pressure control (Table 1).

As can be seen from the presented table, there was a lack of effective control of blood pressure with an insufficient decrease in both systolic blood pressure

Table 1

The study of 24-hour blood pressure monitoring and blood pressure variability before treatment

Indicators of 24-hour blood pressure monitoring	I Group (n=29)	II Group (n=33)
Systolic blood pressure		
24-hour	140.23±1.6	139.34±1.23
day	144.51±1.23	142.35±1.36
night	135.21±1.34	134.25±1.34
Diastolic blood pressure		
24-hour	88.31±1.32	87.34±1.35
day	86.45±1.34	88.11±1.34
night	80.31±1.24	80.54±1.53
Average blood pressure		
24-hour	100.23±1.3	102.12±1.51
day	105.67±1.34	107.12±1.23
night	98.31±1.23	96.78±1.52
Variability systolic blood pressure		
24-hour	17.64±0.98	17.38±0.72
day	17±1.1	16±1.22
night	13.9±1.44	12.65±0.93
Variability diastolic blood pressure		
24-hour	13.21±0.67	13.46±0.83
day	15.33±0.73	15.3±0.97
night	9.94±0.98	9.32±0.72
Variability pulse blood pressure		
24-hour	17.76±0.7	17.84±0.62
day	10.82±0.82	10.81±0.73
night	12.71±0.71	11.87±0.83

and diastolic blood pressure at night in both groups of the study. An unfavorable prognostic characteristic was also an increase in most indicators of blood pressure variability.

Self-monitoring of blood pressure, heart rate and office measurement of blood pressure and heart rate after 2 weeks of therapy showed that out of 29 patients in group 1, the primary goal of blood pressure control (less than 140/90 mm Hg) was achieved by 21 patients. The remaining 8 patients were transferred to high-dose triple therapy with an increase in the dose of perindopril and amlodipine to 10 mg. The heart rate in patients of this group before inclusion in the study and after 2 weeks of treatment was below 80 beats per minute. In the second group of the study, 26 patients out of 33 patients achieved the primary goal of controlling blood pressure (less than 140/90 mm Hg), and 22 patients achieved decrease in resting heart rate below 80 beats per minute after 2 weeks of treatment. In this connection, in the future, in patients who did not reach the target level of blood pressure and/or heart rate, the dose of bisoprolol was increased to 10 mg and / or amlodipine to 10 mg.

Follow-up visits after 4 and 8 weeks showed that the use of triple therapy by the end of the 8th week of treatment allowed the patients of group 1 to achieve a blood pressure level of less than 140/90 mm Hg in 26 (89.6%) patients. Subsequently, a fourth reserve antihypertensive drug was added to 3 patients. In the 2nd group of the study, dose adjustment of one or two components of antihypertensive therapy by the end of the 8th week of treatment made it possible to achieve a blood pressure level of less than 140/90 mm Hg in 31 (93.9%) patients, heart rate was less than 80 and less than beats per minute in all studied patients. Subsequently, a fourth reserve antihypertensive drug was also added to 2 patients of this group.

Analysis of daily blood pressure indicators after 8 weeks of treatment showed that in both study groups, the achievement of office blood pressure control was accompanied by a statistically significant decrease in all daily blood pressure indicators (table 2).

Against the background of therapy in both groups, there was also a significant decrease in most

Table 2

Indicators of daily monitoring of 24-hour blood pressure before treatment and during therapy

Indicators blood pressure	I Group (n=29)		II Group (n=33)	
	before treatment	during therapy	before treatment	during therapy
Systolic blood pressure				
24-hour	140.23±1.6	118.84±1.23*	139.34±1.23	121.21±1.28*
day	144.51±1.23	122.79±1.58*	142.35±1.36	125.25±1.38*
night	135.21±1.34	110.57±2.05*	134.25±1.34	115.94±1.87*
Diastolic blood pressure				
24-hour	88.31±1.32	74.95±0.94*	87.34±1.35	72.16±1.2*
day	86.45±1.34	78.75±1.25*	88.11±1.34	75.25±1.38*
night	80.31±1.24	67.61±1.26*	80.54±1.53	66.34±1.59*
Average blood pressure				
24-hour	100.23±1.3	89.57±1.23*	102.12±1.51	88.56±1.18*
day	105.67±1.34	93±1.28*	107.12±1.23	91.59±1.21*
night	98.31±1.23	81.54±1.44*	96.78±1.52	82.44±1.43*

Note: ** - p<0.05 in relation to the indicators before treatment*

TABLE 3

Blood pressure variability before and during therapy

Indicators blood pressure	I Group (n=29)		II Group (n=33)	
	before treatment	during therapy	before treatment	during therapy
Variability systolic blood pressure				
24-hour	17.64±0.98	11.82±0.75	17.38±0.72	12.41±0.53***
day	17±1.1	11.34±0.57	16±1.22	11.34±0.57***
night	13.9±1.44	11.97±0.85	12.65±0.93	10.97±0.85
Variability diastolic blood pressure				
24-hour	13.21±0.67	9.88±0.52***	13.46±0.83	9.88±0.52***
day	15.33±0.73	10.28±0.71***	15.3±0.97	8.88±0.66***
night	9.94±0.98	7.31±0.74**	9.32±0.72	7.21±0.58**
Variability pulse blood pressure				
24-hour	17.76±0.7	8.7±0.59*	17.84±0.62	8.5±0.49*
day	10.82±0.82	8.58±0.5	10.81±0.73	8.63±0.56
night	12.71±0.71	9.45±0.6	11.87±0.83	9.53±0.69

*NOTE: *** p<0,001 ** p<0,005 *p<0,05*

indicators of variability blood pressure (table 3).

In both study groups, the indicators of diastolic blood pressure variability significantly decreased both in general for 24 hours and during the day and night periods, as well as the variability of pulse pressure. In the second group of the study, there was also a significant decrease in the variability of systolic blood pressure both in general per day and during the daytime period.

Against the background of antihypertensive therapy in both groups of the study, there was a significant and reliable ($p<0.05$) increase in all parameters for assessing the quality of life, which reflects the effectiveness of the treatment of hypertension in patients who underwent coronavirus infection in increasing satisfaction with their lives and improving social functioning. Data on the dynamics of quality of life indicators against the background of ongoing treatment are presented in table 4.

Against the background of the therapy in the two study groups, the indicator of the general state of health did not differ significantly ($p>0.05$). Analyzing the significance of differences in the effectiveness of therapy, we found a significantly ($p<0.05$) more pronounced increase in the parameters of role functioning due to the physical and emotional components of health, social functioning and mental health in patients of the II group of the study. In this group, the assessment of pain intensity and vital activity during treatment also revealed a significantly ($p<0.05$) more significant increase in comparison with patients of I group, which characterizes the high efficiency of combination therapy using a beta-blocker in increasing the social activity of patients and improving somatic health of patients with coronavirus infection.

Integral indicators of QoL, reflected in the form of summing scales characterizing physical and mental health, are presented in table 5.

Against the background of antihypertensive therapy in two groups, the parameters of the men-

TABLE 4.

Assessment of quality of life under the influence of various variants of combined antihypertensive therapy

Scales (points)	I Group (n=29)		II Group (n=33)	
	Before	During	Before	During
Physical functioning	38.43±3.41	45.43±3.17*	37.78±3.47	63.47±3.52#
Role functioning due to physical condition	17.86±3.89	45.00±5.47*	17.36±3.81	78.47±4.16#
Pain intensity	39.61±3.99	48.44±2.85*	38.65±4.34	65.22±3.16#
General health	31.03±2.32	39.00±2.98*	31.14±3.56	41.83±2.39#
Vital activity	33.71±2.39	43.14±2.50*	33.19±2.71	57.64±2.72#
Social functioning	40.00±4.19	55.71±3.07*	39.93±4.30	67.36±2.52#
Role functioning due to emotional state	20.00±4.34	59.05±5.32*	19.44±4.45	70.37±5.70#
Mental health	41.71±2.75	47.66±2.56*	40.78±2.74	60.67±2.76#

NOTE: 1)*- $p<0.05$ in relation to the indicators before treatment in I group 1; 2) # - $p<0.05$ in relation to the indicators before treatment in II group.

Table 5.

Assessment of the physical and mental components of health during treatment in patients with arterial hypertension

	I Group 1n=29)		II Group (n=33)	
	Before treatment	During treatment	Before treatment	During treatment
The physical component of health	43.21±1.50	44.40±1.61	42.77±1.46	50.13±1.51*#
Mental component of health	33.46±1.63	41.06±1.58*	33.32±1.57	46.50±1.44*#

Note: *1) *- p<0.05 in relation to the indicators before treatment in two groups; 2) # - p<0.05 in I and II groups during therapy.*

tal component of health improved significantly (p<0.05), while in II group, during treatment, we revealed a significantly (p<0.05) higher indicator of the mental component, which possibly reflects better tolerance and comfort when taking a combination of perindopril, bisoprolol, amlodipine. The assessment of indicators of the physical component of health in I group did not reveal significant differences before treatment and against the background of antihypertensive therapy, and in II group, treatment with hypertension was accompanied by a significant (p<0.05) improvement in the physical component of health, while the assessment of the physical component in group 1 was significantly (p<0.05) lower than in II group (in I group - 44.40±1.61 points, in II group - 50.13±1.51 points, p<0.05).

Most of the patients included in the study reported good tolerability of the treatment. There were no significant side effects that required discontinuation of ongoing therapy in patients included in the study. After 8 weeks of observation, high adherence to the use of triple therapy was maintained.

Conclusion:

In patients with uncontrolled arterial hypertension who underwent coronavirus infection, the use of the analyzed three-component therapy options - perindopril / indapamide / amlodipine and perindopril / bisoprolol / amlodipine, made it possible to achieve the target level of blood pressure in 89.6% and 93.9% of cases of observation, respectively.

In both study groups, the achievement of office blood pressure control was accompanied by a statistically significant decrease in all its daily indicators.

Against the background of antihypertensive therapy in both groups of the study, there was a significant and reliable (p<0.05) increase in all parameters for assessing the quality of life, which reflects the effectiveness of the treatment of arterial hypertension in patients who have undergone coronavirus infection in increasing satisfaction with their lives and improving social functioning.

Therapy with the use of perindopril, bisoprolol, amlodipine was accompanied by the achievement of significantly (p<0.05) higher rates of mental and physical health components.

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