ORIGINAL ARTICLE

TREATMENT OPTIMIZATION IN MANAGEMENT OF COMBINED PATHOLOGY – ARTERIAL HYPERTENSION AND POST-COVID SYNDROME IN ELDERLY PATIENTS

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ABSTRACT

The aim: Purpose of the study. Our research is aimed at the increase in the treatment effectiveness for combined pathology, namely, arterial hypertension (AH) and post-COVID syndrome in elderly patients at the stage of providing medical care by family medicine general practitioners with the use of statins, antiplatelet agents, as well as endothelial-protective drug – L-arginine and anxiolytic effect – mebicar against the background of basic antihypertensive therapy.

Materials and methods: The study included treatment and observation of 50 elderly patients with hypertension and post-COVID syndrome. The average age was 68.7±1.89 years.

Results: The use of mebicar with moderate tranquilizing (anxiolytic) effect and endothelium-protector – L-arginine in the comprehensive treatment of elderly patients with combined pathology – AH and post-COVID syndrome contributed to the elimination of the main clinical symptoms (headache, poor sleep) in a shorter time; provided significant decrease in the level of systolic blood pressure, reactive anxiety, the decrease in total blood cholesterol, and improvement in blood rheology.

Conclusions: Treatment optimization for combined pathology – arterial hypertension and post-COVID syndrome in elderly patients with the use of L-arginine and mebicar in comprehensive treatment, improves the quality of patients' life, reduces the treatment duration.

KEY WORDS: arterial hypertension, L-arginine, post-COVID syndrome, mebicar

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INTRODUCTION

Despite the significant progress in understanding epidemiology, pathophysiology and risks associated with the increased blood pressure, arterial hypertension (AH) remains a serious global problem [1]. The prevalence of hypertension in people of retirement age exceeds the average by 1.8 times [2,3]. According to the World Health Organization, the number of elderly and senile people will increase to almost 40% over the next decades [4,5]. At the same time, coronavirus disease (COVID-19) is the extremely serious problem in connection with pandemic in the world. The causative agent of coronavirus infection (COVID-19), as a rule, severely affects elderly patients over 65 years of age [6]. Moreover, patients after the acute phase of COVID-19 present with the signs of chronic disease exacerbations, the increase in the severity of functional and morphological disorders experienced before the onset of coronavirus infection [7]. The relevance of the problem consists in unclear understanding the ways and approaches in diagnosis and management of post-COVID syndrome [7]. Post-COVID syndrome is characterized by complaints of constant fatigue, anxiety and weakness. More often post-COVID syndrome manifests in the form of lung damage, mental disorders and asthenia [8-10]. Currently, the treatment of post-COVID syndrome in patients with cardiovascular pathology becomes the urgent issue, especially in the family medicine practice. The main pathomorphological process and the trigger mechanism of post-COVID syndrome is endotheliitis, resulting from direct infection of endothelial cells by SARS-CoV-2 virus (or indirect – by cytokines and free radicals through immune responses) which causes the development of generalized endothelial dysfunction, that in turn disrupts microcirculation, vasoconstriction and leads to the further development of organ ischemia, inflammation and tissue edema, transition of the smoldering systemic inflammation to post-COVID syndrome [8,10]. AH destroys the architectonics of endothelial cells followed by the increased production of vasoconstrictor endothelin-1 and vascular remodeling

with the decrease in vascular elasticity [11]. It should be noted that L-arginine (Tivortin aspartate) not only improves the condition of the endothelium, but also reduces the manifestations of systemic inflammation and oxidative stress, the formation of post-COVID syndrome. [8]. L-arginine is a conditionally essential amino acid, which is an active and multifaceted cellular regulator of many essential functions in the organism, plays antihypoxic, membrane stabilizing, antioxidant and detoxification actions [12]. Currently, it has also been proven that morbidity and mortality from cardiovascular diseases are largely associated with psychological factors, in particular, a significant prevalence of depression and anxiety symptoms has been detected among patients with AH [13]. The data of recent studies suggest that long-term psychological stress caused by activation of the hypothalamic-pituitary-adrenal axis, low-intensity inflammation, leads to endothelial dysfunction and steady increase in the blood pressure (BP) [13]. According to research data, in patients with arterial hypertension, the frequency of anxiety disorders was 1.5 times higher than in patients with normal blood pressure [1]. Therefore, the comprehensive treatment of such patients should include drugs with tranquilizing effect which reduce the anxiety. In clinical practice, they use mebicar (adaptol) for astheno-vegetative syndrome elimination. It has moderate tranquilizing (anxiolytic) effect, relieves the feelings of anxiety, fear, internal emotional stress and irritation [14].

THE AIM

Purpose of the study. Optimization of treatment and improvement of the quality of life of elderly patients with combined pathology – arterial hypertension (AH) and post-covid syndrome by general practitioners of family medicine with the use of additional drugs – with the endothelium-protective effect of L- arginine and mebicar with a sedative effect.

MATERIALS AND METHODS

The research presented includes observation and treatment of 50 elderly patients for hypertension with post-COVID syndrome. The average age was 68.7±1.89 years. The diagnosis was verified on the basis of complaints, anamnesis data (coronavirus disease (COVID-19) experienced over the past 3-6 months), physical examination, general clinical and laboratory-instrumental methods (complete blood count, ECG, echocardiography CS, CRP, coagulograms, lipidograms, urea, residual nitrogen). The study included elderly patients experiencing hypertension with post-COVID syndrome with preserved ejection fraction (EF) of the left ventricle (40%). All patients underwent a preliminary screening test for SARS-CoV-2 antigen using rapid tests for SARS-CoV-2 antigen, a negative result was obtained, which ruled out recurrence of COVID-19. The psychological state of elderly patients with comorbid pathology – hypertension and COPD – was assessed with Ch. D. Spielberger – Yu. L. Khanin questionnaire [14,15]. When interpreting the test results, they use the following scores: less than 30 points – low anxiety; 31-45 points – moderate anxiety; 46 or more points – high anxiety.

The life quality assessment at the beginning and during the treatment was conducted applying SF-36 questionnaire which is considered the“gold standard” [3]. The SF-36 questionnaire has 3 levels: 1) questions; 2) 8 scales; 3) 2 total measurements combining the scales. There are 36 questions in the questionnaire, 35 of which are used to process scores according to 8 scales, which are grouped into two general indicators: “Physical component of health”, including scales: General health (GH); Physical functioning (PF); Role Physical Functioning (RP); Pain intensity (Bodily pain – BP); and “Psychological component of health”, including scales: Mental Health (MH); Vitality (VT); Role functioning caused by emotional state (Role-Emotional – RE); Social Functioning (SF) [16]. Each scale has a different number of questions. The indicators of each scale fluctuate between 0 and 100 points (relative units), where 100 represents full health. One question of the questionnaire (number 2), concerning comparison of the health state at a given time with the previous year, does not belong to any scale and is assessed separately. The SF-36 questionnaire makes it possible to quantify QoL according to the indicated scales [3].

The patients were distributed into two groups: the first – control group (n=25) – was prescribed comprehensive basic antihypertensive therapy, statins, antiplatelet agents (telmisartan/amlodipine, rosuvastatin, cardiomagnyl). The second group – the main group (n=25) was prescribed the basic therapy and, additionally, solution of L-arginine 4.2%, 10 ml 2 times a day as well as mebicar 500 mg, 1 tablet 2 times a day. The groups were age and gender comparable. The observation period lasted 1 month.

The survey data were processed considering the special algorithm developed for assessing QoL according to SF-36. These data are presented in the middle and standard pardon of the middle. In order to directly establish the nature of the interrelationship, we performed a correlation analysis between groups of inde-

Table I. Clinical indicators in patients of the main and control groups

Indicators	Control group		Main group	
BP systolic mm.Hg	179.8±1.52*	134.1±1.23	177.9±1.02*	128.6±1.28**
BP Diastolic mm.Hg	95,13±3.22*	76.0±3.7	95,27±3.24*	69.6±4.33
RA points	48.4±1.24*	42.93±1.13	48.13±1.36*	39.22±1.41**
APTT sec.	19.87±1.01	22.96±2.01	19.64±0.86*	25.49±1.81
Total cholesterol mmol/l	4.83±0.4	3.97±0.22	4.75±0.30*	3.81±0.17

* p<0.05 - differences are significant between groups of patients before and after treatment;
** p<0.05 - differences are significant between the patients of the main and control groups after treatment.

Table II. Indicators of the quality of life of elderly patients with AH and post-COVID syndrome (main and control groups)

Questionnaire scales SF 36	Control group		Main group	
	Before treatment	After treatment	Before treatment	After treatment
1. General health - GH	24,07±2,52*	36,17±3,17	25,53±2,38*	39,6±4,01
2. Role-Physical Functioning - RP	24,73±2,12*	37,63±2,68	24,84±2,53*	40,13±3,17
3. Physical Functioning - PF	22,27±4,55*	35,6±3,64	26,07±4,02*	38,79±3,49
4. Bodily pain - BP	24,73±3,195*	35,33±1,98	26,73±2,98*	42,73±2,31**
5. Vitality - VT	24,53±3,48*	36,93±2,34	25,67±2,58*	43,22±2,17
6. Role-Emotional - RE	25,47±2,97 *	37,53±2,85	26,3±1,97*	41,82±2,12
7. Mental Health - MH	27,4±3,01*	35,13±2,13	26,93±2,98*	44,6±3,04**
8. Social Functioning - SF	28,27±4,16	37,07±1,71	26,47±2,72*	42,51±1,95**

*p<0.05 - differences are significant between groups of patients before and after treatment;
** p<0.05 - differences are significant between the patients of the main and control groups after treatment.

pendent samples with a match coefficient Spearman correlations. statistical significance intergroup viability was assessed using the Mann-Whitney method. Statistical analysis were carried out with the help of the program «Statistica 6.0» (StatSoft Inc., USA, serial No. RGXR412D674002FWC7). For all types of analysis, the statistically significant values were taken into account with equal significance less than 0.05.

RESULTS

The comparative analysis of the main clinical and laboratory parameters determined that patients of the main group who received L-arginine and mebicar against the background of basic therapy had significant differences in the timing of headache subsiding, sleep improving, decrease in BP as well as the level of reactive anxiety (RA), decrease in the level of total cholesterol in the blood (p<0.05) compared with the control group of patients. Thus, the average time for headache subsiding in patients of the main group was 6.4±0.79 days versus 8.83±0.71 days in patients of the control group (p<0.05); sleep normalization – 7.0±0.73 days versus 9.3±0.77 days in patients of the control group (p<0.05). The data obtained convincingly indicate that the comprehensive antihypertensive therapy which includes the use of L-arginine and mebicar contributed to a more rapid elimination of clinical manifestations when managing the combined pathology – hypertension and post-COVID syndrome in elderly patients.

Patients of the main group had significant decrease in systolic blood pressure (SBP) compared with patients in the control group (p<0.05). Thus, in patients taking L-arginine and mebicar in addition to treatment, SBP decreased by 32.4% (from 177.9±3.98 to 120.3±1.79 (p<0.05), while in patients of the control group – by 29.9% (from 179.8±5.9 to 126.1±2.29 mm Hg (p<0.05). Diastolic blood pressure (DBP) decreased by 27% in the main group patients (from 95.27 ± 3.24 to 69.6±4.33 (p<0.05), while in patients of the control group – by 20.11 % (from 95.13±3.22 to76.0±3.7) (p<0.05). The research data indicate that the comprehensive therapy which includes L-arginine contributed to the increase in endothelium-dependent vasodilation, which coincides with the authors' opinion [13,16].

The examination data determined that the elderly patients with hypertension and post-COVID syndrome presented with the high level of reactive anxiety (RA), which changed during treatment. The main group patients

developed more significant decrease in RA ($p<0.05$) during the treatment compared with the control group patients. Thus, in the main group patients, the level of RA decreased by 18.6% (from 48.13±1.36 to 39.22±1.41) ($p<0.05$) ($p<0.05$), while in the control group patients – by 11.7% (from 48.4±1.24 to 42.73±1.48) ($p<0.05$). The data obtained make it possible to state that reactive anxiety is a very mobile trait and is characterized by reversibility upon normalization of the somatic state of a person [17]. The main group patients developed significant increase in APTT level after therapy, namely, by 29,7% (from 19.64±0.86 before treatment; 25.49±1.81 – after therapy) ($p<0.05$), which indicates the improvement in blood rheology and a positive effect on the anticoagulant system parameters. While in the control group patients, APTT increased insignificantly by 11.5% (from 19.87±1.01 to 22.96±2.01) ($p>0.05$).

After treatment, the main group patients presented with significant decrease in the level of total cholesterol by 19,8% (from 4.75±0,30 mmol/l to 3.81±0,17 mmol/l) ($p<0.05$), while the cholesterol level did not decrease significantly in the control group patients, namely, by17.81% (from 4.83±0.4 to 3.97±0.22) ($p>0.05$). The decrease in cholesterol level ($p<0.05$) indicates the positive effect of L-arginine on lipid metabolism, which coincides with the scientists' view [18]. The data of research are presented in the Table I. Considering that the ultimate goal of any therapy is to increase the life expectancy of patients and improve its quality, we studied QoL of patients before and after the course of therapy. The data obtained are presented in Table II.

DISCUSSION

After comprehensive treatment, compared to the control group, patients in the main group showed a significant increase in indicators, according to the following scales: Pain intensity (Bodily pain – BP), Mental Health (MH), Social Functioning (SF). ($p<0.05$), which indicates a significant improvement in the quality of life in this category of patients.

There were correlative dependences between the levels of systolic BP and RA in the main group patients ($r=0.392$; pbefore treatment, which proves the expediency of applying the drug with a moderate tranquilizing (anxiolytic) effect – mebicar and endothelial protector – L-arginine in the comprehensive treatment of elderly patients with combined pathology – hypertension and post-COVID syndrome.

Thus, comprehensive examination of elderly patients with combined pathology – hypertension and post-COVID syndrome using questionnaires – Ch.D. Spielberger – Y.L. Khanin, and the SF-36 questionnaire, allows to assess the level of reactive anxiety, the quality of life in this category of patients, with the aim of developing a rational complex therapy.

Given the important role of endothelial nitric oxide production disorders in the pathogenesis of hypertension, the feasibility of using drugs that are its donors is justified. Such drugs include L-arginine [19,20]. L-arginine can be recommended for the purpose of: normalizing high blood pressure; prevention of the formation and development of atherosclerotic plaques and normalization of elevated cholesterol levels; protection of the heart and blood vessels in conditions of oxidative stress; reducing the risk of thrombosis; maintenance of normal blood circulation and oxygen supply to various organs and tissues; general strengthening of the body and improvement of immunity; improvement of microcirculation in the tissues of the central nervous system, which enhances the metabolism in neurons, contributes to the improvement of cognitive functions – memory, attention, mental activity [19] .

The results of the conducted research allow us to recommend L-arginine in the complex treatment of elderly patients with combined pathology – hypertension and post-covid syndrome.

At the same time, in the treatment of psychosomatic disorders and the normalization of the body's adaptive capabilities in a wide range of pathological conditions, according to the data of scientists, the use of the drug mebikar is justified. According to the results of the authors' research [14, 21] mebikar helps to reduce anxiety symptoms, it also has an antihypertensive effect, which makes it possible to recommend mebikar in the complex treatment of elderly patients with combined pathology – hypertension and post-covid syndrome.

The results of the conducted studies show that the optimization of the treatment of elderly patients with combined pathology – arterial hypertension and post-covid syndrome with additional use of drugs – L-arginine and mebikar use on the background of basic therapy contributed to the improvement of the quality of life of patients and due to:

- elimination of the main clinical manifestations in a shorter time: (the average duration of headache cessation in patients of the main group was 6.4±0.79 days, against 8.83±0.71 days in patients of the control group ($p<0.05$) average terms of normalization of sleep – 7.0±0.73 days, against 9.3±0.77 days in patients of the control group ($p<0.05$);
- more significant decrease in the level of systolic blood pressure by 32.4%, (while in patients of the control group – by 29.9%) ($p<0.05$).

– more significant reduction in the level of reactive anxiety by 18.6%, (while in patients of the control group – by 11.7%) ($p<0.05$),

– a significant increase in the level of PT – by 29.7% ($p<0.05$), a significant decrease in the level of total cholesterol by 19.8% ($p<0.05$), while in patients of the control group these indicators improved without statistical significance.

Positive clinical dynamics in patients who received complex therapy with the use of L-arginine and mebicar contributed to shortening the duration of treatment by 1.8 days.

CONCLUSIONS

Optimization of treatment of combined pathology – arterial hypertension and post-covid syndrome in elderly patients with additional use of L-arginine and mebicar drugs to the basic therapy contributes to the improvement of the quality of patients life, due to the regression of the main clinical manifestations of the disease in a shorter time, a significant decrease in the level of blood pressure and reactive anxiety, shortening the period of treatment of patients.

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