Chapter 23

EVALUATION OF THE EFFECTIVENESS OF COMPLEX TREATMENT OF PATIENTS WITH ARTERIAL HYPERTENSION WITH CONCOMITANT CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Voloshyna O. B., Nazaruk T. O., Zbitnieva V. O.
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INTRODUCTION

The prevalence of arterial hypertension (AH) worldwide is high and continue storise rapidly[1]. According to the World Health Organization, chronic obstructive pulmonary disease (COPD) is the third leading cause of death worldwide, causing 3.23 million deaths in 2019[2].

The combination of hypertension with COPD is associated with an increased risk of cardiovascular complications[3]. COPD is diagnosed in every fourth patient with hypertension aged from 25 to 64 years, which necessitates early diagnosis, treatment and rehabilitation of a patient with this comorbid pathology.

The frequent combination of AH and COPD causes a number of difficulties in choosing therapy in this category of patients, in particular due to the need to choose anti-hypertensive and bronchodilator drugs more carefully and to assess the effectiveness of complex treatment[4].

[1] Williams B. et al. 2018 ESC/ESH Guidelines for the management of arterial hypertension: The Task Force for the management of arterial hypertension of the European Society of Cardiology (ESC) and the European Society of Hypertension (ESH). European Heart Journal. 2018. №39(33). P. 3021-3104. https://doi.org/10.1093/eurheartj/ehy339

[2] Global Initiative for Chronic Obstructive Lung Diseases (GOLD) Global strategy for diagnosis, management, and prevention of chronic obstructive pulmonary disease [updated 2023]. URL: https://goldcopd.org/wp-content/uploads/2023/03/GOLD-2023-ver-1.3-17Feb2023_WMV.pdf

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[4] Feshchenko Yu.I., Gavrisyuk V.K., Dzublik O.Ya., Mostovoy Y.M., Pertseva T.O., Polyanska M.O., Yachnik A.I., Yashina L.O. Adapted clinical setting: chronic obstructive pulmonary disease (Part 1). *Ukrainian Pulmonary Journal.* 2019. №2. P. 5-17. DOI:10.31215/2306-4927-2020-109-3-5-36

Current international guidelines for the treatment of internal diseases emphasize the need to improve the quality of life of patients as a result of effective comprehensive treatment.

1. The problem's prerequisites emergence and the problem's formulation

The improvement of the complex treatment of this comorbid pathology is associated with the use of drugs that can further improve the functionality of the cardiorespiratory system due to the multifactorial effect on various physiological functions and on the links of the pathogenesis of all diseases and improve the quality of life of these patients[5]. In view of this, several publications on the effectiveness of the use of magnesium compounds in the treatment of patients with various pathologies are noteworthy[6].

Magnesium is a natural calcium antagonist, glutamate NMDA receptor blocker, which explains its vasodilating, antioxidant, anti-inflammatory, vegetative-regulating effect[7]. The positive effects of magnesium have been attributed to its effects on physiological functions such as impulse conduction, blood pressure, heart rate, and muscle contraction[8].

The use of magnesium compounds in patients with arterial hypertension is associated with its multifactorial positive effect on smooth muscle cells, endothelial dysfunction, renin-aldosterone-angiotensin system, reduced sensitivity of the cardiovascular system to catecholamines, etc. Studies show that the use of various magnesium compounds is accompanied by a decrease in blood pressure (systolic – by 1.3–5.6 mm Hg, diastolic – by 1.4–3.4 mm Hg)[9].

Hypomagnesemia has been found to be one of the significant risk factors for COPD exacerbations[10].

In recent years, there have been several publications on the effectiveness of magnesium compounds in the treatment of patients with COPD. In particular, in a randomized, double-blind, placebo-controlled, cross over study

[5] Hogea S.P., Tudorache E., Fildan A.P., Fira-Mladinescu O., Marc M., Oancea C. Risk factors of chronic obstructive pulmonary disease exacerbations. Clin Respir J. 2020. №14. P. 183-197. DOI: 10.1111/crj.13129

[6] Makwana S., Patel A., Sonagara M. Correlation between serum magnesium level and acute exacerbation in patients with chronic obstructive pulmonary disease (COPD). Cureus. 2022. №14(6). doi:10.7759/cureus.26229

[7] Mathew A.A., Panonnummal R. 'Magnesium'-the master cation-as a drug-possibilities and evidences. Biometals. 2021. №34(5). P. 955-986. doi:10.1007/s10534-021-00328-7

[8] Blitz M., Blitz S., Hughes R. et al. Aerosolized magnesium sulfate for acute asthma: a systematic review. Chest. 2005. №128(1). P. 337-344. doi:10.1378/chest.128.1.337

[9] Voloshyna O.B. Vegetative dysfunctions after infections and possibilities of their correction in general practice (literature review). Family medicine. 2019. №1. P. 52-61. URL: http://nbuv.gov.ua/UJRN/simmed_2019_1_10

[10] Do Amaral A.F., Rodrigues-Júnior A.L., Terra F.J., Vannucchi H., Martinez J.A. Effects of acute magnesium loading on pulmonary function of stable COPD patients. Med Sci Monit. 2008. #14(10). URL: https://pubmed.ncbi.nlm.nih.gov/18830192/

in which 22 male COPD patients (64+/-6 years, FEV1: 49+/-20%) received an intravenous infusion of 2 g of magnesium sulfate or placebo. Intravenous administration of Mg in stable patients with COPD resulted in improvements in lung function and respiratory muscle strength[11].

A literature review analyzed the results of 10 double-blind, placebo-controlled clinical trials conducted in 7 countries from 2004 to 2018, which investigated the efficacy of intravenous or nebulizer magnesium sulfate (MS) in patients with COPD. It was found that MS infusions led to a decrease in the duration of hospital stay by an average of 2.7 days, reduction of dyspnea. The combined use of MS infusions plus MS nebulizer administration did not differ in effectiveness from the nebulizer administration of ipratropium and was accompanied by a decrease in the severity of dyspnea and the need for bronchodilators[12].

In a recently published study was shown that hypomagnesemia was reported in 57% of patients with exacerbation of COPD. The duration of hospital stay (more than seven days) in patients with hypomagnesemia (80.7%) was significantly higher than in patients with normomagnesemia (55.8%). The authors concluded that hypomagnesemia is common in acute exacerbations of COPD. Detectable magnesium levels are associated with length of hospital stay but are not associated with mortality in patients with exacerbations. The use of magnesium compounds in patients with arterial hypertension is associated with its multifactorial positive effect on smooth muscle cells, endothelial dysfunction, renin-aldosterone-angiotensin system, reduced sensitivity of the cardiovascular system to catecholamines, etc. In addition, the use of various magnesium compounds is accompanied by a decrease in blood pressure (systolic – by 1.3–5.6 mm Hg, diastolic – by 1.4–3.4 mm Hg)[13].

2. Analysis of existing methods of solving the problem and formulation of proposals for the optimal solution of the problem of assessing the effectiveness of complex treatment of comorbid pathology

The analysis of available publications related to the assessment of the effectiveness of complex treatment of this comorbid pathology indicates the need to reduce the frequency and intensity of clinical symptoms, increase the

[11] Nazaruk T.O. The effectiveness of the use of magnesium compounds in the complex treatment of patients with arterial hypertension with concomitant chronic obstructive pulmonary disease. Lviv Clinical Bulletin. 2023. No. 3-4 (43-44). P. 24-28. http://dx.doi.org/10.25040/lkv2023.03-04.024

[12] Ni H., Aye S.Z., Naing C. Magnesium sulfate for acute exacerbations of chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2022. № 5(5). doi:10.1002/14651858.CD013506.pub2

[13] Makwana S., Patel A., Sonagara M. Correlation between serum magnesium level and acute exacerbation in patients with chronic obstructive pulmonary disease (COPD). Cureus. 2022. №14(6). doi:10.7759/cureus.26229

functionality of the cardiorespiratory system, which leads to an improvement in the quality of life of patients. In particular, it was established that there is a relationship between the level of blood pressure and the functional state of the respiratory system[14].

The main goal of pulmonary rehabilitation for COPD, according to GOLD, is to reduce symptoms, improve quality of life, physical and emotional participation in daily activities. Pulmonary rehabilitation covers a number of non-pulmonary problems that are not addressed by COPD drug therapy, including intolerance of physical exertion, relative social isolation, deterioration of mental health (especially depression), muscle loss, and weight loss[15].

The results of some studies show that pulmonary rehabilitation in patients with hypertension with concomitant COPD not only improves the functional state of the lungs, but also helps to reduce blood pressure and vascular stiffness[16].

A review of retrospective cohort study[17] involving 2962 patients with COPD II and III and comorbidities, including 61% of patients with arterial hypertension was carried out. Age, sex, FEV1, respiratory function evaluation questionnaire of the hospital of St. George (SGRQ) and modified shortness of breath questionnaire (MRC), 6-minute walk test, Charlson comorbidity index were assessed. Although comorbidities in no way interfered with pulmonary rehabilitation in this group of patients, less than half of the patients had positive results. Researchers attribute this to the aggravating course of hypertension and COPD.

It is important to note that the use of β-adrenomimetics in patients with COPD can lead to hypomagnesemia. Therefore, patients with COPD may be recommended to use magnesium supplements, preferably in the form of vitamin-mineral complexes[18]. The use of magnesium preparations is also

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[18] Durlach J., Pagès N., Bac P., Bara M., Guiet-Bara A. Beta-2 mimetics and magnesium: true or false friends?. Magnes Res. 2003. №16(3). P. 218-233. URL: https://pubmed.ncbi.nlm.nih.gov/14596327/

advisable in patients taking M-cholinolytics. The addition of magnesium to the complex therapy of COPD cannot only reduce the negative effect of these drugs on the state of cardio-vascular system, but also reduce the clinical manifestations of COPD, increase tolerance to physical exertion, improve bronchial patency and indicators of external respiration: FEV1 and FEV1/FVC[19].

To diagnose and assess the effectiveness of treatment of comorbid pathology, it is important to use adequate functional tests that allow you to assess the general state of the body, its reserve capabilities, determine the features of adaptation to physical activity and identify hidden disorders of the functions of organs and systems[20].

To determine the functional state of the respiratory system, determine sensitivity to hypoxia, hypercapnia and volitional qualities of the patient, the Stange test (voluntary breath retention on inspiration) or the Genchi test (breath retention on exhalation) are used[21]. The adaptation of the respiratory system to physical activity is more often determined using the Serkin test[22], which allows you to assess the duration of breath holding, namely: after 5 minutes of rest in a sitting position, after a standardized load (20 squats in 30 seconds) and in a standing position for 1 minute of rest.

However, while allowing for a partial assessment of the function of the respiratory system, these tests in no way allow to assess the body's hemodynamic reserves in response to physical exertion.

To determine the level of physical performance and impaired tolerance to physical exertion in patients with concomitant pathology of hypertension and COPD, it is advisable to use cardiopulmonary tests with physical activity. The easiest to perform and do not require complex equipment are functional tests with walking: samples with 12, 9, 6, 5 and 2-minute walking, tests with a fixed distance, tests with a given walking speed (shuttle test with an increasing

[19] Do Amaral A.F., Rodrigues-Júnior A.L., Terra F.J., Vannucchi H., Martinez J.A. Effects of acute magnesium loading on pulmonary function of stable COPD patients. Med Sci Monit. 2008. #14(10). URL: https://pubmed.ncbi.nlm.nih.gov/18830192/

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walking pace)[23]. The most common of these is the 6-minute walk test[24]. However, the assessment of the distance in these samples allows us to determine only the submaximal tolerance of physical activity for the performance of daily functions, so it in no way provides information directly about the state of the respiratory and cardiovascular systems.

Until recently, it was believed that the 6-minute walk test (6 MW) more accurately reflects the state of functional physical activity in patients with COPD than the 2-minute walk test (2 MW)[25].

Despite the fact that this test is quite simple to perform, it does not control the respiratory rate and cardiovascular rate, so it is not suitable for patients with concomitant pathology of hypertension and COPD.

In sports medicine, to determine the ability of the cardiovascular system to recover after physical exertion, a standardized test with physical activity is widely used – a test with a squat (Martine-Kushelevsky), in which only one degree of load is used – 20 squats in 30 seconds[26].

However, this test only determines the response of the cardiovascular system in indicators of blood pressure and heart rate and does not take into account the indicators of the respiratory system. In addition, the average level of physical activity (20 squats) may be too high for patients with cardiorespiratory pathology.

To assess the function of the respiratory system, the spirometry method is used, including in outpatient practice. This method is used mainly for diagnosing the presence of bronchial obstruction, and for differential diagnosis of bronchial asthma and chronic obstructive pulmonary disease (with salbutamol). It is important that the determination of forced expiratory volume in 1 second (FEV1) by this method is recommended to be carried out at rest.

However, the use of spiroergometry, i.e. simultaneous veloergometry and spirometry, is limited by the simultaneous availability of expensive equipment and cannot be widely used in outpatient practice. With this in mind, we have

[23] Vagaggini B., Taccola M., Severino S. etal. Shuttle walking test and 6-minute walking test induce a similar cardiorespiratory performance in patients recovering from an acute exacerbation of chronic obstructive pulmonary disease. Respiration. 2003. №70(6). P. 579-584. doi:10.1159/000075202

[24] Carter R., Holiday D.B., Nwasuruba C., Stocks J., Grothues C., Tiep B. 6-minute walk work for assessment of functional capacity in patients with COPD. Chest. 2003. №123(5). R. 1408-1415. doi:10.1378/chest.123.5.1408

[25] Enright P.L. The six-minute walk test. Respir Care. 2003. №48(8). P. 783-785. URL: https://pubmed.ncbi.nlm.nih.gov/12890299/

[26] Sports medicine: Textbook for students and doctors/ edited by V.M. Sokruta. Donetsk: "Kashtan". 2013. 472 p.

proposed a new method for determining the cumulative adaptation of the cardio-respiratory system during physical exertion[27].

The implementation of this technique makes it possible to simultaneously assess both the function of the respiratory and cardiovascular systems, which is more acceptable in patients with concomitant pathology of arterial hypertension and COPD.

Taking into account the fact that there is a positive course of certain symptoms of comorbid pathology, accompanied by an improvement in quality of life, in particular physical performance, it would also be advisable to provide an objective assessment of changes in the main clinical and functional indicators of these diseases during physical exertion.

Aim. The aim of this study was to estimate the effectiveness of the complex treatment on clinical and functional parameters and quality of life of patients with arterial hypertension combined with COPD.

Material, methodology and methods. The study, the protocol of which was previously approved by the Commission on Bioethics of the Odessa National Medical University, was carried out on an outpatient basis of the outpatient department of the University Clinic ONMedU. The study included 60 women and men aged from 45 to 74 years with stage II arterial hypertension[28] with concomitant clinical group B COPD (GOLD 2) with a duration of both nosologies of at least 1 year based on inclusion and no exclusion criteria. Patients continued to receive basic treatment with antihypertensive and bronchodilator drugs at a stable dose that was not changed for 1 month prior to enrollment in the study. The mean age of patients with arterial hypertension with concomitant COPD was 64.32 ± 1.25 years.

The exclusion criteria were: myocardial infarction or stroke within the last 6 months; heart failure with reduced ejection fraction and functional class ≥ 3; severe COPD or infectious exacerbation of COPD; active chronic viral hepatitis with alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels three times higher than the normal limit; chronic renal failure with glomerular filtration rate below 60 ml/min; severe allergy or history of intolerance to the medications (or components) that patients are taking in this study; oncological diseases; other comorbidities in a state of exacerbation or decompensation.

[27] Voloshyna O.B., Dychko T.O., Lysiy I.S., Dukova O.R., Chaika A.O., Zbitneva V.O. Stalemate. for the invention 119478 Ukraine, IPC A61B 5/091 (2006.01) A61B 5/02 (2006.01) G01N 33/497 (2006/01). The method of complex diagnosis of adaptation of respiratory function and hemodynamics to dosed physical load. The applicant and patent owner is Odesa National Medical University. No. u2017 03987; statement 24/04/2017; published 25.06.2019, Bull. No. 12

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Patients with hypertension with concomitant COPD were divided into 2 subgroups, depending on the rehabilitation treatment: group 1 (control) – 30 patients received antihypertensive therapy (fixed combination of losartan 50–100 mg with hydrochlothiazide 12.5–25.5 mg), lipid-lowering therapy (atorvastatin 10 mg per day) and bronchodilator therapy (fixed combination of fenoterol hydrobromide 50 μg and ipratropium bromide 20 μg, 1 ing. 2 times a day and salbutamol as needed); Group 2 (main group) – 30 patients who, in addition to similar antihypertensive and bronchodilator treatment, additionally received a fixed combination of magnesium and vitamin B6 (MgB_6) (Mg – 47 mg and vitamin B6 – 5 mg) 2 tabs 2 times a day for 4 weeks. Patients were given recommendations for lifestyle and work correction, dosed physical activity.

In all patients, anamnesis, subjective and objective clinical parameters were analyzed, height and body weight were measured, tobacco smoking index was calculated, office blood pressure (BP) indicators were determined, clinical and biochemical laboratory blood tests were performed.

Electrocardiographic examination (ECG) at rest was performed in 12 conventional leads.

Spirometric examination was performed with the help of a computer spirograph "SpirobankG/MIR" (Italy) and its program equipment winspiro PRO. The reversibility of bronchial obstruction was determined using β 2-agonist salbutamol (400.0 μg). After spirometry, a thorough analysis of the results was carried out to determine the type of ventilation disorders.

The degree of impairment of the function of external respiration was determined according to the GOLD-2014 classification[29]. At $FEV_1/FVC<0.70$:

- GOLD 1 – $FEV_1>80\%$ of the proper values;
- GOLD 2 – $50\%<FEV_1<80\%$ of the proper values;
- GOLD 3 – $30\%<FEV_1<50\%$ of the proper values;
- GOLD 4 – $FEV_1\leq30\%$ of the proper values.

In all patients, the COPD Assessment Test (CAT) questionnaire[30] was used to determine the impact of COPD on their daily lives, to determine these verity of dyspnea – a modified scale of the British Medical Research Council (mMRC)[31].

[29] Global Initiative for Chronic Obstructive Lung Diseases (GOLD) Global strategy for diagnosis, management, and prevention of chronic obstructive pulmonary disease [updated 2023]. URL:https://goldcopd.org/wp-content/uploads/2023/03/GOLD-2023-ver-1.3-17Feb2023_WMV.pdf

[30] Global Initiative for Chronic Obstructive Lung Diseases (GOLD)/ Global strategy for diagnosis, management, and prevention of chronic obstructive pulmonary disease [updated 2018]. URL: https://goldcopd.org/wpcontent/uploads/2017/11/GOLD-2018-v6.0-FINAL-revised-20-Nov_WMS.pdf

[31] Global Initiative for Chronic Obstructive Lung Diseases (GOLD) Global strategy for diagnosis, management, and prevention of chronic obstructive pulmonary disease [updated 2023]. URL: https://goldcopd.org/wp-content/uploads/2023/03/GOLD-2023-ver-1.3-17Feb2023_WMV.pdf

The establishment of clinical group B in patients with COPD was carried out on the basis of a cumulative analysis of the obtained spirometry data and the results of the CAT and mMRC questionnaires. That is, according to the GOLD-2014 classification (and the GOLD-2021 revision)[32]:

– Group A included patients with exacerbations ≤1 time per year, few symptoms: 0–1 point on the mMRC scale or <10 points on the CAT questionnaire and measures of external respiratory function: $FEV_1/FVC \leq 70\%$ and $FEV_1 > 50\%$ of the appropriate values.

– Group B included patients with exacerbations ≤1 time per year, a high number of symptoms: >2 points on the mMRC scale or >10 points on the CAT questionnaire and measures of external respiratory function: $FEV_1/FVC \leq 70\%$ and $FEV_1 > 50\%$ of the appropriate values.

– Group C included patients with exacerbations ≥2 times a year, few symptoms: 0–1 point on the mMRC scale or <10 points on the CAT questionnaire and measures of respiratory function: $FEV_1/FVC \leq 70\%$ and $FEV_1 < 50\%$ of the appropriate values.

– Group D included patients with exacerbations ≥2 times a year, a high number of symptoms: >2 points on the mMRC scale or >10 points on the CAT questionnaire and measures of external respiratory function: $FEV_1/FVC \leq 70\%$ and $FEV_1 < 50\%$ of the appropriate values.

In all patients, the adaptation of respiratory function and hemodynamics to dosed physical activity (spirohemodynamic test) was assessed by simultaneous determination of FEV_1 and blood pressure measurement, which consisted in the measurement of blood pressure being carried out simultaneously with spirometry before and after exercise[33]. At the same time, blood pressure was measured according to the standard method on the shoulder, and FEV_1 was determined as a percentage of the proper values. The test was evaluated as follows: if with an increase in systolic blood pressure by less than 10–15% after physical exertion (5–10 squats) and FEV_1 more than 5–10% of the baseline level, a normal type of adaptation of respiratory function and hemodynamics was diagnosed, with an increase in systolic blood pressure of more than 15% with normal changes in FEV_1, a hypertensive type of adaptation was recorded, and in the absence of an increase in FEV_1, or even a decrease, an obstructive type of adaptation was stated.

[32] Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease 2021. URL: https://goldcopd.org/gold-reports/gold-report-2021-v1-0-11nov20_wmv/

[33] Voloshyna O.B., Dychko T.O., Lysiy I.S., Dukova O.R., Chaika A.O., Zbitneva V.O. Stalemate. For the invention 119478 Ukraine, IPC A61B 5/091 (2006.01) A61B 5/02 (2006.01) G01N 33/497 (2006/01). The method of complex diagnosis of adaptation of respiratory function and hemodynamics to dosed physical load. The applicant and patent owner is Odesa National Medical University. No. u2017 03987; statement 24/04/2017; published 25.06.2019, Bull. No. 12

In all patients, quality of life (QoL) indicators were analyzed according to the EQ-5D questionnaire[34]. The questionnaire consists of two parts. The first includes five sections, which are related to mobility, self-care ability, activity in daily life, feelings of pain/discomfort, and anxiety/depression. Each section has five answer options according to the degree of severity. The second part is represented by a visual analogue scale (VAS) from 0 to 100, on which the patient notes the general state of his health at the time of the interview. The questionnaire was filled out by the patient himself.

Statistical processing of the obtained data was carried out using computer programs Microsoft Excel 2013 (Microsoft Corporation, USA, 2013) and Statistica6.0 (StatSoft, version 13.3.721). The normality of the distribution of quantitative traits was assessed using the Shapiro–Wilk test. The indicators are given as the mean value and the standard error of the mean value ($M \pm m$). The probability of the difference in the indicators was calculated using the $\chi 2$ criterion and the Student's t-test with a normal distribution of values. The results of comparisons were considered reliable if $p<0.05$[35].

Results. The study showed that as a result of treatment in both groups of patients, subjective improvement was observed, which was manifested in a decrease in the number of complaints of headache, shortness of breath, coughing attacks, and an improvement in household performance. However, in patients of the control group, a positive dynamics of subjective data was observed in a smaller number of patients, which was reflected in the absence of significant changes in the group as a whole. In particular, in patients with arterial hypertension associated with COPD, who additionally took a fixed combination of magnesium with vitamin B6 (MgB6), a significant decrease in complaints was observed (Table 1).

As can be seen from Table 1, in the patients of the main group, who received a fixed combination of MgB6 (FC MgB6) in addition to the basic treatment, compared to the control group, the frequency of complaints decreased: headache – from (80.0±7.3) to (46.7±9.1) ($p<0.01$), heart attacks from (60.0±8.9) to (30.0±8.4) ($p<0.02$), cough – from (90.0±5.5) to (46.7±9.1) ($p<0.001$), shortness of breath during physical exertion from (76.7±7.7) to (36.7±8.8) ($p<0.002$), sleep disturbances from (70.0±8.4) to (30.0±8.4) ($p<0.002$), manifestations of depression/anxiety from (60.0±8.9) to (20.0±7.3) ($p<0.001$). In the control group of patients, a decrease in complaints was also observed, but their dynamics was unreliable. In particular, in the control group, after treatment, there was a decrease in headache complaints – from (80.0±7.3) to (76.7±7.7) ($p>0.5$), palpitations attacks from (63.3±8.8) to (56.7±9.0) ($p>0.5$), cough – from (86.7±6.2) to (73.3±8.1) ($p>0.1$), shortness

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of breath during physical exertion from (73.3±8.1) to (66.7±8.6) (p>0.5), sleep disturbances from (66.7±8.6) to (56.7±9.0) (p>0.2), manifestations of depression/anxiety from (53.3±9.1) to (46.7±9.1) (p>0.5).

Table 1

Dynamics of complaints in patients with arterial hypertension with concomitant COPD depending on the type of treatment, %

Complaints	Maingroup (n=30)	Control group (n=30)
Headache	80,0±7,3 46,7±9,1*	80,0±7,3 76,7±7,7
Increased fatigue	76,6±7,7 53,3±9,1	70,0±8,4 56,7±9,0
Attacks of heart palpitations	60,0±8,9 30,0±8,4*	63,3±8,8 56,7±9,0
Violation of heart rhythm	43,3±9,0 36,7±8,8	46,7±9,1 40,0±8,9
Discomfort in the chest	73,3±8,1 43,3±9,0	70,0±8,4 63,3±8,8
Cough	90,0±5,5 46,7±9,1*	86,7±6,2 73,3±8,1
Shortness of breath during physical exertion	76,7±7,7 36,7±8,8*	73,3±8,1 66,7±8,6
Sleep disturbance	70,0±8,4 30,0±8,4*	66,7±8,6 56,7±9,0
Depression / anxiety	60,0±8,9 20,0±7,3*	53,3±9,1 46,7±9,1
Swelling on the limbs	53,3±9,1 43,3±9,0	46,7±9,1 33,3±8,6

Note 1. The numerator shows the data before treatment;

Note 2. The denominator shows the data after treatment;

Note 3. The significance of the difference between the indicators before and after treatment is less than 0.05 is marked.*

The effectiveness of the treatment in patients of the main group was also evidenced by a significant improvement in quality of life indicators (QoL) according to the results of the EQ-5D questionnaire, which was manifested in the improvement of household and social adaptation, reduction of disease manifestations, reduction of anxiety, improvement of sleep, etc. The integral index of QoL according to the EQ-5D questionnaire significantly decreased in the main group of patients from 1.8±0.02 to 2.2±0.04 after treatment (p<0, 001), and almost did not change in the control – from 1.7±0.06 to 1.8±0.07 (p>0.2). According to the results of the 100-point visual analogue

scale (VAS) of the EQ-5D questionnaire, the overall assessment of their condition by patients with hypertension with concomitant COPD showed a significant improvement in patients of the main group – from (52.6±3.4) points to (74.2±3.8) points ($p<0.001$) after treatment, and in the control group – from (47.4±3.4) points to (54.3±3.1) points ($p>0.1$).

Improvement of the subjective state in patients with hypertension and COPD of the main group was observed against the background of reliable dynamics of blood pressure. Specifically, the mean systolic blood pressure (SBP) level decreased from (160.3±2.1) mmHg up to (143.0±2.1) mmHg ($p<0.001$), diastolic blood pressure (DAT) – from (92.8±2.4) mmHg up to (85.6±3.6) mmHg ($p>0.1$). In patients with hypertension and COPD of the control group, a decrease in average SBP levels was also observed, but not significantly – from (161.4±3.1) mmHg up to (149.3±3.1) mmHg ($p>0.2$), and DAT – from (93.4±3.0) mmHg up to (88.1±2.2) mmHg ($p>0.1$). The target blood pressure level was achieved in 25 (83.3±6.8%) patients of the main group and only in 8 (26.6±8.1%) patients of the control group ($p<0.001$).

Analysis of ECG indicators showed that a significant decrease in the incidence of heart rhythm disturbances was observed in the examined patients after treatment, primarily in the main group of patients with arterial hypertension and COPD. Thus, in the main group of patients with hypertension associated with COPD, who additionally took MgB6, there was a significant decrease in the frequency of tachycardia from (23.3±7.7)% to (3.3±3.3)% ($p<0.02$) and supraventricular extrasystole from (36.7±8.8)% to (13.3±6.2)% ($p<0.05$). In control, a decrease in tachycardia frequency and supraventricular extrasystole was unreliable: from (30.0±8.4)% to (26.7±8.1)% ($p>0.5$) and from (30.0±8.4)% to (23.3±7.7)% ($p>0.5$), respectively. Almost half of the patients in the intervention group also had an improvement in repolarization processes in the left thoracic ECG leads, as evidenced by a 0.5–1 mm increase in the amplitude of the T wave, which was negative or isoelectric in leads V_{5-6} before treatment (respectively in the main group – in (46.7±9.1)% of patients, and in the control group – only in (16.7±6.8)%, ($p<0.02$)). However, the incidence of depression in the left thoracic leads changed insignificantly in both groups: in the intervention group before treatment it was (63.3±8.8), after treatment – (50.0±9.1)% ($p>0.2$), and in the control group before treatment – (56.7±9.0)%, and after treatment – (43.3±9.0)% ($p>0.2$).

To determine the effectiveness of the treatment in all patients, indicators of the function of external respiration were determined. The results of the spirographic examination are presented in the table.

Table 2

Dynamics of spirometry indicators and their ratio in patients with arterial hypertension with concomitant chronic obstructive pulmonary disease depending on complex treatment, %

Indicators	Maingroup (n=30)	Control group (n=30)
FEV_1, %	55,9±3,0 65,8±4,4*	59,2±4,3 63,1±4,7
FVC, %	89,0±3,9 90,6±4,6	89,8±4,4 92,0±4,0
FEV_1/FVC, %	62,3±3,1 71,6±3,4*	66,4±4,7 68,3±4,0

Notes: 1. The numerator shows the data before treatment. 2. The denominator shows the data after treatment. 3. The significance of the difference between the indicators before and after treatment is less than 0.05 is marked. 4. FEV_1istheforced expiratory volume in 1 sec. 5. FVC is the forced vital capacity of the lungs.*

As can be seen from the table, in the main group of patients with arterial hypertension with concomitant COPD, the forced expiratory volume in 1 s (FEV_1) ($p<0.05$) and, respectively, FEV_1/FVC ($p<0.05$) significantly increased, which indicated a decrease in bronchial obstruction. In the control group, there were no significant changes in these indicators.

When analyzing the BP response and respiratory function, a hypertensive type of adaptation was observed in the majority of patients in both the main and control groups (Table 3).

As shown in Table 3, the normal type of adaptation was registered only in 4 (18.2%) patients of the main group and 3 (15.0%) patients of the control group ($p>0.5$). The obstructive type of adaptation was also observed in a smaller number of patients (6 (27.3%) of the main group and 4 (20.0%) patients of the control group ($p>0.5$), respectively). The smaller proportion of obstructive adjustment disorders in our study can be explained by the fact that, according to the inclusion and non-inclusion criteria, patients with concomitant COPD of clinical groups A and B were randomized to this study, in which airway obstruction is not as significantly impaired as in patients of clinical groups C and D.

After complex restorative treatment in the main group, there was a positive trend in both indicators of external respiratory function (Table 4) and blood pressure in response to dosed physical activity (Table 5).

Table 3

Frequency of detection of violations of adaptation to dosed physical load of respiratory function and blood pressure in patients with arterial hypertension with concomitant chronic obstructive pulmonary disease (n, %)

The option of adaptation	Criteria for evaluating indicators after dosed physical activity		Maingroup (n=22)	Control group (n=20)
	Systolic blood pressure– SBP (increase from baseline, %)	The volume of forced exhalation In the first second – FEV_1 (increase from the initial level, %)		
Normal	<10 – 15%	> 5 – 10%	4 (18,2%)	3 (15,0%)
Hypertensive	> 15%	> 5 – 10%	12 (54,5%)	13 (65,0%)
Obstructive	< 10 – 15%	Increase < 5% or decrease from base line	6 (27,3%)	4 (20,0%)

Table 4

Dynamics of FEV_1 and FVC indicators and their ratio during physical exertion in patients with hypertension with concomitant COPD depending on the type of restorative treatment (M±m)

Indicators	Main group (n=22)		Control group (n=20)	
	Before treatment	After treatment	Before treatment	After treatment
FEV_1, % of the proper value	63,5±10,2 58,7±9,4	72,3±9,9 67,5±8,9*	64,2±9,3 60,3±8,9	67,0±10,2 61,9±9,7
FVC, % of the proper value	80,6±12,0 82,6±10,7	83,1±10,2 84,3±9,5	83,2±11,6 85,4±10,2	86,5±9,8 87,2±9,1
FEV_1/FVC	78,8±9,4 71,0±9,6	87,0±9,2 80,1±9,2*	77,2±10,2 70,6±9,0	77,5±9,8 70,9±8,8

Note 1. The numerator contains data before physical activity;

Note 2. The denominator shows the data after physical exertion;

Note 3. The significance of the difference between the indicators before and after treatment is less than 0.05 is marked.*

The data shown in Table 4. show that after treatment in patients with hypertension and concomitant COPD of the main group, the indicators of external respiration significantly improved: FEV_1 – from (58.7±9.4) to (67.5±8.9) ($p<0.05$) and FEV_1/FVC – from (71.0±9.6) to (80.1±9.2) ($p<0.05$).

Table 5

Dynamics of office blood pressure indicators in patients with hypertension with concomitant COPD depending on the type of treatment in response to physical exertion (M±m)

Indicators	Main group (n=22)		Control group (n=20)	
	Before treatment	After treatment	Before treatment	After treatment
Systolic BP, mm Hg	159,3±2,4 169,5±1,8	141,0±2,7 159,6±1,3*	160,1±4,3 166,3±2,4	159,3±4,1 163,6±3,1
Diastolic BP, mm Hg	91,3±3,4 90,8±3,1	87,6±3,6 88,5±2,7	92,4±4,4 92,7±2,6	89,1±3,2 90,6±2,3

Note 1. The numerator contains data before physical activity;

Note 2. The denominator shows the data after physical activity;

Note 3. The significance of the difference between the indicators of the main and control groups less than 0.05 is marked.*

Improvement in clinical and functional parameters was observed against the background of an increase in the level of magnesium in the blood of patients of the main group. After the treatment, an increase in the level of magnesium in the blood serum was observed: in patients of the main group – from (0.71±0.04) to (0.91±0.07) mmol/l ($p<0.02$), and in patients of the control group these changes were not so significant – from (0.73±0.07) to (0.76±0.08) mmol/l ($p>0.5$).

It is the increase in magnesium levels that can explain the significant decrease in blood pressure in patients of the main group compared to the control group. It is believed that an increase in the extracellular concentration of magnesium improves blood circulation, reduces vascular resistance and increases the capacity of peripheral, renal, coronary and cerebral blood vessels, lowers blood pressure[36].

Thus, the use of MgB6 in the complex treatment of patients with hypertension with concomitant COPD made it possible to improve the clinical course of comorbid pathology, improve spirometry indicators and blood pressure, and improve the quality of life of patients with these diseases. Assessment of the effectiveness of rehabilitation treatment, which includes not only the data of quality of life questionnaires, but also the results of the study of changes in the functional state of the cardiorespiratory system, allows you to objectively assess the adaptive capabilities of the body patients with this comorbid pathology. In addition, the determination of the response of blood pressure and FEV_1 in patients to standardized physical activity makes it possible to determine the prevailing disorders of blood pressure regulation or respiratory function in comorbid pathology, which allows timely detect the

[36] González a J.A., Garciaa CH., Gonzalezb PA, Garciac C.M., Jiménezd A. Electof. Intravenous Magnesium Sulfate on Chronic Obstructive Pulmonary Disease Exacerbations Requiring Hospitalization A Randomized Placebo-Controlled Trial Volume 42, Issue 08, August 2006.

priority are as for the construction of comprehensive rehabilitation treatment of patients with hypertension with concomitant COPD.

CONCLUSIONS

1. Measurement of blood pressure and FEV_1 during standardized two-stage exercise test makes possible to determine the priority areas for improving the complex treatment and its effectiveness of patients with hypertension with concomitant COPD.
2. Complex treatment of patients with arterial hypertension and chronic obstructive pulmonary disease, in which a fixed combination of magnesium and vitamin B6 is added to the basic treatment, can improve the clinical and functional parameters of the comorbid pathology.

SUMMARY

It is known that when arterial hypertension (AH) is combined with chronic obstructive pulmonary disease (COPD), there is not only a worsening of both diseases, but also an increase in the risk of cardiovascular complications. It has been established that the use of various magnesium compounds is accompanied by a decrease in blood pressure in patients with hypertension, as well as an improvement in respiratory function in patients with COPD.

The aim of this study was to estimate the effectiveness of the complex treatment on clinical and functional parameters and quality of life of patients with arterial hypertension combined with COPD

Materials and methods. 60 patients with hypertension and concomitant COPD of clinical group B (GOLD 2) were examined. Subjective and objective clinical data, office blood pressure (BP) level and the results of home blood pressure monitoring, spirometry at rest and during physical exertion, electrocardiography (ECG), laboratory parameters, EQ-5D, mMRC, CAT questionnaires were analyzed.

Results. Analysis of the study results shows that measurement of blood pressure and FEV_1 during standardized two-stage physical activity makes it possible to determine the priority areas for improving the comprehensive rehabilitation treatment of patients with hypertension with concomitant COPD and to objectivize the assessment of the effectiveness of treatment of this comorbid pathology.

The complex treatment of patients with hypertension and COPD, in which a fixed combination of magnesium and vitamin B6 is added to the basic treatment, can improve the clinical course of comorbid pathology, bioelectrical activity of the heart, further reduce blood pressure, improve spirometry and quality of life of patients.

Conclusions. 1. Measurement of blood pressure and FEV_1 during standardized two-stage exercise test makes possible to determine the priority areas for improving the complex treatment and its effectiveness of patients with hypertension with concomitant COPD. 2. Complex treatment of patients with arterial hypertension and chronic obstructive pulmonary disease, in

which a fixed combination of magnesium and vitamin B6 is added to the basic treatment, can improve the clinical and functional parameters of the comorbid pathology.

The authors emphasize the absence of a conflict of interest.

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Information about the authors:
Voloshyna Olena Borysivna,
https://orcid.org/0000-0002-7685-7313
Doctor of Medical Sciences, Professor,
Head of the Department of General Practice,
Odessa National Medical University
2, Valikhovsky Lane, Odesa, 65062, Ukraine

Nazaruk Tetiana Oleksandrivna,
https://orcid.org/0009-0009-3482-3623
Assistant Professor at the Department of General Practice,
Odessa National Medical University
2, Valikhovsky Lane, Odesa, 65062, Ukraine

Zbitnieva Viktoriia Olehivna,
https://orcid.org/0000-0001-9656-4860
Candidate of Medical Sciences,
Assistant Professor at the Department of General Practice,
Odessa National Medical University
2, Valikhovsky Lane, Odesa, 65062, Ukraine