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PECULARITIES OF THE CLINICAL COURSE OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE IN HYPERTENSIVE PATIENTS

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Ключевые слова: *хроническое обструктивное заболевание легких, гипертоническая болезнь, сочетанное течение*

Abstract. Pecularities of the clinical course of chronic obstructive pulmonary disease in hypertensive patients. Arkhipkina O.L. *Nowadays, the problem of comorbid chronic obstructive pulmonary disease (COPD) and arterial hypertension (AH) is considered from the point of view of the presence of common risk factors and pathogenetic mechanisms. The aim of the study was to investigate cardiorespiratory system function in patients with COPD and AH and to analyze the main cardiovascular risk factors. 284 patients with COPD were divided into 2 groups: the main group - 167 patients with COPD and concomitant hypertension, the comparison group - 117 patients with COPD and normal blood pressure values. An analysis of the clinical picture of COPD revealed that patients with AH more often had exacerbation of underlying disease, more expressed clinical manifestations of the disease, differed in phenotypic distribution of patients. All patients with COPD showed a tendency to increase in arterial pressure, blood glucose level and total cholesterol compared with the control group with enhanced tendency in hypertensive patients. In addition, in hypertensive group the patients had a higher body mass index and smoked intensively. According to EGC data, the majority of patients with COPD experienced tachycardia, arrhythmias and conduction disturbances, hypertrophy of ventricules, which occurred more often in hypertensive patients. Pulmonary function was characterized both by obstructive and restrictive changes that were more expressed in the comorbidity. Thus, in the presence of AH the clinical manifestations of COPD varied, demonstrating the contribution of vascular pathology to the respiratory disorders in those patients. The combined course of COPD with AH is characterized by a modification of clinical manifestations of the disease and COPD was associated with increased cardiovascular risk in patients examined.*

Реферат. Особенности клинического течения хронического обструктивного заболевания легких у больных гипертонической болезнью. Архипкина О.Л. *Сегодня проблему коморбидного течения хронического обструктивного заболевания легких (ХОЗЛ) и гипертонической болезни (ГБ) рассматривают с позиции наличия общих факторов риска и патогенетических механизмов. Целью работы было изучение особенностей функционирования кардиореспираторной системи у больных с ХОЗЛ и ГБ и анализ основных факторов сердечно-сосудистого риска. Было обследовано 284 пациента с ХОЗЛ, которые были разделены на 2 группы: основная группа - 167 больных с ХОЗЛ и сопутствующей ГБ, группа сравнения – 117 больных ХОЗЛ с нормальными значениями артериального давления. Анализ клинической картины ХОЗЛ выявил, что у больных на фоне ГБ достоверно чаще наблюдаются обострения основного заболевания, наблюдается ухудшение клинических проявлений болезни, меняется фенотипическое распределение больных. У всех больных ХОЗЛ выявлена тенденция к повышению артериального давления, глюкозы крови и общего холестерина по сравнению с контролем с наивысшими значениями в основной группе. К тому же больные имели больший индекс массы тела и интенсивнее курили в группе с ГБ. Согласно данным ЕГК, у большинства больных ХОЗЛ наблюдалась тахикардия, нарушения ритма и проводимости, гипертрофия миокарда желудочков, что чаще имело место при наличии ГБ. Функция легких, кроме обструктивных изменений, характеризовалась еще и рестриктивными, что более выражено было при сочетанной патологии. Таким образом, при наличии ГБ клинические проявления ХОЗЛ менялись, демонстрируя влияние сосудистой патологии на респираторные нарушения этих больных. Выводы: Сочетанное течение ХОЗЛ с ГБ характеризовалось модификацией клинических проявлений заболевания, а ХОЗЛ ассоциировалось с увеличением сердечно-сосудистого риска обследованных пациентов.*

Chronic obstructive pulmonary disease (COPD) remains one of the most common pathologies of the respiratory organs with a tendency to further increase in morbidity in persons of working age, characterized by chronic progressive course and requires lifelong treatment. Given the fact that the disease is diagnosed with spirometry, it is difficult to assess the true prevalence of COPD among the population, and early manifestations of the disease often remain underestimated by clinicians [9]. One of the main complaints of patients is shortness of breath, which is often considered by doctors as a manifestation of heart failure. It is known that comorbidity is more likely to be a rule for COPD, since 88% of these patients have at least one chronic concomitant disease [2, 7], and the leading place here belongs to cardiovascular disease, which is the leading cause of death in the world as well as in Ukraine in particular (67.3%) [1]. Today, the problem of comorbidity of COPD and cardiovascular pathology is discussed in terms of development of conditions under COPD that promote the development of endothelial dysfunction, atherosclerosis, arterial hypertension. In the structure of cardiovascular diseases, hypertension disease (HD) is a key factor of their progression and complications. HD does not cause diagnostic difficulties and is modified, but the number of patients who reach the target values of blood pressure is insignificant. Given the poor control of blood pressure, most pathological mechanisms continue to affect the patient. In addition, COPD and HD have much in common: from risk factors to pathogenetic mechanisms that include systemic (low-grade) inflammation, hypoxia, oxidative stress, endothelial dysfunction. It is assumed that the treatment of each disease will contribute to the improvement of the concomitan disease course due to the impact on the common pathogenetic components and reduction of load on the cardiopulmonary

system in general. However, it should not be forgotten about the potentially negative effect of the medication treatment of both diseases on the comorbid clinical course of each of them. Thus, to minimize the adverse prognosis for patients with comorbid pathology, the most important problem is the recognition of comorbidity, adequate treatment of both diseases and the prevention of complications. Consequently, management of a patient with a comorbid pathology, especially in terms of inclusion of interrelated systems remains the complicated issue for a clinician.

The purpose of this work was to study the features of the functioning of the cardiopulmonary system in patients with COPD with HD and analysis of the main cardiovascular risk factors in these patients.

MATERIALS AND METHODS OF RESEARCH

The survey involved 284 adult COPD patients who were divided into two groups, depending on the presence of hypertension. The main group consisted of 167 patients with COPD and concomitant HB stage II, and a comparison group - 117 patients with COPD with normal blood pressure. All the patients had a confirmed diagnosis of COPD of group B. In accordance with the criteria of the GOLD – Global Initiative for Obstructive Lung Disease (2015) and the Order of the Ministry of Health of Ukraine dated June 27, 2013 N 555 and at the time of inclusion in the study were in the phase of remission of the underlying disease, that is more than 4 weeks after the end of treatment or 6 weeks from the onset of pre-exacerbation in the absence of treatment. Diagnosis of HD I-II stage of 1-3 degrees was established after a detailed clinical and instrumental examination based on the Order of the Ministry of Health of Ukraine N 384 dated May 24, 2012. The study did not involve patients with concomitant diseases of the respiratory system (bronchial asthma, tuberculosis, pneumonia, cancer, etc.), HD stage III, symptomatic arterial hypertension, clinically expressed forms of ischemic disease, structural heart diseases, decompensated chronic heart failure (more than CF IIA). The control group consisted of 38 normotensive people without signs of bronchial obstruction, which were undergoing an annual medical examination. This research was carried out at the Clinic of the Research Institute of Occupational Hygiene and Occupational Diseases of the KhNMU. Comprehensive study of patients included a detailed collection of complaints, anamnesis of the disease, external examination, and the identification of cardiovascular risk factors. Electrocardiography in 12 standard leads was performed on the apparatus Heart Mirror. The respiratory function was determined by means of spiroographic complex SPIROCOM. Statistical analysis of the results of experimental studies was carried out using a computer software package for the statistical information processing of Statistica 6.1 (StatSoft, Inc., USA).

RESULTS AND DISCUSSION

Among the surveyed in all groups men dominated: 67.07% in the main group and 74.36% – in the comparison group (tab.). The average age of patients with COPD was 52.4±3.18 years, and with combined pathology – 55.47±5.17 years, the control group – 54.16±5.31. Thus, the population of patients with COPD is predominantly represented by men of mature age, which coincides with the traditional notions of this disease [5], and such unmodified factors as age and gender have no significant effect on the presence of hypertension in COPD patients.

According to the anamnesis, the duration of COPD among the clinical groups did not differ. In the majority of patients in the main group, the diagnosis of HD was established at the same time (14.97%) or after verifying COPD (65.27%) and only in 19.76% preceeded respiratory system disease. Considering that the basis for irreversible obstruction of COPD has been formed over decades, the slow development of symptoms and underestimation of clinical symptoms by doctors, which is often the cause of COPD hypodiagnosis, it can be safely stated that this disease manifests before HD. Thus, the patients of all the examined groups had a long history of bronchopulmonary disease. Complaints of cough and/or shortness of breath were over the course of 12.4±2.13 years in patients with isolated COPD and 13.87±3.5 years in patients with combined pathology. One of the factors for the development of COPD in the examined individuals was the air pollution with silicon dust in the workplace in the past. The average length of service in the harmful conditions of the patients in the comparison group was 17.35±2.31 years and 18.06±3.84 years and statistically did not differ between the groups. Thus, the analysis of anamnestic data of patients with COPD did not differ significantly depending on the presence of HD. The analysis of the frequency of exacerbations showed that patients with a comorbid pathology on average were significantly more exacerbated as compared with the isolated COPD course. The burdened family history of cardiovascular diseases (CVD in a family history: up to 55 years for men and up to 65 years for women) was in 68 (40.72%) patients of the main group, while in the comparison group only in a quarter of patients – 31 (26.5%).

Clinical characteristic of the examined patients (M±m)

	Control group (n=38)	Group of comparison (n=117)	Main group (n=167)
Men/women	**29/11**	**87/30**	**112/55**
Age, years	**54,16±5,31**	**52,4±3,18**	**55,47±5,17**
Duretion of COPD, years	**-**	**5,3±2,4**	**7,1±3,4**
COPD exacerbations per year	**-**	**0,8±0,3**	**1,4±0,2****
Duretion of HD, years	**-**	**-**	**3,8±1,6**
Duration of smoking, years	**7,05±1,63**	**25,16±2,81***	**23,5±2,51***
Smoking index, pack/year	**6,02±1,3**	**26,5 ± 2,4**	**33,1 ± 2,4*,****
BMI, kg/m^2	**26,7±2,41**	**29,4±3,27**	**32,5±2,14***
SBP, mm Hg.	**127,5±3,7**	**134,9±3,51***	**147,23±5,14*,****
DBP, mm Hg.	**82,6±4,7**	**86,3±2,16**	**93,85±1,36*,****
Glucose on empty stomach, mmol/l	**4,5±0,2**	**5,7±0,8***	**6,1±0,4***
3X mmol/l	**4,8±0,9**	**6,2±1,2**	**6,1±1,4**
HBR per min.	**74,2±3,5**	**84,4±3,6***	**92,8±3,2*,****
FEV$_1$, %	**102,7±1,54**	**73,3±2,7***	**68,5±1,38*,****
FIVC, %	**101,5±2,37**	**59,28±3,48***	**52,17±2,21*,****

N o t e s : * – the difference is significant with the control group, p <0.05, ** – the difference is significant between the clinical groups, p<0.05.

An assessment of common risk factors for COPD and CVD was also conducted. Among patients with COPD only, 43.59% were smokers at the time of the examination, 32.48% smoked in the past. In the main group, the number of smokers and those who smoked was statistically higher (36.53% and 56.89% respectively, p<0.05). Duration of smoking in both groups did not have a significant difference, but the tobacco smoking index was significantly higher in the group where, along with COPD, there was HD. So, the intensity of smoking was more pronounced in patients with a combined pathology and, probably, was associated with the development of HD in these patients [6, 8].

Clinical manifestations of COPD in patients of a comparison group were typical complaints of permanent cough in 79 (67.52%) subjects, with expectoration – in 54 (46.15%), mainly in the morning – in 68 (58.12%) and shortness of breath on physical activity – in 102 (87.18%). The most common features of the combined course were cough – in 118 (70.66%) of the subjects, of unproductive character – in 120 (71.86%) and disturbed patients during the day – 112 (67.07%), shortness of breath – in 164 (98.2%).

Several COPD phenotypes have been verified among COPD patients: with predominance of chronic bronchitis, with dominance of emphysema and a mixed variant (i.e. patients in whom the prevalence of bronchial or emphysematous variant is imossibly to clearly identify). Thus, among patients with isolated COPD, the majority had a bronchial variant of the phenotype (47.86%), and the proportion of emphysematous and mixed variant accounted for 28.21% and 23.93% respectively. In the group where COPD was combined with HD, the situation was the opposite. The main group was represented mainly by patients with emphysematous (36.53%) and mixed variant (40.12%), and bronchial was observed only in 23.35% of patients.

It is common knowledge that overweight and obesity reliably increase the risk of cardiovascular events, even in the absence of hypertension or metabolic disorders [4]. BMI significantly exceeded the control group's rates in patients with concomitant HD, and in the comparison group did not differ between the groups. However, among patients with COPD, obesity (BMI≥30 kg/m^2) was in 30 (25.64%), and among patients with HD – in 61 (36.53%). Patients with insufficient body weight were not found in any group. Chinese scientists conducted a meta-analysis [3], the results of which indicate a negative effect of excess body weight and obesity on the course of COPD in the form of frequent exacerbations and a rapid decrease in FEV$_1$ values. In addition, obesity per se is associated with shortness of breath, which worsens the clinical picture of such patients.

Measurement of blood pressure revealed that the mean values of brachial systolic and diastolic pressure in the examined groups of comparison were within the established norm, but according to the generally accepted gradation corresponded to high normal pressure, and the value of systolic pressure was significantly different from that of control. In patients with a diagnosis of HD and COPD, the figures for arterial pressure were respectively the highest. All patients with HD received baseline antihypertensive therapy, but, unfortunately, target blood pressure figures were achieved only in 58 (34.73%) patients in the main group. Among variants of hypertension in 80 (73.4%) patients of the main group systole-diastolic variant prevailed. The isolated systolic version was in 19 (17.43%), and diastolic – in 10 (9.17%).

According to the results of the laboratory-instrumental study, it was found that in all patients with COPD, the average blood glucose values were significantly higher compared to the control group. Among patients in the comparison group, compensated diabetes mellitus type II was found in 16.24% (19 patients), and in patients of the main group – in 26.95% (45 patients). The level of total cholesterol exceeded the permissible values in patients of both clinical groups, however, there was no statistically significant difference between the observation groups. It should be noted that among patients of the comparison group, lipid-reducing medication was received by 63 (53.85%) patients, and in the main group – 147 (88,02%). Given the use of hypolipidemic drugs, the correct assessment of lipid metabolism is not possible, but the very fact of using this group of drugs by half of patients with COPD and almost by all patients with COPD combined with HD indicates a high activity of atherogenesis in the examined COPD patients.

According to the electrocardiographic study, sinus rhythm was in 109 (93.19%) patients with COPD and 124 (74.25%) patients with a combined course. Patients in both clinical groups were prone to tachycardia: heart rate per minute in the comparison was 84.4±3.6 and significantly differed from the main group – 92.8±3.2 ($p<0.05$). Such a trend may be explained by the presence of ventilatory disorders with the development of hypoxia in patients with COPD and baseline therapy with β-adrenomimetics, and especially abuse of those ones by patients. Impairment of cardiac rhythm and conduction was recorded in 36 (30.77%) patients in the comparison group and in 79 (47.30%) patients in the main group. ECG signs of right ventricular hypertrophy were found in 18 (15.38%) patients with COPD only, and in combined course – 38 (22.75%). The left ventricular myocardial hypertrophy is found in 6 (5.13%) persons in the comparison group and in the naturally larger proportion of patients with GC-98 (58.68%). Signs of damage to the myocardium were not recorded in any patient.

The analysis of the functional state of the broncho-pulmonary system expectedly revealed obstructive and restrictive changes in the patients of both groups of observation. When comparing key indicators, it was found that FEV_1 and FIVC were the lowest in the main group, while the ratio of FEV_1 to FIVC lost its diagnostic value. The greater severity of restrictive changes can be explained by the prevalence of emphysematous phenotype in patients in the main group. On the other hand, an increase in rigidity of the pulmonary tissue in patients with pathology of the cardiovascular system is possible due to interstitial pulmonary edema. Given that decompensated patients were not involved in the study, such manifestations may be due to past cardiac episodes in patients with HD. In addition, left ventricular insufficiency can increase the manifestations of bronchial obstruction and, as a result, accelerate the reconstruction of the bronchial tree due to external compression, mucosal swelling and hyperreactivity. Consequently, the presence of HD with the development of heart failure aggravates the ventilation disorders of COPD.

The analysis of the clinical picture of COPD has found that in patients with HD background exacerbation of the underlying disease is observed significantly more commonly, classic manifestations of the disease are more pronounced, phenotypic distribution of patients is different. All patients with COPD have a tendency to increase in blood pressure, blood glucose and total cholesterol compared with the control which is mostly presented in the hypertension group. In addition, the patients had a higher body mass index and more intensely smoked in the presence of HD. According to the EGC, most patients with COPD experienced tachycardia, rhythm and conduction disturbances, ventricular myocardial hypertrophy, which often occurred in the presence of HD. The function of the lungs, except obstructive changes, was also characterized by restrictive ones, especially in combined pathology. Thus, in the presence of HD the clinical manifestations of COPD changed, which demonstrates the effect of vascular pathology on respiratory disturbances in these patients.

CONCLUSION

The combined course of COPD with HD was characterized by the modification of clinical manifestations of the disease, and COPD was associated with an increase in cardiovascular risk in the examined patients.

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