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Use of Ivabradine in Patients with Cardiorespiratory Pathology

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Abstract: Chronic obstructive pulmonary disease (COPD) remains a critical medical and social challenge due to its high prevalence, significant impact on work incapacity, and its role as a leading cause of mortality. This is further complicated by frequent comorbidities such as coronary heart disease (CHD) and metabolic syndrome (MS), which exacerbate cardiovascular risks and hinder effective management. This study aimed to evaluate the efficacy of ivabradine in preventing cardiovascular complications in patients with COPD combined with CHD and MS.

The study included 114 patients: 76 with COPD and CHD (Group I) and 38 with COPD and MS (Group II). Ivabradine was administered at 5 mg twice daily, and outcomes were assessed after three months. Clinical and instrumental evaluations revealed significant improvements in both groups, including reduced frequency of angina attacks, decreased nitrate use, and improved heart rate regulation. Holter monitoring demonstrated a reduction in painless myocardial ischemia duration by 47.6% in Group I and 54.3% in Group II ($p < 0.05$).

Patients exhibited improved oxygenation (increased PaO2 and decreased PaCO2), enhanced exercise tolerance, and reduced pulmonary artery pressure. Importantly, ivabradine showed no adverse effects on bronchial patency. These findings underscore the efficacy of ivabradine in optimizing hemodynamic parameters, improving exercise capacity, and preventing cardiovascular complications in COPD patients with comorbid conditions.

Conclusion: Ivabradine at 5 mg twice daily is a promising antianginal treatment for patients with COPD and cardiorespiratory pathologies, effectively reducing angina frequency, improving lung function, and mitigating cardiovascular risks without compromising bronchial health.

Keywords: ivabradine, chronic obstructive pulmonary disease, metabolic syndrome, prevention of cardiovascular complications.

Introduction. At present, there is no doubt about the undeniable medical and social significance of chronic obstructive pulmonary disease (COPD), which in the structure of morbidity is among the leaders in the number of days of incapacity for work and causes of disability, occupying fourth-fifth place among other causes of death. The main contingent of patients with COPD, despite the significant "rejuvenation" of the disease in recent years, are people over 45 years old, it is in this age category that a frequent combination of COPD with cardiac pathology is observed, and, in particular, with such diseases as coronary heart disease (CHD) [4]. In combination, they make up about 62% in the morbidity structure of patients in older age groups, and in the structure of mortality from various causes - more than 50%. Another significant problem of our time is obesity and the development of metabolic syndrome (MS), the growth rate of the prevalence of which in the next 25 years, in the absence of its effective prevention, may increase by more than 50% [8, 9].

A meta-analysis of large-scale studies conducted recently showed that 15-22.6% of people in the age group of 30-69 years in developed countries have signs of MS, while in the USA this figure reaches 24%. Taking into account the frequent combination of MS and breathing disorders during sleep, the danger of the simultaneous occurrence of COPD and MS in patients becomes clear.

In addition, one of the leading syndromes of both COPD and coronary heart disease is hypoxia, which, when combined, leads to rapid progression of atherosclerosis and the formation of cardiovascular complications. MS, the obligatory manifestations of which are impaired glucose tolerance or type II diabetes mellitus, as well as arterial hypertension, can also contribute, apparently, to the more rapid formation of cardiovascular pathology in patients with COPD. In this regard, the organization of the optimal treatment process associated with combined pathology remains the most complex problem of modern practical medicine [1, 2].

Formation of treatment tactics in this case requires the doctor to have extensive knowledge of related disciplines in the absence of standards for the treatment of combined pathology. Currently, there are standards for the treatment of patients with coronary heart disease, COPD, rhythm disorders and MS. However, none of these protocols take into account the possibility of combined pathology, which makes their direct use impossible. The issues of treating coronary heart disease against the background of COPD (beta-blockers, ACE inhibitors, long-term use of diuretics, often nitrates - against the background of taking Sildenafil) remain problematic, as well as COPD against the background of coronary heart disease (negative effect of bronchodilators) and MS in the presence of broncho-obstructive pathology (glucocorticosteroids increase blood glucose levels, affect the level of blood pressure). Objective of the study. The objective of this study was to investigate the effect of ivabradine

(coraxan, servier) on the prevention of cardiovascular complications in patients with COPD against the background of ischemic heart disease and COPD in combination with MS.

Material and methods of the study. A total of 114 patients were included in the study, of which 76 people (55 men and 21 women) were people with COPD in combination with ischemic heart disease (group I) and 38 patients (28 women and 10 men) - with COPD against the background of MS (group II).

The average age of patients did not exceed 55.6+ 2.2 years and 50.1+ 2.6 years, respectively. Among the patients included in the examination, all patients with COPD had a moderate severity of the disease and respiratory failure no higher than the second degree (DNIIst.), stable angina of functional class II was observed in 62 patients and functional class III - in 14 patients from the first group. All patients were prescribed ivabradine at a dose of 5 mg 2 times a day.

The prescription of coraxan to the subjects from the second group was due to persistent sinus tachycardia, which is, apparently, one of the compensatory mechanisms of chronic respiratory failure. The effectiveness of the therapy was assessed 3 months after the start of treatment.

All patients in both groups underwent a comprehensive clinical and instrumental examination, including general and biochemical blood tests, electrocardiography (ECG), Holter (daily) monitoring of ECG and blood pressure (BP) [3]. The gas composition of capillary (conditionally arterial) blood - PaO2 and PaCO2 (mm Hg) was studied on the analyzer of blood gases, electrolytes and metabolites "Medica Easytraf Analyser - 2002" (USA) according to the method described in the instructions for the device, blood saturation - using a pulse oximeter PNOSK-22 (Russia), the function of external respiration (FER) - using a computer spirograph (Pulmo 236, USA). To determine tolerance to physical activity, all patients underwent a 6-minute walk test (before and after treatment with "Coraxan"), the level of pressure in the pulmonary artery was determined by echocardiography (the average pressure in the pulmonary artery was calculated using the formula proposed by A. Kitabatake et al., 1983)

Results and discussion. All patients in the first group, starting from the second week of treatment, showed a significant ($p<0.05$) decrease in the number of angina attacks per week (from 11.2+1.9 to 5.6+1.6) with a simultaneous decrease in the nitrate dose by an average of 6.7+1.2 tablets per week and a decrease in the average heart rate, both at rest and during exercise, from 92.6+2.2 to 75.4+1.8 and from 119.9+3.2 to 95.9+2.8 beats/min, respectively, which was due to the main mechanism of action of the drug - inhibition of I(f) channels of the sinus node of the heart, and, as a consequence, a decrease in myocardial oxygen requirements. According to Holter ECG monitoring, patients in both

the first and second observation groups showed a decrease in the periods of painless myocardial ischemia by an average of 47.6% in patients with COPD against the background of coronary heart disease (from 67.2+3.5 min per day to 35.2+3.0 min per day, $p<0.05$) and by 54.3% in those examined with COPD and MS (from 62.2+4.5 min per day to 28.4+2.1 min per day, $p<0.05$), which in most cases occurred in patients of the second group before the administration of coraxan, mainly at night or after asthma attacks. Such an improvement in the oxygen supply to the myocardium was associated with a change in the blood gas composition of the examined patients (an increase in PaO2 by 15.6% and a decrease in PaCO2 by 12.6%) against the background of a decrease in the average heart rate; the disappearance of the hyperdynamic type of blood circulation associated with tachycardia led to an improvement in the conditions for blood oxygenation in the lungs and a decrease in the hypoxic load on the tissues and organs of patients. In addition, the normalization of hemodynamic parameters apparently led to a significant decrease in pulmonary artery pressure in patients of both groups

After a month of treatment with Coraxan, positive dynamics in the change of blood gas homeostasis of patients was observed - an increase in tolerance to physical activity in all examined patients. At the same time, the distance covered by patients in 6 minutes with angina pectoris II FC increased by 156.6 + 9.6 m, III FC - by 101.3 + 5.6 m and in patients from the second group - by 164.7 + 8.6 m.

After a course of treatment with ivabradine, all patients included in the examination showed normalization of the circadian index - 1.26 + 0.2 [5, 6].

In addition, it was found that in patients with COPD against the background of MS after treatment with ivabradine, the number of patients with unfavorable BP profiles significantly ($p < 0.05$) decreased (Table 2). In none of the patients included in the study did the use of Coraxan lead to deterioration of bronchial patency, which was confirmed by clinical manifestations of the disease and data from objective and instrumental examinations.

In our opinion, the stable course of respiratory failure in patients of the observation groups was associated with improved hemodynamics in the pulmonary circulation and the absence of an effect on bronchial patency from ivabradine.

Conclusions

1. Ivabradine is an effective antianginal drug for cardiorespiratory pathology, significantly reduces the frequency of angina attacks and the time of painless myocardial ischemia, optimizes ventilation-perfusion ratios in the lungs, has a positive effect on the blood pressure profile in patients with COPD against the background of metabolic syndrome, increases patients' tolerance to physical activity and reduces their risk of sudden coronary death.
2. Ivabradine at a dose of 5 mg 2 times a day can be used in patients with broncho-obstructive diseases and in patients with cardiorespiratory pathology for the prevention of cardiovascular complications

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