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COMBINED THERAPY WITH SILDENAFIL FOR SEVERE PULMONARY HYPERTENSION WITH COPD

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Abstract: This article presents the results of a study devoted to an urgent problem in modern medicine, such as chronic obstructive pulmonary disease and chronic pulmonary hypertension. Despite the many drugs used for this disease, it is not completely possible to cure it, which was the reason for further research in terms of the complex use of some drugs. As a result of many years of research, the effectiveness of the drug sildenafil in our republic, as in many others, has been proven, it was decided to introduce it into the standards for the treatment of this disease.

Key words: CHP, COPD, chronic airway obstruction, sildenafil, iloprost.

Relevance. Phosphodiesterase-5 inhibitors (PDE5I) represent an important new class of drugs for the treatment of pulmonary hypertension [1,8,10]. Sildenafil, a selective PDE5I, through its action, causes a selective reduction in pulmonary vascular resistance and improves symptoms and physical performance in patients with chronic pulmonary hypertension (CPH). Recent clinical trials have clearly demonstrated the efficacy and safety of sildenafil in CPH, so its use in this disease has recently been approved [2,3,9]. Current guidelines from several major specialized societies include sildenafil for the treatment of CPH, which is supported by a large body of evidence [4,5,6,7]. Sildenafil can also be combined with other medications and may also be effective in other forms of pulmonary hypertension.

Purpose: To evaluate the safety and efficacy of oral sildenafil alone and in combination with inhaled loprost for the treatment of pulmonary hypertension associated COPD.

Material and methods of research. The material for the study was 125 patients observed in the regional multidisciplinary clinical hospital of Bukhara city. We divided them into 2 groups - the first group with a history of COPD (chronic obstructive pulmonary disease) (60 patients). Of them with severe pulmonary arterial hypertension (n=36), chronic thromboembolic pulmonary hypertension (n=23) or pulmonary hypertension due to left pulmonary artery aplasia (n=1), all classified as NewYorkHeartAssociation class III or IV. The second group without COPD (65 patients). Written consents for examination were taken from all patients. All patients received nitric oxide by inhalation and iloprost in aerosol form (inhaled dose of 2.8 mcg). They were then randomized to receive 12.5 mg sildenafil orally, 50 mg sildenafil, 12.5 mg sildenafil plus inhaled iloprost, or 50 mg sildenafil plus inhaled iloprost.

Systemic and pulmonary arterial pressure, pulmonary artery occlusion pressure, cardiac output, central venous pressure, peripheral arterial oxygen saturation, and arterial and mixed venous blood gases were measured during right heart catheterization using a Swan-Ganz catheter.

Results. In order of systematic order of pulmonary vasodilatory activity (maximal reduction in pulmonary vascular resistance and increase in cardiac index), 50 mg sildenafil plus iloprost was the most effective,

followed by 12.5 mg sildenafil plus iloprost. Iloprost alone and 50 mg sildenafil were almost equally effective but were less effective than the combination regimens, and the least effective treatments were 12.5 mg sildenafil and nitric oxide.

In our observed patients we studied bad habits worsening gas exchange in lungs, and also blood tests were taken to study lipid spectrum and all indicators concerning metabolism. All data of the obtained results are shown in Table 1.

Criteria studied	**COPD (*n = 60*)**	**no COPD. (*n = 65*)**	**Differences between groups**
Age, years	79 (7)	77 (6)	0,023
Men	46 (61,2)	40(41,1)	<0,001
Smoking status*			<0,001
Didn't smoke	31 (18,8)	12 (37,5)	
Didn't smoke	10 (64,8)	3 (57,1)	
Current smoker	17 (16,4)	8 (5,4)	
Smoking cigarettes, a pack of years	2 (36,6)	2 (19,1)	<0,001
Body mass index, kg / m 2	25,9 (5,6)	26,9 (4,8)	0,034
Hypertension †	37 (52,7)	18 (49,4)	0,443
Mean systolic blood pressure, mm Hg.	152,0 (23,0)	153,0 (28,0)	0,472
Mean diastolic blood pressure, mm Hg.	83,0 (15,0)	84,0 (14,0)	0,664
Diabetes ‡	27 (16,4)	20 (12,4)	0,182
Serum glucose, mmol/L	5,5 (0,9)	5,5 (0,8)	0,178
Total cholesterol in serum, mmol/L	5,3 (1,4)	5,3 (1,5)	0,446
High-density lipoprotein-cholesterol in serum, mmol/L	1,4 (0,6)	1,4 (0,5)	0.200
Triglycerides in serum, mmol/L	1,2 (0,6)	1,2 (0,7)	0,152
Serum creatinine, mkmol/L	81,0 (27,5)	81,0 (25,0)	0,150
Hematocrit,%	44,0 (4,0)	44,0 (5,0)	0,085

Reliability of results $p \leq 0.05$

As can be seen from the table, all parameters in the second group without COPD were almost at the reference values. The influence of smoking is of particular importance, since most patients with COPD are current or former smokers, and smoking has been previously identified as a risk factor, which once again proves its influence on chronic pulmonary hypertension.

In patients receiving 50 mg sildenafil plus iloprost, the maximal change in pulmonary vasodilatory activity was -44.2% (95% CI, -49.5% to -38.8%) vs. %) in response to nitric oxide. When 50 mg of sildenafil plus iloprost was administered, the area under the curve of reduction in pulmonary vasodilatory resistance exceeded that when 50 mg of sildenafil alone and iloprost alone were administered together, the vasodilatory effect lasted more than 3 hours, and systemic blood pressure and arterial oxygenation were maintained. No serious adverse events occurred.

Conclusion: Although limited by a small sample and lack of long-term follow-up, the study shows that oral sildenafil is a potent pulmonary vasodilator that acts synergistically with inhaled iloprost to cause severe pulmonary vasodilation in both severe pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension.

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