

EFFICACY EVALUATION OF TREATMENT OF PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE BY DYNAMICS OF CLINICO-FUNCTIONAL AND LABORATORY PARAMETERS**Kulik E.G., Pavlenko V.I., Naryshkina S.V.**

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Abstracts The presented article contains the results of a study that studies the effect of long-term pharmacotherapy with the inclusion of roflumilast on clinico-functional and laboratory parameters in patients with severe COPD, high-risk. In the course of the examination, it was established that the long-term inclusion in the basic therapy of the anti-inflammatory drug roflumilast leads to more significant changes in clinical, functional and laboratory parameters than the conventional pharmacological scheme. There was also a significant improvement in the quality of life of patients and a reduction in episodes of exacerbations in 6 months.

Key words: chronic obstructive pulmonary disease, inflammation, therapy, roflumilast.

Introduction Chronic obstructive pulmonary disease (COPD) continues to be one of the global problems of the world, especially in developing countries. Taking into account the scale of complications of the disease and the level of disability, the issues of rational drug therapy of patients at any stage remain relevant. At the present time during the treatment of COPD, no drug is able to prevent a decline in pulmonary function in the future [4]. Considering the fact that modern treatment is based not only on spirometric indicators, but on a comprehensive assessment of the patient's condition, the authors propose a correction of already existing schemes by means of new groups of drugs, among which the phosphodiesterase 4 (PDE4) inhibitor roflumilast takes its place. The evidence available up to date that were obtained in large clinical trials on a broad patient population indicate the strong potential of roflumilast as the first representative of a conceptually new class of drugs aimed at treating COPD-specific inflammation [3]. Consequently, further study of the efficacy of roflumilast in actual clinical practice is important today [6, 7].

Aim of studies: evaluate the effect of long-term drug therapy using roflumilast on clinico-functional and laboratory parameters in patients with COPD severe course, high risk.

Material and methods: 69 patients with COPD severe course, high risk who received treatment in pulmonology department and outpatient department of the Far Eastern Scientific Centre of Physiology and Pathology of Respiration in 2012-2015, mainly men (82.5%) aged 42 to 76 years, participated in this study. Duration of the disease was 10.81 ± 0.75 years. The diagnosis of COPD was made according to the criteria of the Global Initiative for COPD (GOLD) 2013. At the time of admission to the hospital, all patients, depending on the volume of therapy, were divided by a simple blind method into two groups: 1st group (n = 31) - individuals receiving first-choice drugs according to GOLD (2013); in the scheme for treatment of patients of the 2nd group (n = 38), an additional oral phosphodiesterase 4 roflumilast inhibitor was added in the proportion of 500 µg daily for 6 months. By sex composition, duration of COPD, history of smoking and basic therapy, the groups were equivalent. Complex clinico-instrumental and laboratory research of patients was carried out twice – during the admission to the hospital and after 6 months. The frequency of COPD exacerbation was estimated for 6 months. The control group consisted of 15 smoking volunteers aged 40 to 65 years.

The patient screening program included: the determination of the intensity of clinical symptoms by means of a marked gradation with specific assessment tests of the effect of COPD on the patient's condition (CAT and mMRC); spirometry with the instrument "Erich JAEGER GmbH" (Germany).

To assess the severity of nonspecific inflammatory reactions, the following actions were performed [1]: a clinical blood test and a biochemical blood test (fibrinogen, CRP) using highly sensitive test systems "Biochem-mack" (Austria). Control and correction of treatment was carried out once a month at an outpatient stage.

The obtained data were processed by non-parametric variation statistics methods with the use of the application software package Statistica 10.0. The quantitative data are presented as an average and 95% of confidence interval. As a comparison of independent samples, Mann-Whitney U test was in use. Differences were considered to be authentic at $p < 0.05$.

Results of studies and discussion

During admission to the hospital, all patients expressed complaints of cough predominantly with scanty, difficult to separate phlegm of mucus or puromucous nature (86.4%) and exertional dyspnea of varying intensity. In the setting of already administered therapy, it was noted that the inclusion in the basic therapy of the anti-inflammatory drug roflumilast for a long period of time (6 months) leads to more significant changes in clinico-functional and laboratory parameters than the conventional pharmacological scheme (Table 1). For example, in the 2nd group of patients, in comparison with the 1st group, there was less intensity of cough by 21.4% ($p < 0.01$), dyspnea by 12.6% ($p < 0.01$), phlegm - by 5.6% ($p < 0.05$). (Table 1.)

A notional and significantly greater increase in the initial index of FEV1 ($p < 0.01$) was obtained in patients from the 2nd group, while in the patients of the 1st group only the dynamics of the studied index with a tendency to statistically significant ones ($p > 0.05$) was revealed.

When comparing the results of the conducted therapy, it has been established that under any of the selected treatment regimens the concentration of biomarkers of systemic inflammation significantly declines [5]; however, in the setting of taking the oral PDE-4 inhibitor, roflumilast, the effect was the most favorable. The laboratory examination of patients of the 2nd group enabled to reveal a statistical decrease in the content of the initial leukocyte level by 24.3% ($p < 0.001$), C-reactive protein by 37.3% ($p < 0.0001$) and fibrinogen by 8.6% ($p < 0.05$), while in the 1st group, correspondingly, 11.6% ($p < 0.01$), 27.9% ($p < 0.001$) and 5.0% ($p > 0.05$).

In the setting of administration of roflumilast during the observed period, COPD exacerbation in patients of the 2nd group was not noted. While 12 patients of the 1st group had an exacerbation of the disease [2].

After treatment, the improvement in CAT values was revealed in comparison with initial data in all study groups with

Table 1. The main clinico-functional and laboratory parameters of patients after 6 months of treatment (M and \pm 95% CI)

Indices	groups	initially	after 6 months	% of decrease	p1
Cough (points)	1 st	2,19[1,95-2,4]	1,71[1,46-1,96] **	21,9	<0,01
	2 nd	2,17[1,81-2,52]	1,23[0,99-1,47] ***	43,3	
Cough (points)	1 st	2,41[1,99-2,84]	2,19[1,95-2,43]	8,75	<0,05
	2 nd	2,37[2,06-2,68]	2,03[1,87-2,19] *	14,3	
Phlegm (points)	1 st	2,65[2,40-2,89]	2,42[2,17-2,66]	8,68	<0,01
	2 nd	2,58[2,4-2,78]	2,03[1,87-2,19] **	21,3	
Dyspnea according to mMRC scale (points)	1 st	22,71[20,6-24,8]	20,48[18,9-20,1] *	9,8	<0,001
	2 nd	20,67[18,7-22,5]	14,4[12,2-16,7] ****	30,3	
FEV ₁ (% D)	1 st	40,5[39,3-43,7]	41,5[38,7-42,3]	2,4	<0,01
	2 nd	43,3[41,2-45,3]	49,4[45,9-52,9] **	14,1	
FEV ₁ /FVC (% D)	1 st	54,6[51,3-57,7]	57,0[53,4-60,6]	9,1	>0,05
	2 nd	51,7[47,6-55,9]	58,5[53,7-63,2] *	11,3	
Leukocytes (10 ⁹ / L)	1 st	8,67[8,07-9,28]	7,66[7,33-8,19] **	11,6	<0,01
	2 nd	8,63[8,03-9,23]	6,53[5,99-7,07] ***	24,3	
C-reactive protein (g / L)	1 st	11,11[10,34-11,89]	8,00[6,66-9,37] ***	27,9	<0,05
	2 nd	11,12[10,20-12,04]	6,97[5,98-7,96] ****	37,3	
Fibrinogen (g / L)	1 st	4,16[3,81-4,52]	3,95[3,53-4,36]	5,0	>0,05
	2 nd	4,21[3,91-4,51]	3,85[3,45-4,24] *	8,6	

Note: symbol * indicates the differences between the indices in the groups before and after treatment (*-p<0,05, **-p<0,01, ***-p<0,001, ****- p<0,0001); p1- the level of significance of differences between the 1st and 2nd groups after the treatment; FEV₁ – forced expiratory volume in 1 second; FVC – forced volume vital capacity.

the greatest dynamics in the 2nd group (p <0.0001). The statistical significance between the 2nd and 1st groups after treatment was p <0,01.

As the state of patients improved in the course of the treatment, the need for short-range bronchodilators decreased, which enabled to reduce the single and daily doses in both groups, while in the 2nd group it was more significant (p <0.001).

Conclusions

Thus, the inclusion of a PDE-4 inhibitor in the comprehensive treatment of patients of a high-risk category with severe COPD leads to a more pronounced regression of the symptoms of the disease and the degree of their effect on the health of patients, reducing the activity of systemic inflammation, enables to slow the progression of bronchial obstruction and reduce the risk of exacerbations of the disease in future.

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THE SOFTWARE SCORING OF THE PULMONARY ARTERY

THROMBOEMBOLISM RISK IN ONCOLOGY

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Abstract The problem of the thromboembolism of the pulmonary artery (TEPA) is still not solved and quite urgent especially for patients with malignant tumors. The risk of TEPA at this patients' rank is about 10-40% and 10% with lethal outcome without adequate prophylaxis. The TEPA prophylaxis is based on the stratification of the risk level that is subsequently depends on quality and quantity of the risk factors for every case personally.

Key words: thromboembolism of the pulmonary artery, risk, oncology, colorectal cancer, software

Objective To optimize the program of the thromboembolic complications for the patients with oncological disease of colorectal localization.

Materials and methods To gain the purpose we created and registered the software for TEPA risk calculation (The certificate of Russian state software registration for IBM N2015619184, 26.08.2015). This software gives us ability to calculate the risk factors of the TEPA for every patient personally and after all to get standard scheme of the TEPA prophylaxis and treatment personally with considering of patient's weight and age.

Results and discussion The retrospective analysis of the colorectal cancer cases (n=41) were made. We found these TEPA risk factors: the age of 61-80 years in 67%, obesity – 45%, heart diseases – 33%, the surgical intervention duration more than 1 hour – 75%, varicose disease of the legs – 45%. The combination of the 2 risk factors was found in 20% and 3 risk factors in more than 62,5%. Thus, the high risk of TEPA (IIC, IIIA, B, C by Samama, 1999) was no less than in 17,5% cases with the risk of TEPA in 5 – 10%, and lethal TEPA in 1 – 5%. The patients with high risk of TEPA must pass through active methods of TEPA prophylaxis such as pharmacotherapy.

Thus, our software gives ability to doctors of every specialty to calculate the risk of the thromboembolic complications with mathematical accuracy and objectively get personified program of TEPA prophylaxis and treatment by actual national recommendations with considering the patients' weight and age. This is especially actual for the medical institutions without cardiovascular surgeons in stuff who are responsible for TEPA stratification in routine conditions.

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RESULTS OF IMMUNOFERMAL ANALYSIS IN CHILDREN RELATING TO THE GROUP OF FREQUENT PATIENTS

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Key words: often ill children, TORCH infections, enzyme immunoassay.

Summary: Children who are prone to frequent acute respiratory infections (ARI) are often called sick. Frequent ARI can lead to disruption of the physical and neuropsychological development of children. One of the reasons is the presence of a TORCH infection in a child. For the diagnosis of TORCH infections, the enzyme immunoassay is used to determine the levels of the Ig classes of IgM and IgG that appear at different stages of the immune response and are in the blood at different times. The article reflects the results of analysis of 50 case histories of children