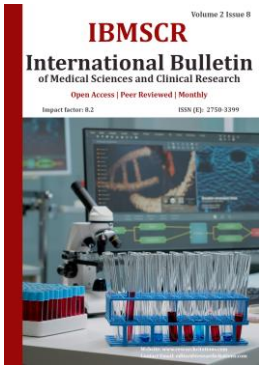

CLINICAL EFFICACY OF THE DOMESTIC MUCOLYTIC DRUG ASCEIN (N-ACETYLCYSTEINE) IN THE COMPLEX TREATMENT OF PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Musaeva L.J.
Abdumajidova N.X.
Avazova G.N.
Tashkent Medical Academy, Uzbekistan
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Abstract

Chronic obstructive pulmonary disease (COPD) is one of the most common pathologies of the respiratory system and is often the cause of disability and mortality of this category of patients. An unfavorable prognosis is often due to late diagnosis of COPD. Over the past decade, certain successes have been achieved in the study of pathogenesis, clinic, early diagnosis and treatment of COPD. COPD therapy includes pharmacological and non-pharmacological approaches that can significantly reduce clinical symptoms and reduce the frequency of exacerbations of the disease. Mucolytic therapy such as N-acetylcysteine, ambroxol, or carbocysteine may also be considered in patients with chronic bronchitis. Our study showed that when N-acetylcysteine was included in the complex treatment of moderate COPD in the acute stage, SpO2 levels significantly increased, shortness of breath, cough symptoms and the amount of sputum excreted decreased, which significantly improves the clinical picture and quality of life of patients.

Keywords: chronic obstructive pulmonary disease, treatment, mucolytic therapy, N-acetylcysteine

Introduction

Currently, chronic obstructive pulmonary disease (COPD) is a global problem. The level of prevalence, morbidity and mortality of COPD varies not only by country, but also by region within one country. The prevalence of COPD is directly related to the prevalence of smoking. In addition, in many countries, the main risk factors include environmental air pollution. According to WHO, today COPD is the 3rd leading cause of death in the world, about 2.8 million people die from COPD annually, which is 4.8% of all causes of death. According to experts' forecasts, by 2030 the disease will take the third place among the causes of death in the world [4]. The main cause of death in patients with COPD is the progression of the underlying disease. About 50-80% of COPD patients die from respiratory causes: either during exacerbations of COPD, or from lung tumors (from 0.5 to 27%), or from other respiratory problems.

In Uzbekistan, as in the whole world, there is an increasing increase in patients with respiratory diseases. This is due to pronounced solar radiation, high air temperature, dustiness, combined exposure to pesticides. Respiratory diseases in the Republic of Uzbekistan occupy the first place in the structure of morbidity of the population. Mortality from respiratory diseases ranks second in the country, giving way to cardiovascular diseases [1].

COPD therapy includes pharmacological and non-pharmacological approaches. Pharmacological methods of treatment include the appointment of bronchodilators, combinations of inhaled GCS and long-acting bronchodilators, phosphodiesterase-4 inhibitors, theophylline, as well as vaccination against influenza and pneumococcal infection. Non-pharmacological methods include smoking cessation, pulmonary rehabilitation, oxygen therapy, respiratory support and surgical treatment [3].

Therapy of exacerbations is considered separately. The appointment of mucolytic drugs is recommended for patients with COPD with bronchitic phenotype and frequent exacerbations, especially if therapy with inhaled glucocorticosteroids is not carried out [6,7].This group includes several substances with different mechanisms of action. The regular use of mucolytic drugs in COPD has been studied in several studies, but contradictory results have been obtained [5].

The pharmacological activity of N-acetylcysteine suppresses oxidative stress, acting as a cell-permeable amino acid precursor of glutathione and breaking disulfide bonds, which leads to depolarization of mucoproteins and a decrease in sputum viscosity. As a result, mucociliary clearance increases and sputum discharge improves. In addition, N-acetylcysteine suppresses the formation of pro-inflammatory cytokines, such as IL-8 and TNF-α, thereby exerting anti-inflammatory activity. Due to the mechanism of action aimed at increasing glutathione, improving the response of T-lymphocytes and modulating inflammation, N-acetylcysteine can be used in the complex treatment of COPD.

The aim of this study was to evaluate the clinical efficacy of ascein (T-acetylcysteine) in the complex treatment of moderate COPD in the acute stage.

Materials and methods

The study included adult patients (n = 50; median age – 63 (52; 75) years; body mass index (BMI) – 30 (27.1; 33.1) kg / m2; duration of illness before hospitalization – 7 (6; 8) days)with moderate COPD. The patients were treated in the pulmonology department of the multidisciplinary clinic of the Tashkent Medical Academy.

After the diagnosis of COPD was confirmed, the patients were divided into 2 observation groups: 1st control group (n = 25) – patients receiving standard COPD therapy (bronchodilators - long-acting β2-agonists, long–acting anticholinergic drugs, inhaled corticosteroids, antibacterial drugs); 2nd (n = 25) - patients who, in addition to bronchodilating therapy, were prescribed the mucolytic drug ascein (ATM Farm, Uzbekistan). The drug was prescribed 1 powder 200 mg 3 times a day for 10 days.

Initially and after 10 days of treatment, the dynamics of clinical symptoms of the disease (the severity of cough, shortness of breath and the amount of sputum released) were determined. The assessment of respiratory symptoms was carried out in points — from 0 (absence of a symptom) to 3 (significant severity of the symptom). Pulse oximetry with measurement of blood oxygen saturation was used to detect respiratory insufficiency (RI) and assess the severity of hypoxemia. Pulse oximetry was performed using a pulse oximeter of the MEDICOM130T series. Respiratory insufficiency was determined in accordance with the severity classification based on pulse oximetry (SpO2). To assess the nutritional status of patients, the BMI indicator was used, which was calculated according to the generally accepted formula: BMI = body weight (kg) / height (m)2.

The Statistica for Windows 13 program was used for statistical processing of the obtained results. The confidence interval for the difference of averages was calculated.

Results

The groups were comparable in age, severity of COPD and other clinical indicators (Table 1); no significant differences were found ($p > 0.05$).

Table 1. Initial clinical characteristics of the examined patients.

Indicators	Group 1 (basic therapy) n = 25	Group 2 (basic therapy + ascein) n = 25	p
	M ± SD	M ± SD	
Age, years	59(53,5±12,1)	64 (61,0 ± 12,8)	0,007
BMI, kg / m2	28,8 (27,79 ± 3,62)	30,2 (30,4 ± 3,0)	0,006
Duration of the disease Before hospitalization, days	6,8 (6,5 ± 1,51)	7,5 (7,0 ± 1,7)	0,41
RR	25 (23,2 ± 1,12)	24 (24,1 ± 0,5)	0,15
HR	90 (86,30 ± 7,53)	89 (83,8 ± 7,3)	0,23
SpO2, %	93 (92,20 ± 1,3)	92 (91,6 ± 0,5)	0,39
Body temperature,˚ C	37,6 (37,10 ± 0,41)	37,8 (37,6 ± 0,5)	0,08
Cough	2,81 (2,51± 0,49)	2,82 (2,83 ± 0,45)	0,01
Sputum	1,59(1,58±0,37)	1,62 (1,55±0,96)	0,03
Shortness of breath	2,7 (2,65±0,52)	2,8 (2,74±0,48)	0,01

Note: BMI – body mass index; SpO2 – blood oxygen saturation; RR – respiratory rate; HR – heart rate; M ± SD – mean standard deviation; p – statistical significance of differences between the experimental and control groups.

As can be seen from the table, comparable results of initial clinical and functional indicators were noted in all observation groups.

As a result of treatment, a statistically significant change in all the considered indicators was demonstrated in both groups. However, it is worth noting that the analysis revealed intergroup differences in the intensity of changes in a number of indicators (Table 2).

Table 2. Dynamics of indicators after treatment.

Indicators	Group 1 (basic therapy) n = 25	Group 2 (basic therapy + ascein) n = 25	p
RR	18 (17,91 ± 0,65)	17 (16,7 ± 0,82)	0,07
HR	77 (73,34 ± 7,21)	78 (72,6 ± 8,16)	0,06
SpO2, %	96 (96,23 ± 1,10)	97 (97,0 ± 0,9)	0,02
Body temperature,˚ C	36,6 (36,60 ± 0,12)	36,6 (36,6 ± 0,11)	0,06
Cough	2,13 (2,09 ± 0,72)	1, 49 (1,52± 0,67)	0,02
Sputum	1,10 (0,96±0,05)	0,7 (0,65±0,03)	0,03
Shortness of breath	2,4 (2,37±0,49)	2,1 (2,0±0,34)	0,05

In all patients with extreme COPD severity, cough was constant, productive, with difficult-to-separate mucopurulent sputum, intensified at night and combined with shortness of breath. As a result of the use of ascein in the complex therapy of 49 (98%) patients, an improvement in sputum discharge was noted ($p<0.05$), while cough became more rare and

productive, the number of wet wheezes noticeably decreased during physical examination, the tolerance of physical exertion increased, the change in the nature of sputum to a mucous consistency occurred faster, by the 10th day of treatment.

In patients receiving basic bronchodilation therapy in combination with ascein, after 10 days of follow-up, a significant positive dynamics of cough reduction was established. In this group of patients, there was a decrease from 2.83 ± 0.45 to 1.52 ± 0.67 points. In the first group of patients receiving traditional therapy, there was a tendency to reduce cough, but it did not reach statistically significant values. Already 10 days after the addition of ascein at a dose of 600 mg to basic therapy, shortness of breath (from 2.8 to 2.1 points) and sputum secretion (from 1.6 to 0.7 points) also decreased in patients. The improvement of sputum discharge at the beginning of treatment was replaced by a decrease in its separation.

The level of SpO2 in each patient of the basic treatment group increased by an average of 2.95 ± 1.37 % ex. – from 93 (91; 95) to 96 (95; 97)% (the change is statistically significant – $p < 0.001$), at the same time, the increase in this indicator in the ascein group averaged 4.6 ± 1.21% – from 92 (92; 93) to 97 (96; 98)% ($p < 0.001$). The difference between the intensity of growth is statistically significant ($p = 0.001$). As a result of the different intensity of the increase, the SpO2 index after treatment of patients in the ascein group became statistically significantly higher compared to the control group -97 (96; 98)% vs 96 (96; 97)% ($p = 0.02$).

The drug was well tolerated, no serious side effects were registered in any treatment group.

Discussion

Against the background of treatment, a statistically significant change in all the considered indicators was demonstrated in both groups. The results of the study indicate a positive effect of the inclusion of the drug ascein in the complex therapy of patients with exacerbation of COPD. One of the most sensitive and indicative criteria of treatment is the degree of reduction in the severity of cough and sputum, as well as shortness of breath in persons with bronchial obstruction. According to the results of this study, a statistically significant decrease in the symptoms of cough, shortness of breath, and a decrease in the amount of sputum excreted in patients receiving the mucolytic drug ascein in addition to basic therapy was demonstrated. The improvement of sputum discharge is associated with a decrease in the viscosity and adhesiveness of bronchial secretions, as a result of which sputum is more easily separated when coughing. Due to the increased motor activity of the cilia of the ciliated epithelium for the evacuation of less viscous secretions, the drug also has a distinct mucokinetic effect [2].

The positive effect of ascein is also evidenced by the indicator of blood oxygen saturation. After treatment in patients of the second group, this indicator became statistically significantly higher than in the control group. The mechanism of realization of this effect is probably primarily associated with the effect on mucociliary clearance and indirectly with a decrease in local inflammation in the tracheobronchial tree. Also, the positive effect of caffeine is associated with the antioxidant properties of the drug, since it directly neutralizes free radicals and, in addition, is a precursor of glutathione, the main thiol–free cell antioxidant. Consequently, ascein can restore the impaired redox status of the cell, modify the cascade of inflammatory reactions in COPD by inhibiting signal transmission factors in the cell and expression of pro-inflammatory genes.

Conclusion

The study showed that with the inclusion of acein in the complex treatment of moderate COPD at the stage of exacerbation, the SpO2 level significantly increased, shortness of breath, cough symptoms and the amount of sputum excreted decreased, which significantly improves the clinical picture and quality of life of patients.

A good tolerance profile and absence of pronounced side effects were also noted.

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