UDC 616.24-007.272-036.12:615.835.56-085

O. B. Iaremenko[1], N. M. Kuzmenko[1], G. L. Gumeniuk[2,3], D. V. Dobrianskyi[1], R. I. Ilnitskyi[1], O. I. Magas[1]

[1] Bogomolets National Medical University, Kyiv
[2] phthisiology and pulmonology named after F. G. Yanovsky NAMS of Ukraine, Kyiv
[3] Shupyk National Medical Academy of Postgraduate Education, Kyiv

COMPARATIVE EFFECTIVENESS OF APPLICATION OF ACETYLCYSTEIN IN PERORAL AND INHALATION FORM FOR NEBULIZER THERAPY IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Key words: *COPD, acetylcysteine, nebulizer therapy, mucolytics* .

Chronic obstructive pulmonary disease (COPD) is a widespread disease that can be prevented and treated and is characterized by persistent respiratory symptoms and the constraint of airway patency due to pathological changes in the airways and/or alveoli caused by significant exposure to harmful particles and gases [8]. The main symptoms of the disease are dyspnea, which progresses over time and increases during exercise, chronic cough, which may be intermittent and unproductive, prolonged secretion of sputum. If dyspnoea occurs most often in COPD, the productive cough bothers about 30 % of patients, its severity may change over time, and appearance may precede changes in the parameters of the lung function for many years [8].

According to recent international recommendations [8], bronchodilators (β2-agonists, cholinolytics) are used in a stable state to treat patients with COPD on a regular basis to prevent and reduce the severity of symptoms. But even on the background of regular intake of basic inhalation therapy, some patients continue to complain of cough with difficult expectoration. This hypersecretion is due to an increase in the number of goblet cells and submucosal glands in response to chronic irritation of the respiratory tract mucus with tobacco smoke and other harmful agents. For the category of patients who do not receive inhaled glucocorticoids, additional use of mucoactive drugs is advisable. Mucolytics violate the structure of the mucus gel, reduce its viscosity and elasticity, and thus improve viscoelastic properties of sputum, which facilitates the cleaning of respiratory tract [17]. Effective mucolytics with the best evidence base include acetylcysteine and carbocysteine. According to the results of studies [8, 4], oral administration of acetylcysteine or carbocysteine can reduce the severity and frequency of exacerbations of COPD [5, 15]. However, due to heterogeneity of the population, dosage regimen and concomitant therapy remain unresolved regarding the contingent of patients requiring additional mucolytics, as well as insufficient data about the effect of drugs on quality of life [15].

There are separate studies which investigate the effectiveness and safety of mucolytic drugs, primarily acetylcysteine and its derivatives, in inhalation form by nebulizer technology [23, 2]. These studies were performed in patients with cystic fibrosis and in healthy subjects, although some authors extrapolated the positive results obtained in the contingent of patients with COPD [18]. For now no randomized controlled trials have been conducted to evaluate the benefit and safety of N-acetylcysteine or similar mucolytic drugs for inhalation use in the treatment of any respiratory disease. We did not find any studies in which in the comparative aspect was studied the effect of acetylcysteine administered orally and in inhalation form on clinical status, lung ventilation and quality of life in patients with COPD.

www.search.crossref.org
DOI: 10.31655/2307-3373-2019-1-15-21

Aims. Determine the efficacy and safety of inhaled nebulizer application of acetylcysteine compared with its oral administration in patients with COPD in a patient's stable condition.

Materials and methods. The study included 31 patients with spirometry-confirmed COPD and complaints on cough with viscous sputum excretion. Among them, 26 were men (83.9 %) and 5 women (16.1 %) aged 50 to 78 years (63.5 ± 6.7 years on average), with a duration of illness from 1 to 14 years (7,6 ± 3.6).

By random sampling two groups of patients were formed. In the first of them (n = 13), patients received acetylcysteine orally, in the second (n = 18) – inhalation with a nebulizer. Patients in the first group received oral acetylcysteine in the form of a powder (ACC 200, Salutas Pharma GmbH, Germany), pre-dissolved in a glass of water 200 mg 3 times a day after eating for 10 days. Patients in the second group received a 10-day course of treatment with acetylcysteine by inhalation using a 3 ml 10 % solution (Ingamyst, Yuriia-Farm, Ukraine) in a single session 2 times a day (morning and evening); the duration of the inhalation session was 7–10 minutes. As can be seen from the data given, the daily dose of acetylcysteine in both groups was the same — 600 mg. During treatment with acetylcysteine all patients continued to receive baseline therapy in the unchanged regimen (long-acting cholinolytics, long-acting β_2-agonists, combination thereof and inhaled glucocorticoids in combination with long-acting β_2 agonists).

To evaluate the severity of the symptoms and the efficacy of the treatment, the data of validated questionnaires were analyzed: for the overall assessment of the COPD — COPD Assessment Test (CAT) severity and the Modified Medical Research Council Dyspnea Scale (mMRC) [3,13], for assessing the dynamics of respiratory symptoms – focused on patients with COPD Clinical COPD Questionnaire score (CCQ) [21, 10]. Additionally, a 6-minute walk test was performed [6].

The severity of the day and night coughing also assessed on a scale [1]. In order to objectify the changes in the parameters of the lung function, spirometry was performed (SPIROKOM, "KhAI-MEDICA", Ukraine) according to the standard protocol [8, 11].

All of the above studies as well as a sputum analysis were performed before and immediately after the completion of the 10-day course of treatment. In the sputum analysis the number of leukocytes was measured on the mucus expressed in numbers 1, 2, 3, 4 in accordance with the results of the quartile distribution of the resulting variation series. In addition, spirometry was performed 2 hours after the first reception of acetylcysteine by oral or inhalation route.

The evaluation of acetylcysteine tolerance was carried out after the first application of the drug and after the entire course of treatment according to the results of the patient survey, laboratory and instrumental data.

The statistical processing of data were performed by methods of descriptive statistics, the nature of the data distribution was estimated by the graphical method and using the Kolmogorov-Smirnov and Shapiro-Wilk criteria. Average values are presented in the form of mean value and standard error of the mean value (±σ), qualitative — in %. For data processing with normal distribution parametric methods were used. For comparison of two independent groups of patients t-test for independent groups was used, to compare the results of initial and re-examination of patients - paired t-test was used. In the nature of the distribution of data other than normal nonparametric statistical methods Mann-Whitney's criterion, Wilcoxon's criterion were used. The difference was considered probable at $p < 0.05$. The statistical analysis was performed using the standard program package Microsoft Office Excel 2016 (Microsoft Corp., USA) and Statistica 10.0 (StatSoft Inc., USA).

Results. Characteristics of patients before inclusion in the study are given in Table 1.

As can be seen from the table, in the group of patients taking acetylcysteine by inhalation, the number of female participants was higher compared to the oral group ($p < 0.05$), although there was no statistically significant difference in the number of men in both groups. For all other indicators, including the results of all questionnaires, a 6-minute walk and spirometry test, as well as the number of GOLD-grade patients in group B (from 2 and 10 points according to the mMRC and CAT questionnaires respectively with frequency of exacerbations not requiring hospitalization for the last 12 months, no more than one [8]) and group D (from 2 and from 10 points according to the mMRC and CAT questionnaires, respectively, with the frequency of exacerbations without hospitalization in the last 12 months more than 2, or the presence of exacerbations, which requires hospitalization), the groups receiving inhaled and oral acetylcysteine were comparable.

Table 2 shows the results of a 10-day course of treatment with acetylcysteine. In the group of patients receiving acetylcysteine orally, a significant improvement in the patients' condition was noted by the CCQ questionnaire (decrease by 15.1 %, $p < 0.04$). According to other questionnaires, the results of a 6-minute walk test, the severity of the symptoms of day and night cough and spirometric indices significant dynamics was not recorded. Instead, in the group of patients receiving acetylcysteine by inhalation, there were significant positive changes in the results of the CAT questionnaire (a 16.8 % decrease compared to baseline) and a decrease in the symptoms of night cough (by 36.4 %). In this case, the score according to mMRC, CCQ, and daytime cough symptoms did not change significantly. In addition, there was a decrease in the manifestations of bronchial obstruction – an increase in the average FEV_1 by 10 % ($p = 0.01$). An important consequence of inhaled therapy should be considered as a significant reduction in the number of leukocytes in the sputum. There was no statistically significant difference in dynamics of the indicators between the groups.

Also, an estimate of changes in spirometric indices was made immediately after 2 hours of the first drug administration (Table 3). The data in the table show the absence of reliable changes in FEV_1 due to the single oral or inhaled use of acetylcysteine. This may indicate that the increase in the values of FEV_1 after the completion

ISSN 2307-3373 DOI: 10.31655/2307-3373-2019-1-15-21

Table 1. Clinical and demographic characteristics of COPD patients included in the study

Indicators		Patients receiving acetylcysteine therapy	
		Oral (n = 13)	Inhalation (n = 18)
Women, %		7,7	22,2*
Men, %		92,3	77,8
Age, years ($\overline{X}$ ±σ)		62,5 ± 7,95	64,3 ± 5,68
Duration of the disease, years ($\overline{X}$±σ)		7,7 ± 3,79	7,6 ± 3,55
CAT, points		21,0 ± 7,92	23,56 ± 3,81
mMRC, points		2,08 ± 1,12	2,56 ± 0,86
CCQ, points		26,92 ± 12,74	31,33 ± 9,83
Day cough, points		2,15 ± 0,55	2,67 ± 0,97
Night cough, points		1,08 ± 0,95	2,17 ± 1,34
6-minute walk test, m ($\overline{X}$ ± σ)		255,85 ± 37,03	252,39 ± 36,52
FEV_1**	L	1,48 ± 0,54	1,10 ± 0,56
	%	46,88 ± 18,18	38,95 ± 16,52
Clinical group B, %		61,5	72,3
Clinical group D, %		38,5	27,7

Примітки. * p < 0,05; ** FEV_1 — – forced expiratory volume in the first second.

Discussion. OThe obtained results indicate that oral administration of acetylcysteine at an average therapeutic dose (600 mg/day) for 10 days improved the quality of life of patients with COPD assessed by the CCQ questionnaire, although it did not affect the severity of COPD symptoms determined by the CAT questionnaire and mMRC, exercise tolerance, cough frequency in the daytime and at night. At the same time indicators of the lung function also remained unchanged. In contrast to the oral administration, the inhalation route of the drug was accompanied by a significant positive change in the results of the CAT questionnaire, manifestations of cough at night and improved values of spirometry. Consequently, acetylcysteine in both its variants had a positive effect on the clinical status of patients, but when it was administered orally, it limited itself to only quality of life indicators, while the 10-day course of inhalation by a nebulizer was associated with improved airway patency and COPD symptoms, including night cough, reduction of inflammatory characteristics of sputum. The absence of significant differences in the dynamics of the studied parameters between groups is probably due to a small sample of patients.

In studies of other authors, inconsistent data were obtained about the efficacy of oral acetylcysteine in patients with COPD [20, 26, 12]. Only with prolonged use of the drug in medium and high doses [16], changes in spirometric parameters (reduction of the progression of FEV1 decrease), improvement of quality of life and reduction of the frequency of exacerbations of the disease were detected.

Table 2. Changes in clinical, spirometric and laboratory parameters in patients with COPD under the influence of a 10-day course of treatment with acetylcysteine orally and by inhalation ($\overline{X}$ ± σ)

Indicators		Patients receiving acetylcysteine therapy						
		Oral (n = 13)			Inhaled (n = 18)			
		before treatment	after treatment	p_1	before treatment	after treatment	p_1	p_2
CAT, points		21,00 ± 7,92	19,54 ± 7,40	0,273	23,56 ± 3,81	20,17 ± 6,18	0,012	0,198
mMRC, points		2,08 ± 1,12	2,00 ± 0,82	0,940	2,56 ± 0,86	2,17 ± 1,15	0,156	0,53
CCQ, points		26,92 ± 12,74	23,38 ± 13,06	0,042	31,33 ± 9,83	28,17 ± 9,81	0,104	0,748
Day cough, points		2,15 ± 0,55	2,08 ±0,76	0,123	2,67 ± 0,97	2,22 ± 0,88	0,938	0,27
Night cough, points		1,08 ± 0,95	0,69 ± 0,75	0,219	2,17 ± 1,34	1,38 ± 1,14	0,010	0,319
6-minute walk test, m		255,9 ± 37,0	256,4 ±3 8,2	0,356	252,4 ± 36,5	256,3 ± 36,8	0,067	0,561
FEV_1	L	1,48 ± 0,54	1,46 ± 0,52	0,542	1,1 ± 0,56	1,21 ± 0,58	0,01	0,201
	%	46,88 ± 18,18	45,33 ± 19,31		38,95 ± 16,52	42,95 ± 17,7		
Number of leukocytes in sputum, quartiles		3,69 ± 0,63	3,17 ± 1,11	0,297	3,28 ± 1,13	2,88 ± 1,36	0,031	1,0

p_1 — the significance of the difference in the indicators before and after treatment in the group (Wilcoxon criterion) , p_2 — the significance of the difference in the changes in the parameters in the treatment process between the groups (Mann-Whitney Criterion).

of the course of treatment in the inhaled group of acetylcysteine was a cumulative result not related to the direct, associated with the inhalation procedure, effect on bronchial patency.

The tolerability of course treatment with acetylcysteine was generally satisfactory. During the administration of oral drug 3 patients (23 %) noted periodic discomfort in the stomach area, which was resolved on its own. Two patients who received nebulizer therapy (11 %) reported a slight deterioration of the condition immediately after inhalation of the drug (increasing of cough), which self-limited for several tens of minutes. Some patients noted an unpleasant odor of the drug, but this did not affect the adherence to therapy, all patients had a full course of treatment.

Таблиця 3. Зміни показника $ОФВ_1$ через 2 години після першого застосування ацетилцистеїну

The route of administration		FEV_1 before treatment	FEV_1 after the first administration
Oral	l	1,48 ± 0,54	1,47 ± 0,62
	%	46,88 ± 18,18	46,53 ± 20,29
Inhaled	l	1,10 ± 0,56	1,07 ± 0,52
	%	38,95 ± 16,52	38,33 ± 16,33

Примітка. Всі зміни статистично не значущі (p > 0,05).

DOI: 10.31655/2307-3373-2019-1-15-21 ISSN 2307-3373

At short-term treatment (up to 4 weeks) of patients with COPD without exacerbation the drug (200 mg three times a day) did not demonstrate the ability to influence on the clinical condition of patients and on the parameters of spirometry. Positive effects of acetylcysteine with long-term use are associated with the presence of as antioxidant and anti-inflammatory properties. The drug is a thiol-containing compound, therefore it can acts as an antioxidant, increasing intracellular production of glutathione, whose molecule is one of the important elements of pulmonary antioxidant defense, thereby reducing inflammation and reducing the frequency of exacerbations of the disease [5, 16]. Our data on the absence of significant effects on symptoms of COPD and spirometry rates coincide with those of other researchers [12] who used 600 mg of acetylcysteine per day orally for 4–8 weeks.

We did not find the results of studies of the use of acetylcysteine with a nebulizer in patients with COPD in a stable condition. The effectiveness and safety of using acetylcysteine in the form of metered dose inhalers in patients with chronic bronchitis was determined [7]. Significant changes were not detected, the use of the drug was safe, and the frequency of exacerbations could not be estimated due to the short-term course of treatment. Also, the effectiveness of inhaled mucolytic therapy in patients with cystic fibrosis, bronchiectasis [24], idiopathic pulmonary fibrosis (IPF) [25, 19] and healthy subjects [23] was investigated. The safety of use and the positive effect of the drug on the parameters of lung function tests were established. Thus, according to the meta-analysis [25], acetylcysteine slows down the pace of decline in predicted vital capacity of the lungs (VC) in patients with ILF, and inhales of mucolytics along with perfinidone are capable to reduce the rate of annual decline in forced VC [19]. Our data about positive dynamics in the form of reducing the symptoms of the disease, improving the indicators of pulmonary lung tests with a 10-day course of acetylcysteine using a nebulizer in general coincides with the results of the above studies, although they were performed in patients with other pulmonary diseases. Interestingly, similar to our results regarding the reduction of cough after inhalation of acetylcysteine, we found in the experimental study of Pappova L. [14], which demonstrates the effect of acetylcysteine inhalations on the mechanisms of respiratory tract protection in animals – a decrease in the severity of cough. Researchers believe that the reason for the use of acetylcysteine by inhalation is the higher potential of its mucolytic action in direct contact with mucus associated with the presence of a sulfhydryl group in the molecule. This group opens disulfide bonds in the mucus, thereby reducing its viscosity [9]. In addition, the drug has antioxidant and anti-inflammatory properties, which can be more fully implemented at the local, rather than systemic application. As evidence of this assumption, we can consider our data on the reduction of leukocyte count in the sputum precisely with the inhalation rather than the oral route of application of acetylcysteine. Further clinical studies are needed to determine the benefits of the inhalation route and the oral route and to determine the mechanisms of these potential benefits.

Conclusions

1. In patients with COPD without exacerbation but in the presence of sputum the inhalation use of acetylcysteine with a nebulizer for 10 days has a wider range of exposure to the manifestation of the disease compared with the oral administration of the drug in the same daily dose: significantly improve not only indicators of quality of life questionnaires and symptoms of the disease, but also symptoms of night coughing and lung function (FEV_1).

2. After one (first) use of acetylcysteine both orally and in inhalation spirometry (FEV_1), does not significantly change.

3. The tolerance of acetylcysteine in both its variants is satisfactory, side effects develop infrequently and are not an obstacle to course treatment.

REFERENCES

1. Chuchalyn A.H. Pulmonolohyia: nats. ruk. Kratkoe yzdanye pod red. A.H. Chuchalyna (Pulmonology: nat. edition ed. A.G. Chuchalina). Moskva. HƏOTAR-Medya, 2014. 800 s.
2. App E. M., Baran D., Dab I. et al. Dose-finding and 24-h monitoring for efficacy and safety of aerosolized Nacystelyn in cystic fibrosis. Eur Respir J. 2002. Vol. 19. P. 294–302.
3. Barr J. T., Schumacher G. E., Freeman S. American translation, modification, and validation of the St. George's Respiratory Questionnaire. Clin Ther. 2000. Vol. 22(9). P. 1121–45.
4. Cazzola M. et al. Impact of Mucolytic Agents on COPD Exacerbations: A Pair-wise and Network Meta-analysis. COPD. 2017. Vol. 14(5). P. 552–563. DOI: 10.1080/15412555.2017.1347918.
5. Cazzola M. et al. Influence of N-acetylcysteine on chronic bronchitis or COPD exacerbations: a meta-analysis. Eur Respir Rev. 2015. Vol. 24. P. 451–461.
6. Dajczman E., Wardini R., Kasymjanova G., Préfontaine D., Baltzan M. A., Wolkove N. Six minute walk distance is a predictor of survival in patients with chronic obstructive pulmonary disease undergoing pulmonary rehabilitation. Can Respir J. 2015. Vol. 22(4). P. 225–229. DOI: 10.1155/2015/280187.
7. Dueholm M., Nielsen C., Thorshauge H., Evald T., Hansen N. C., Madsen H. D., Maltb N. N-acetylcysteine by metered dose inhaler in thetreatment of chronic bronchitis: a multi-centre study. Resp Med. 1992. Vol. 86. P. 89–92.
8. Global initiative for chronic obstructive lung diseases (GOLD). Global strategy for diagnosis, management and prevention of chronic obstructive lung diseases. NHLB/WHO workshop report. URL: https://goldcopd.org/gold-2017-global-strategy-diagnosis-management-prevention-copd/
9. Jargin S. V. On the use of acetylcysteine as a mucolytic drug. J Invest Biochem. 2016. Vol.2. P. 52–53. DOI: 10.5455/jib.20160929024258.
10. Kon S. et al. The Clinical COPD Questionnaire: response to pulmonary rehabilitation and minimal clinically important difference. Thorax. 2014. Vol. 69. P. 793–798.
11. MacIntyre N. R. Spirometry for the Diagnosis and Management of Chronic Obstructive Pulmonary Disease. Respiratory Care. 2009. Vol. 54. P. 1050–1057.
12. Millar A. B., Pavia D., Agnew J. E., Lopez-Vidriero M. T., Lauque D., Clarke S. W. Effect of oral N-acetylcysteine on mucus clearance. Br J Dis Chest. 1985. Vol. 79(3). P. 262–6.
13. Morishita-Katsu M., Nishimura K. The COPD assessment test and St George's Respiratory Questionnaire: are they equivalent in subjects with COPD? Int J Chron Obstruct Pulmon Dis. 2016. Vol. 11. P. 1543–1551. DOI: 10.2147/COPD.S104947.
14. Pappová L., Kazimierová I., Kocmálová M. Effect of inhaled and oral n-acetylcysteine on airway defense mechanism. Eur. Pharm. J. 2017.Vol. 64. P. 17–21. DOI: 10.1515/afpuc-2017-0002. DOI: 10.1515/afpuc-2017-0002.
15. Poole P., Chong J., Cates C. J. Mucolytic agents versus placebo for chronic bronchitis or chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews. 2015. I. 7. Art. No CD001287.
16. Repine J. E., Bast A., Lankhorst I. Oxidative stress in chronic obstructive pulmonary disease. Am J Respir Crit Care Med. 1997. Vol. 156. P. 341–357.
17. Rogers D. F. Mucoactive Agents for Airway Mucus Hypersecretory Diseases. Respiratory Care. 2007. Vol. 52. P. 1176–1197.
18. Sadowska A. M. et al. Role of N-acetylcysteine in the management of COPD. Int J Chron Obstruct Pulmon Dis. 2006. Vol. 1(4). P. 425–434.

ISSN 2307-3373 DOI: 10.31655/2307-3373-2019-1-15-21

19. Sakamoto S. et al. Effectiveness of combined therapy with pirfenidone and inhaled N-acetylcysteine for advanced idiopathic pulmonary fibrosis: a case-control study. Respirology. 2015. Vol. 20(3). P. 445–52. DOI: 10.1111/resp.12477.
20. Sanguinetti C. M. N-acetylcysteine in COPD: why, how, and when? Multidisciplinary Respiratory Medicine. 2016. Vol. 11. P. 11.
21. Ställberg B., Nokela M., Ehrs P. O., Hjemdal P. and Wikström E. Validation of the Clinical COPD Questionnaire (CCQ) in primary care. Health and Quality of Life Outcomes. 2009. Vol. 7. P. 26.
22. Stey C., Steurer J., Bachmann S., Medici T.C., TrameÁ M.R. The effect of oral N-acetylcysteine in chronic bronchitis: a quantitative systematic review. Eur Respir J. 2000. Vol. 16. P. 253–262.
23. Szkudlarek U., Zdziechowski A., Witkowski K. et al. Effect of inhaled N-acetylcysteine on hydrogen peroxide exhalation in healthy subjects. Pulm Pharmacol Ther. 2004. Vol. 17. P. 155–62.
24. Tarrant B. J., Maitre C., Romero L., Steward R., Button B. M., Thompson B. R., Holland A. E. Mucoactive agents for chronic, non-cystic fibrosis lung disease: A systematic review and meta-analysis. Respirology. 2017. Vol. 22(6). P. 1084–1092. DOI: 10.1111/resp.13047.
25. Tong Sun, Jing Liu, De Wei Zhao. Efficacy of N-Acetylcysteine in Idiopathic Pulmonary Fibrosis. Medicine. 2016. Vol. 95 (19). P. 1–7. DOI: 10.1097/MD.0000000000003629.
26. Turner R. D., Bothamley G. H. N-acetylcysteine for COPD: the evidence remains inconclusive. Resp Med. 2014. Vol. 2. P. 3.
27. Zheng J. P. et al. Twice daily N-acetylcysteine 600 mg for exacerbations of chronic obstructive pulmonary disease (PANTHEON): a randomised, double-blind placebo-controlled trial. Resp Med. 2014. Vol. 2(3). P. 187–194. DOI: 10.1016/S2213-2600(13)70286-8.

COMPARATIVE EFFICIENCY OF ACETYLCALCYTEIN APPLICATION IN ORAL AND INHALATION FORM WITH THE HELP OF NEBULAISER IN PATIENTS WITH COPD

O. B. Iaremenko, N. M. Kuzmenko, G. L. Gumeniuk, D. V. Dobrianskyi, R. I. Ilnytskyi, O. I. Magas

Abstract

Aims. To determine the efficacy and safety of nebulized inhalation of acetylcysteine compared with its oral administration in patients with chronic obstructive pulmonary disease (COPD).

Materials and methods. The study included 31 patients, two groups of patients were formed. In the first of them (n = 13) patients took acetylcysteine orally, in the second (n = 18) — by inhalation with a nebulizer for 10 days with stable basic therapy. To assess the severity of symptoms and the effectiveness of treatment, data from validated questionnaires (CAT, mMRC, CCQ) were analyzed, the severity of day and night cough was assessed on a scale, spirometry and sputum analysis were performed.

Results. Patients who received acetylcysteine orally showed a significant improvement in the condition according to the results of the CCQ questionnaire (a decrease by 15.1 %, $p < 0.04$). According to other methods of diagnostic no significant dynamics was obtained. In the group of patients who received acetylcysteine inhalation, there were significant positive changes in the results of the CAT questionnaire (a decrease by 16.8 % compared with the initial level) and a decrease in the symptoms of nocturnal cough (by 36.4 %). In this case, the score according to mMRC, CCQ, the symptoms of daily cough did not change significantly. A decrease in the manifestations of bronchial obstruction was recorded — an increase in the mean forced expiratory volume in one second (FEV_1) value by 10 % ($p = 0.01$) and decrease of leukocyte count in sputum was obtained. No significant changes of FEV_1 after first oral or nebulized exposure of acetylcysteine were obtained.

Conclusions. Inhalation use of acetylcysteine for 10 days has a wider range of effects on the manifestations of the disease compared with oral administration of the drug in the same dose in patients with COPD without exacerbation but in the presence of sputum. Tolerability of acetylcysteine in both cases of its use is satisfactory, side effects develop rarely.

Key words: COPD, acetylcysteine, nebulizer therapy, mucolytics.

Oleh Borysovych Iaremenko,
Head of the Department of Internal Medicine №3
Bogomolets National Medical University
26, P. Zaporozhets str., Kyiv, Ukraine, 02125, Kyiv City Clinical Hospital № 3.
tel.: (044) 540-96-91, e-mail: o.b.iaremenko@gmail.com
Asthma and allergy, 2019, 1, P. 15–21.

O. B. Iaremenko
ORCID iD
https://orcid.org/0000-0003-2095-5819

N. M. Kuzmenko
ORCID iD
https://orcid.org/0000-0001-5894-0968

G. L. Gumeniuk
ORCID iD
http://orcid.org/0000-0001-8160-7856

D. V. Dobrianskyi
ORCID iD
https://orcid.org/0000-0002-9513-9966

R. I. Ilnitskyi
ORCID iD
https://orcid.org/0000-0003-0264-4814

O. I. Magas
ORCID iD
https://orcid.org/0000-0002-4987-4994

DOI: 10.31655/2307-3373-2019-1-15-21
ISSN 2307-3373