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L. V. Iakovlieva, D. V. Bondarenko, N. A. Barilyuk
National University of Pharmacy, Kharkiv

Evaluation of pharmacotherapy of the chronic obstructive pulmonary disease in hospital

Keywords: *adapted clinical guideline, chronic obstructive pulmonary disease, ABC analysis, VEN analysis, frequency analysis.*

Chronic obstructive pulmonary disease (COPD) is characterized by a stable, progressive restriction of patency and increased chronic inflammatory response of the airways and lungs to the action of harmful particulates and gases. Chronic obstructive pulmonary disease is a major health problem today and one of the major causes of morbidity and mortality worldwide. People suffering from this disease for years have a poor quality of life and die prematurely. Throughout the world, there is a rapid growth of COPD due to prolonged exposure to risk factors and aging of the population [1, 10].

International studies have shown that COPD occurs in 9 –10 % of those over 40, and among smokers – in 15–16 % of individuals [5]. According to the Ministry of Health of Ukraine, in 2010, 420,000 cases of morbidity of COPD have been reported among the adult population, which is 11 % more than in 2009, and the rate of mortality from COPD in 2009 exceeded deaths from bronchial asthma (BA) by 12.6 times [8, 11].

Economic losses due to COPD are several times higher than the damage caused by BA, and, above all, due to a high level of temporary or permanent disability and premature mortality. Economic costs for one patient, associated with COPD, are three times higher than for a patient with BA [7]. The annual costs of the European Union in the amount of EUR 28.5 billion are associated with COPD – due to loss of productivity, EUR 4.7 billion – the cost of outpatient care, EUR 2.9 billion – to stay in hospital and 2.7 billion – on drugs [3].

Pharmacological treatment of COPD is aimed at reducing the symptoms, frequency and severity of exacerbations, improving health status and exercise tolerance. Table 1 lists the MPs recommended for the treatment of stable COPD by the Ukrainian Adapted Clinical Guideline (ACG) for the treatment of COPD in 2013 [1]. The prototype of this guideline is the updated clinical guideline NICE «Clinical Guideline 101 Chronic obstructive pulmonary disease. Management of chronic obstructive pulmonary disease in primary and secondary care. Jun 2010».

Exacerbation of COPD is usually treated with higher doses of short-acting bronchodilators or changing routes of administration of drugs (for example, the transition from metered-dose inhalers to therapy with nebulizer). If no significant contraindications, glucocorticosteroids for oral use with other modes of therapy can be prescribed to all hospitalized patients with exacerbation of COPD. Studies indicate that the use of systemic corticosteroids for exacerbations of COPD shortens recovery, improves lung function and reduces the risk of early recurrence of the exacerbation, treatment failure and increase in the period of treatment in a hospital. The oral use of prednisolone in a dose of 30–40 mg daily for 10–14 days is recommended [1].

The use of antibiotics for exacerbations of COPD is indicated in the presence of clinical signs of bacterial infection, such as an increase in purulent sputum (sputum colour change), sputum volume or increased shortness of breath. The choice of antibiotics for each patient should be carried out individually, in view of bacterial resistance, comorbidities and severity of COPD [1].

Hypercapnic respiratory failure develops in some patients during exacerbations, so non-invasive ventilation (NIV) as well as centrally acting agents for the stimulation of the respiratory center is used to treat this condition. Mucolytics and expectorants are indicated for use

Table 1

Medical preparations for the treatment of stable COPD recommended by the Adapted Clinical Guideline [1, 6]

MP group		INN	Pharmacodynamics
b2-agonists	Short-acting	Fenoterol, Salbutamol	Impact on b2- adrenergic receptors, increasing bronchial smooth muscles
	Long-acting	Formoterol, Indacaterol, Salmeterol	Impact on b2- adrenergic receptors, increasing bronchial smooth muscles, inhibition of the release of histamine and leukotrienes from passively sensitized human lungs; prevention of bronchospasm.
Anticholinergic	Short-acting	Ipratropium bromide	Blocking muscarinic receptors of smooth muscle of the tracheobronchial tree, inhibition of reflex bronchoconstriction.
	Long-acting	Tiotropium bromide	
Combination of short-acting β2-agonists and anticholinergics in one inhaler		Fenoterol/ipratropium	Effect on b2- adrenergic receptors and muscarinic receptors, increasing bronchial smooth muscles
Methylxanthines		Theophylline (sustained-release), Doxofylline	Inhibition of the enzyme phosphodiesterase, increase in intracellular cAMP content, relaxation of the bronchi and elimination of bronchospasm..
Inhaled glucocorticosteroids (GCs)		Beclomethason, Budesonide, Fluticasone	Pronounced local anti-inflammatory and anti-allergic effect, reducing the symptoms and the frequency of exacerbations.
Combination of long-acting β2-agonists and GCs in one inhaler		Formoterol/ budesonide, Salmeterol/ fluticasone	Impact on b2- adrenergic receptors, increasing bronchial smooth muscles, prevention of bronchospasm. Local anti-inflammatory and anti-allergic effect.
Systemic GCs		Prednisolone, Methylprednisolone (oral and injectable form)	Anti-inflammatory, antiallergic, antishock and immunosuppressive action
Phosphodiesterase-4 inhibitors (PDE4)		Roflumilast	Inhibition of PDE4, increase in intracellular level of basic cAMP, attenuation of leukocyte dysfunction associated with COPD, airway cells and pulmonary vascular smooth muscle, prevention of bronchospasm
Nonsteroidal anti-inflammatory drugs		Fenspiride	Antihistamine, antispasmodic effect on smooth muscles of the bronchi and prevention of edema development, reduced secretion of viscous mucus.

in patients with chronic cough and expectoration, but the literature provides studies on their effectiveness in patients with chronic bronchitis, rather than COPD, so ACG gives no unambiguous recommendation for their implementation [1].

The purpose of this study is to conduct analysis of pharmacotherapy of chronic obstructive pulmonary disease and determine the characteristics of consumption of medical preparations (MPs) by hospital patients with this disease.

Materials and methods

The analysis of MP use and evaluation of the cost-effectiveness of COPD treatment in hospital were carried out at the premises of a department of therapeutics of Dimitrov Central Regional Hospital (Donetsk region) from August 2013 to August 2014. 116 medical histories of patients with COPD were retrospectively analyzed. Data on the patient's sex, duration of hospital stay, diagnosis and treatment regimen were taken from each medical history. As a result of processing the data given in the medical histories, it was found that among patients there were more men – 72 persons (62 % of the total number of patients), women – 44 persons (38 %). The average length of stay of patients in hospital was 12 days. Patients had following secondary diagnoses: hypertension, cardiosclerosis, tachycardia, angina, gastritis and anemia. All patients were prescribed 41 TNs MP. In determining the value of the prescribed MPs, the prices as of September 2014 according to Morion research and retrieval system «Likarski zasoby» were used [4]. Expenditure on pharmacotherapy was determined taking into account the course of treatment.

To estimate the cost of drugs for the treatment of COPD, it was decided to conduct a comprehensive analysis using clinical and economic analysis methods – ABC/VEN

and frequency – the results of which enable us to determine rationality of COPD therapy in hospital, the most expensive and commonly prescribed drugs, the degree of implementation of formulary system and ACG recommendations in daily clinical practice. The frequency analysis is an assessment of the frequency of use of certain MPs, which, together with the costs allows determining, whether the bulk of financial resources spent accounts for the MPs recommended by ACG for use to treat COPD [9]. When conducting the frequency analysis, we performed a ranking of MPs by frequency of use – from most to the least frequently used. ABC analysis is the distribution of drugs by the Pareto principle into 3 groups according to the amount of costs of their use: group A (5–10 % MPs of the total range, the costs of which amount to 70–80 %); group B (15–20 % MPs of the total range, the costs of which amount to 15–20 %); group C (70–80 % MPs of the total range, the costs of which amount to 5 –10 %) [9]. ABC analysis allows you to get an accurate and objective pattern of the structure of cost of drugs for the treatment of COPD. VEN analysis allowed us to assess the compliance of patients' pharmacotherapy with ACG recommendations [1, 9]. During the analysis of pharmacotherapy, the conclusion on belonging of medicines to one of the categories (V – vital and N – minor) were made on the basis of the presence or absence of MPs in ACG.

Results and discussion

The analysis showed that a total of 41 MPs by TN, 25 drugs – for the treatment of COPD and 16 MPs – for comorbidities were prescribed to patients. According to the results of frequency analysis, drugs of the following pharmacological groups were most often prescribed to patients with COPD: mucolytics (ambroxol, bromhexine, acetylcysteine) – 113 prescriptions; systemic glucocorticosteroids (prednisolone, dexamethasone) – 101 prescriptions; expectorants (mucaltin) – 49 prescriptions; short-acting β2-agonists (salbutamol) – 36 prescriptions; antibacterial agents (cefoperazone, ceftriaxone, amoxicillin, levofloxacin) – 23 prescriptions. According to the trade names, leaders in prescription rate (93 to 30) are the following drugs (Table 2):

• Dexamethasone-Darnitsa (93 prescriptions), systemic GCs;

• Lasolvan (63 prescriptions), mucolytic;

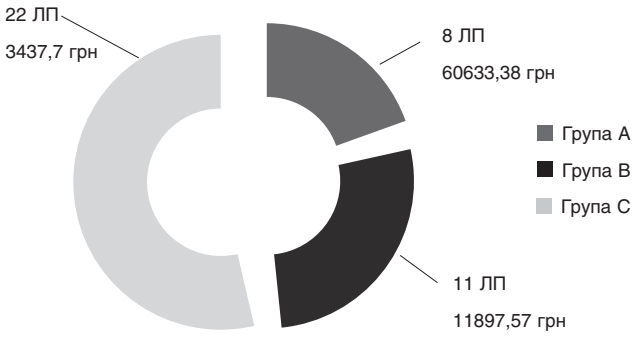

Fig. 1. **The number of drugs and costs in groups A, B, C**

• Mucaltin Galichpharm (49 prescriptions), expectorant;

• Heparin Belmedpreparaty (35 prescriptions), anticoagulant;

• Ambroxol Arterium (30 prescriptions), mucolytic.

The results of the ABC analysis (Table 2) show that a significant proportion of the funds (40.87 %) was spent on 1 MP – Heparin Belmedpreparaty, which was prescribed to 35 patients. Direct anticoagulants are not included into ACG recommendations for the treatment of COPD [1], so in this case the funds were spent inefficiently. The most costly group A included 8 MPs, recommended by ACG, which were prescribed with a frequency of 6 to 63 times, indicating that group A comprised the frequently prescribed MPs for a reasonable price (Lasolvan) and rarely prescribed, but expensive ones (Blicef, Daxas). Group B comprised 11 drugs, among them 5 MPs – for the treatment of COPD, 2 MPs – to prevent adverse reactions (Linex, Suprastin), 4 MPs – for the treatment of comorbidities. The least costly group C (4.53 % of the total costs) included 22 MPs with a frequency of prescriptions from 1 to 30 times (Ambroxol, Arterium). Fig. 1 shows the number of preparations included into the ABC group, and costs thereof.

Drugs for the treatment of comorbidities were included into the group B and C, UAH 6,901.99 were spent on them, accounting for 9.08 % of the total costs.

19 MPs were recommended out of 25 drugs that were used for the treatment of COPD: Ventolin Nebules, Blicef, Hepacef, Daxas, Spiriva, Lasolvan, Symbicort (group A according to ABC analysis); Nebutamol, Levofloxacin, ASS long, Mucaltin (group B); Sulfocamphocaine, Floxium, Prednisolone, Augmentin, Aerofillin, Ambroxol, Bromhexine, Salbutamol (group C), they were assigned rank V. Drugs for the prevention of adverse reactions – Linex and Suprastin (group B), Suprastin tabl. and Aleron (group C) – are not included into ACG recommendations, so these drugs were assigned rank N. Heparin (group A), Dexamethasone-Darnitsa solution for injections (group B), which were used in the treatment of COPD but not included into ACG, were also assigned rank N. According to ACG, replacement of injectable dexamethasone with peroral prednisolone was recommended. Ranking of 16 MPs, which were intended for the treatment of comorbidities, was performed by their presence or absence in the sixth edition of the National Formulary of Ukraine [2]. 10 MPs were assigned rank V, and 6 drugs – rank N.

Conclusions

The analysis of treatment sheets of patients with COPD showed that recommendations of the clinical guideline were insufficiently followed in a department of therapeutics of Dimitrov Hospital, and the pharmacotherapy of COPD in this department needs to be corrected. The analysis showed signs of irrational spending of the budget as 40.87 % of all funds were spent on 1 MP, missing from the clinical guideline. In the analysis, a small number of prescriptions of broncholytic MPs (beta-agonists, anticholinesterase drugs, inhaled glucocorticosteroids,

Table 2

Results of the integrated ABC, VEN and frequency analysis

ABC group	TN MP, dosage form, country of origin	Costs, UAH	Costs, %	Percentage of the total costs of each MP, %	Number of prescri-ptions	V/N rank
Group A	Heparin solution for injections, Belarus	60,633.38	79.81	40.87	35	N
	Blicef inhalation powder, India			7.30	6	V
	Ventolin Nebules, Germany/UK			7.21	29	V
	Hepacef solution for injections, Ukraine			5.84	8	V
	Spiriva inhalation powder, Germany			5.69	12	V
	Daxas tabl., Germany			5.10	6	V
	Lasolvan, lozenges 15 mg, Germany			4.00	63	V
	Symbicort inhalation powder, Sweden			3.81	11	V
Group B	Verospiron tabl.25 mg, Hungary	11,897.57	15.66	2.31	13	V
	Actovegin tabl., Ukraine			2.21	3	N
	Nebutamol solution for inhalation, Ukraine			1.99	16	V
	Levofloxacin tabl., Ukraine			1.33	4	V
	Linex caps.No32, Poland/Slovenia			1.28	6	N
	Dexamethasone, solution for injections, Ukraine			1.25	93	N
	Acc long powder 200 mg, Germany			1.25	12	V
	Creon, caps., Germany			1.19	2	V
	Cordarone tabl., Hungary/Ukraine			1.08	6	V
	Suprastin solution for injections, Germany			0.92	8	N
	Mucaltin tabl., Ukraine			0.86	49	V
Group C	Sidnopharm tabl., Bulgaria	3,437.7	4.53	0.69	19	V
	Sulfocamphocaine, solution for injections, Ukraine			0.58	4	V
	De-nol tabl., Netherlands			0.47	2	V
	Cavinton tabl., Hungary			0.45	3	N
	Floxium tabl.,Ukraine			0.37	2	V
	Augmentin tabl., UK			0.31	3	V
	Aerofillin tabl., Italy			0.30	2	V
	Mexidol tabl., Russia			0.27	2	N
	Prednisolone, tabl., Ukraine			0.22	8	V
	Ambroxol tabl., Ukraine			0.17	30	V
	Cardiomagnyl tabl., Denmark			0.14	4	N
	Suprastin tabl., Hungary			0.12	1	N
	Aleron tabl., India/Iceland			0.08	2	N
	Riboxin solution for injections, Ukraine			0.08	4	N
	Sorbifer tabl., Hungary			0.07	1	N
	Valsacor tabl.,Slovenia			0.06	1	V
	Bromhexine tabl., Ukraine			0.05	8	V
	Furosemide tabl., Ukraine			0.04	4	V
	Lasix tabl., India/Ukraine			0.02	4	V
	Salbutamol spray for inhalation, France			0.02	6	V
	Nimesulide tabl., Ukraine			0.01	1	V
	Analginum tabl., Ukraine			0.01	2	V
Total		75,968.65	100			

xanthines), recommended for the treatment of COPD and included into the regimens of standard pharmacotherapy, was also observed.

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ОЦЕНКА ФАРМАКОТЕРАПИИ ХРОНИЧЕСКОГО ОБСТРУКТИВНОГО ЗАБОЛЕВАНИЯ ЛЕГКИХ В УСЛОВИЯХ СТАЦИОНАРА

Л. В. Яковлева, Д. В. Бондаренко, Н. А. Барылюк

Резюме

Экономические затраты на одного больного, связанные с хроническим обструктивным заболеванием легких (ХОЗЛ), в три раза выше, чем на больного с бронхиальной астмой. Целью данного исследования было проанализировать фармакотерапию пациентов с ХОЗЛ в условиях стационара с помощью клинико-экономических методов (АВС-, VEN- и частотного анализа). Ретроспективно было проанализировано 116 историй болезней. Всего пациентам был назначен 41 лекарственный препарат (ЛП) по ТН, для лечения ХОЗЛ – 25 препаратов, для лечения сопутствующих заболеваний – 16 ЛП. Чаще всего больным назначали муколитики, системные глюкокортикостероиды (ГКС), отхаркивающие средства, β_2-агонисты короткого действия, антибактериальные средства. При проведении анализа было отмечено малое количество назначений бронхолитических ЛП (β_2-адреномиметиков, антихолинэстеразных препаратов, ингаляционных ГКС, ксантинов), которые рекомендованы для лечения ХОЗЛ, поэтому фармакотерапия в данном отделении нуждается в коррекции.

Ключевые слова: *адаптированные клинические рекомендации, хроническое обструктивное заболевание легких, АВС-анализ, VEN-анализ, частотный анализ.*

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Л. В. Яковлева
заслуженный деятель науки и техники Украины,
д-р фарм. наук, профессор
заведующая кафедрой фармакоэкономики
Национальный фармацевтический университет, г. Харьков
ул. Блюхера, 4, Харьков, 61168
тел.: +38(0572)65-88-95
e-mail: feknfau@ukr.net

EVALUATION OF PHARMACOTHERAPY OF THE CHRONIC OBSTRUCTIVE PULMONARY DISEASE IN HOSPITAL

L. V. Iakovlieva, D. V. Bondarenko, N. A. Barilyuk

Summary

Economic costs for one patient, associated with the chronic obstructive pulmonary disease (COPD), are three times higher than for a patient with bronchial asthma. The purpose of this study was to analyze the pharmacotherapy of patients with COPD in hospital using the clinical and economic methods (ABC, VEN and frequency analysis). 116 medical histories were retrospectively analyzed. A total of 41 MPs by TN, 25 drugs – for the treatment of COPD and 16 MPs – for comorbidities were prescribed to patients. Mucolytics, systemic glucocorticosteroids, expectorants, short-acting β_2-agonists and antibacterial agents were prescribed most often. In the analysis, a small number of prescriptions of broncholytic MPs (beta-agonists, anticholinesterase drugs, inhaled glucocorticosteroids, xanthines), recommended for the treatment of COPD, was observed, so the pharmacotherapy in this department needs to be corrected.

Key words: *adapted clinical guideline, chronic obstructive pulmonary disease, ABC analysis, VEN analysis, frequency analysis.*

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L. V. Iakovlieva
Honored Worker of Science and Technology of Ukraine,
D-r of Pharm. Sciences, professor
Head of the Department of Pharmacoeconomics
National University of Pharmacy, Kharkiv
Blucher str., 4, Kharkiv, 61168
tel.: +38(0572) 65-88-95
e-mail: feknfau@ukr.net