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CHRONIC OBSTRUCTIVE PULMONARY DISEASE: PHARMACOEPIDEMIOLOGICAL STUDY OF ANTIBIOTICS IN THE PERIOD OF EXAGENCE

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Abstract:

Chronic obstructive pulmonary disease (COPD) is one of the main causes of death. The risk of death in patients with chronic obstructive pulmonary disease increases depending on the number of cases of exacerbations. Airway obstruction, characteristic of chronic obstructive pulmonary disease, is often aggravated and is associated with a chronic inflammatory reaction. According to the data presented by S. N. Avdeev, 4 biological clusters cause exacerbation of chronic obstructive pulmonary disease: bacterial (11%), eosinophilic (24%), viral (34%), weakly inflammatory (11%). The body reacts to toxins produced by pathogenic microorganisms with an inflammatory reaction, which leads to an exacerbation and a severe course of the disease. The presence of a bacterial factor in the exacerbation of chronic obstructive pulmonary disease requires antibacterial therapy. We studied both from an epidemiological and pharmacoepidemiological point of view and analyzed 788 case histories of patients treated in January- December 2020 in the therapeutic department of the multidisciplinary clinic of Samarkand State Medical University. When analyzing the sensitivity of microorganisms to antibacterial drugs (by the disk-diffuse method, depending on the diameter (mm) in the zone of macroorganism growth suppression based on Sanepidnadzor standards), the following data were revealed: to cefazolin - 65.9%, levofloxacin - 1.7%, cefepime - 3.3%, ceftriaxone - 1.3%. Based on the literature data and the data of our own research, it is advisable to use the drug ceftriaxone from the group of cephalosporins, which is associated with a low resistance of the main pathogens of chronic obstructive pulmonary disease. Irrational dosing, reducing the dose of antibacterial drugs below the doses specified in local and international guidelines and standards, reducing the duration of treatment can cause the development of resistance of microorganisms.

Keywords: COPD, pharmacoepidemiology, cephalosporins, optimization, antibacterial drugs

I. INTRODUCTION

COPD is the cause of the annual death of about 3 million people and accounts for 4.8% of the total mortality, and by 2030 it can reach 4th place in terms of mortality (WHO). One of the main causes of high mortality is the late detection of the disease [3,4,12]. The prevalence of COPD increases depending on age, that is, after 40 years (37%), and also occurs three times more often in men than in women [2,5,11]. The airway obstruction characteristic of COPD is often aggravated and is associated with a chronic inflammatory reaction [3,10,13]. The exacerbation of the disease occurs against the background of weakening of the specific and non-specific protection of the lungs caused by microorganisms with high virulence and damage to the lung tissue. The body reacts to toxins produced by pathogenic microorganisms with an inflammatory reaction, which leads to an exacerbation and a severe course of the disease. Among bacterial pathogens, the main place belongs to H. Influenzae (52%), Moraxella satarrhalis (13%), Streptococcus pneumonia (16.5%) Enterobacteriaceae and Pseudomonas aeruginosa. The presence of a bacterial factor in the exacerbation of COPD requires antibacterial therapy. For this reason, antibacterial therapy also plays an important role in the complex treatment of COPD [1,8]. Conducting antibacterial therapy for COPD helps to reduce the negative effect of bacteria on the lung tissue, prevents the progression of the disease and secondary bacterial infection, reduces damage to the lung tissue. It should also be taken into account that in more than 50-60% of cases, the exacerbation of COPD is not associated with a bacterial infection. According to the data presented by Avdeev S. N., there are 4 biological clusters that cause exacerbation of COPD: bacterial

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(11%), eosinophilic (24%), viral (34%), weakly inflammatory (11%) [6,17,18]. Due to the low effectiveness, it is not recommended to prescribe antibacterial drugs for preventive purposes [2,19,20]. Therefore, the regular use of antibacterial drugs is not always advisable. In most cases, antibacterial therapy is empirical, and the development of resistance of microorganisms to frequently prescribed antibiotics is a serious problem when choosing an antibacterial drug. The resistance of microbes to antibiotics depends on the region, and the resistance in one region may differ from another, so the choice of an antibacterial drug is based on the results of regional pharmacoepidemiological studies, the results of the comparative effectiveness of antibacterial drugs [8,14]. For this reason, a pharmacoepidemiological study of antibacterial drugs used in antibacterial therapy during the exacerbation of COPD was conducted.

II. MATERIALS AND METHODS

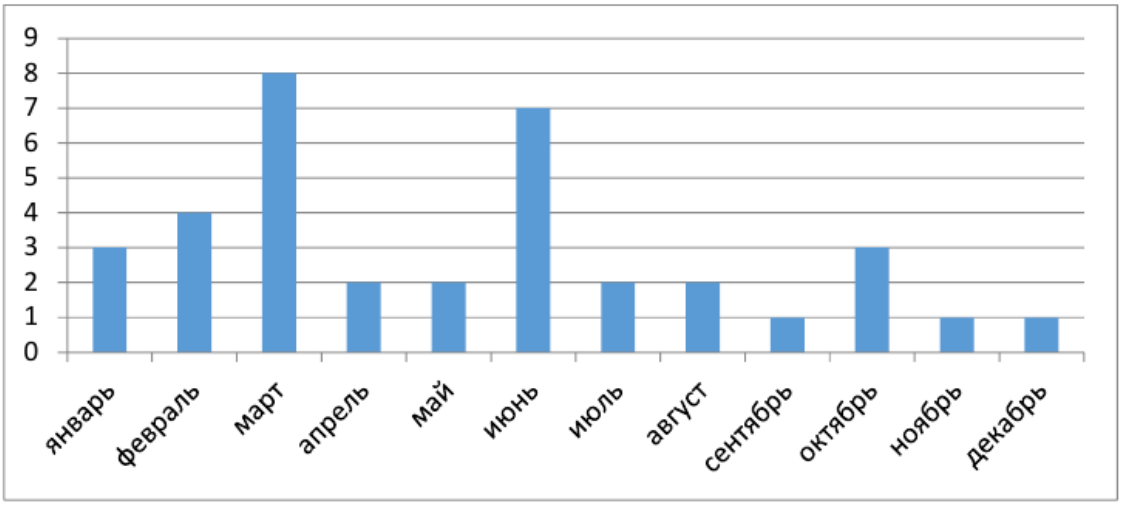
Epidemiological and pharmacoepidemiological analysis of the medical histories of patients with COPD in the aspect of the use of antibacterial agents. A statistical analysis of 788 medical records of patients with COPD treated in January-December 2020 in the therapeutic department of the multidisciplinary clinic of Samarkand State Medical University using the Excel program and IBM in SPSS statistics was carried out.

III. RESULTS

In 2020, 788 patients were treated in the therapeutic department, of which 37 (4.7%) patients were diagnosed with COPD in the acute stage and treated. In 37 patients, 18 (48.6%) COPD was the main disease, in 19 (51.4%) another disease was the main disease, while COPD was identified as a competing or concomitant disease. 22 patients (59.5 %) were men, 15 patients (40.5%) were women of the 37 patients diagnosed with COPD.

Age of patients	up to 40 years old	41-50 ages	51-60 ages	61-70 ages	71 years older
Number of patients	1 (2,7%)	6(16,2%)	6(16,2%)	21 (56,8%)	3(8,1%)

When analyzing patients by month of birth, patients, the following data were obtained:



The analysis of the year-round dynamics of COPD exacerbations in patients shows an increase in exacerbations of the disease in the autumn-winter months:

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	January	February	March	April	May	June	July	August	September	October	November	December
The number of patients who received treatment	9	9	6	0	1	0	1	2	1	2	4	2

The average duration of treatment of patients was 8.8 days, and the number of patients treated for 10 days or more was 14 patients.

Duration of treatment (days)	5	6	7	8	9	10	11	12	13	14	15	16	Total
Number of patients	7	1	6	6	3	5	2	2	1	2	1	1	37

In a comparative study of patients treated in the department for COPD among the urban and rural population, the following results were obtained:

For the year	Total patients	Of which		The average duration of treatment
		Urban population	Rural population	
Total number of patients	788	181	607	7,5
%	100%	23%	77%	
Among them: COPD	37	14	23	8,8
%	100%	38%	62%	

When studying the general blood tests of patients who were treated in the department, it was found in 17 (46%) patients that the ESR was higher than 15 mm/hour. When studying the drugs used in antibacterial therapy during the exacerbation of COPD, the following data were obtained:

Name of the AB of the drug	The number of patients who took the drug	The average duration of treatment (in days)	Average single dose	The average number of receptions per day	Average daily dose
Levofloxacin	5 (11,9%)	6,8	0,5	1	0,5
Metronidazole	2 (4,8%)	6	0,5	1	0,5
Cefazolin	20 (47,6%)	8,4	1	2	2
Cefepime	5 (11,9%)	6,4	1,6	i,6	2,6
Ceftriaxone	8(19%)	6,5	1	1.9	1.9
No AB of the drug is prescribed	2 (4,8%)				

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When used in monotherapy

Name of the AB of the drug	Number of patients	Average duration of treatment
levofloxacin	1	6
metrid	1	6
cefazolin	16	8,9
cefepime	5	6,4
ceftriaxone	7	6,7

When used in combination

Name of the AB of the drug	Number of patients	Average duration of treatment
ccfazolin+levofloxacin	4	7
ceftriaxone+metronidazole	1	6

Compatibility analysis according to international indicators of the volume of use of drugs used in ongoing antibacterial therapy (DDD– http://www.whocc.no/atcddd) showed the following:

Name of the drug	Average single dose	The average number of receptions per day	Average daily dose	DDD (Average daily maintenance dose) p-parenterally; o-orally
Levofloxacin	0,5	1	0,5	0,5 (p/o)
Metrid	0,5	1	0,5	1,5 (P)
Cefazolin	1	2	2	3(P)
Cefepime	1,6	i,6	2,56	4 (p)
Ceftriaxone	1	2	2	2(P)

According to the results of bacteriological sputum culture and analysis of the sensitivity of the identified microbes to antimicrobial drugs in patients treated in the department for COPD, the following results were obtained:

Detected microorganisms:

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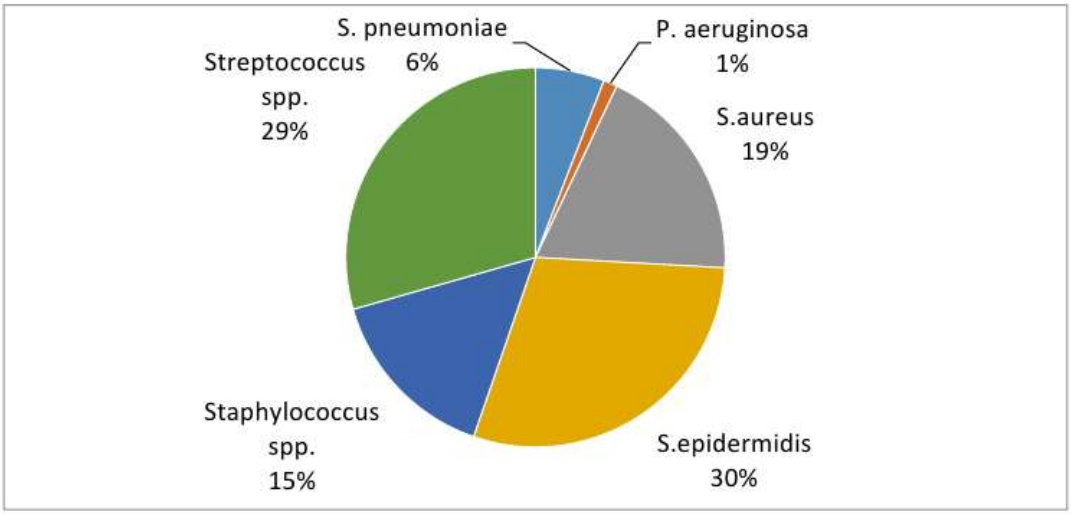

The sensitivity of microorganisms to antibacterial drugs was studied (by the disk-diffuse method depending on the diameter (mm) in the zone of suppression of the growth of macroorganisms based on the standards of Sanitary and Epidemiological Supervision). The analysis of the sensitivity of microorganisms to antibacterial drugs was carried out based on the Recommendations "Determination of the sensitivity of microorganisms to antimicrobial drugs" (version-2021-01) and was divided into the following 2 groups [7,9]:

xx – xx%	- resistant (R)
xx – xx%	- sensitive (S)

	cefepime	ceftriaxone	cefazolin	levofloxacin
S. pneumoniae		30 - 40%	0 - 20%	
		32 - 60%	18 - 60%	
			22 - 20%	
P. aeruginosa	30 - 100%	30 - 100%	18 - 100%	32 - 100%
S. aureus	24 - 33%	28 - 6,7%	0 - 14,3%	18 - 10%
	26 - 33%	30 - 40%	18 - 50%	22 - 20%
	30 - 33%	32 - 53,3%	20 - 7,1%	24 - 40%
			22 - 21,5%	26 - 10%
			28 - 7,1%	28 - 10%
				30 - 10%
S.epidermidis	26 - 20%	26 - 13%	0 - 22,7%	22 - 14,3%
	30 - 60%	28 - 13%	18 - 40,9%	24 - 28,6%
	32 - 20%	30 - 59,6%	20 - 4,5%	26 - 14,3%
		32 - 14,4%	22 - 13,6%	28 - 28,6%
			24 - 18,3%	32 - 14,3%
Streptococcus spp.	26 - 33%	24 - 5%	0 - 14,3%	18 - 10%
	30 - 33%	26 - 15%	18 - 42,9%	22 - 40%
	32 - 33%	30 - 45%	22 - 28,6%	26 - 20%
		32 - 35%	24 - 9,5%	28 - 10%
			28 - 4,7%	30 - 20%
Staphylococcus spp.	18 - 20%	20 - 7,7%	0 - 23%	22 - 10%
	28 - 20%	30 - 38,5%	18 - 30,9%	24 - 10%
	30 - 40%	32 - 53,8%	21 - 7,7%	26 - 10%
	32 - 20%		22 - 23%	28 - 30%
			24 - 15,4%	30 - 30%
				32 - 10%

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IV.DISCUSSION

According to the results of the study, as well as the literature and international studies, it was found that COPD is more common in men than in women [4,11,12]. This can be explained by the fact that smoking (in 80-90% of cases) and professional characteristics (miners, builders, workers of the metallurgical industry) are some of the main external factors of the frequent development of COPD among men [1]. Also, one of the reasons for the high incidence, mainly in people over 40 years old, especially at the age of 61-70 years (56.8%), may be a late diagnosis of patients, late detection of the disease [16]. When analyzing patients by month of birth, patients born in March and June were more susceptible to COPD than patients bom in other months. Frequent exacerbation of the disease, mainly in autumn and winter, can be associated with the fact that both climatic (low temperature, humidity, etc.) and biological (viruses, bacteria, etc.) factors play an important role in the development of the disease [6]. The analysis shows that the average duration of treatment of patients is 8.8 days, which is more than the average duration of treatment (7.5 days) of all patients undergoing treatment in the department. In addition, in 14 out of 37 patients (37.8%), the duration of treatment was more than 10 days, which, in turn, indicates that COPD is a serious pathological condition. The incidence of COPD among the urban and rural population corresponds to the data of the literature and conducted studies. It should be noted that the ratio of urban and rural patients treated in the department is 23%: 77%, and among patients treated for COPD in the department - 38%: 62%. In general blood tests - in 17 (46%) patients with ESR above 15 mm/li, it may indicate the role of microbes in the pathogenesis of the disease and is a relative indication for the use of antibacterial drugs in treatment. In antibacterial therapy during the exacerbation of COPD, cephalosporins were mainly used, and cefazolin was most often prescribed (47.6%).

It should be noted that, although cefazolin belongs to the group of antibacterial drugs with a wide spectrum of action, but mainly has an effect on G-positive bacteria, it is cleaved by the enzyme penicillinase. So it is recommended to use this antibiotic only if the pathogen is known and the sensitivity of the pathogen to the antibiotic is determined [5,14,15]. With cefazolin monotherapy, antibacterial therapy lasted 8.9 days, and with combined use - 7 days. It was found that compared with the average daily dose of antibacterial drugs used in DDD (the international indicator is the average daily maintenance dose) (http://www.whocc.no/atcddd), cefazolin was used in small doses.

When studying sputum tests of patients, the most common pathogens were: S. epidermidis (29.7%), Streptococcus spp. (29.7%), S. aureus (19%). When analyzing the sensitivity of microorganisms to antibacterial drugs (by the disk-diffuse method depending on the diameter (mm) in the zone of macro organism growth suppression based on the standards of Sanitary and Epidemiological Supervision), the following data were revealed: to cefazolin - 65.9%, levofloxacin - 1.7%, cefepime - 3.3%, ceftriaxone - 1.3%. The development of resistance to cefazolin may be associated with improper dosage and irrational use.

V. CONCLUSION

Cefazolin is less effective during exacerbations of COPD, which is associated with a decrease in the susceptibility of microbes to the drug, its pharmacokinetics (the effect of cefazolin depends on maintaining a constant therapeutic concentration in the blood since cefazolin belongs to the group of concentration-dependent antibacterial drugs). It is advisable to use the drug ceftriaxone b from the group of cephalosporins due to the low resistance of the main pathogens of COPD. Irrational dosing, reducing the dose of antibacterial drugs below the doses specified in local and international guidelines and standards, reducing the duration of treatment can cause the development of resistance of microorganisms.

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