ANTIBIOTIC USE AMONG PATIENTS WITH ACUTE EXACERBATION OF COPD IN PULMONARY DISEASES UNIVERSITY CLINICAL HOSPITAL FROM NORTH-EASTERN ROMANIA

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ANTIBIOTIC USE AMONG PATIENTS WITH ACUTE EXACERBATION OF COPD IN PULMONARY DISEASES UNIVERSITY CLINICAL HOSPITAL FROM NORTH-EASTERN ROMANIA (Abstract): **Aims:** Acute exacerbations of Chronic Obstructive Pulmonary Disease (AECOPD) need sometimes hospitalizations and requires five to seven days of oral antibiotics, according to GOLD recommendations. The aim of our study was to find out the most common used antibiotics in patients with AECOPD admitted in a University Clinical Hospital of Pulmonary Diseases from North-Eastern Romania, from June 2014 to May 2019. **Materials and methods:** A descriptive cross-sectional, single-center, retrospective study, conducted among 460 admissions in hospital with J44.0 (COPD with lower airway acute infection) and J44.1 (COPD with acute, nonspecific exacerbation) diagnostics. **Results:** The majority (354; 77%) of admissions were for male; average age was 66 ± 9 years. The preferred antibiotic for first use was ceftriaxone (51%), but the patients were treated also with ciprofloxacin (13%), levofloxacin (12%), ceftazidime, amoxicillin + clavulanic acid or other antibiotics according to antibiograms, with a medium of 10 days treatment. Most of the patients received one antibiotic during hospitalization, 23.9% received two antibiotics and 7.6% of patients received 3 antibiotics. Hospitalization average length was 11 ± 5 days. **Conclusions:** Ceftriaxone was the preferred drug for acute COPD exacerbation treatment for hospitalized patients, while the average hospital length in our study was 11 days. **Keywords**: ANTIBIOTIC USE, ACUTE EXACERBATIONS OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE, LENGTH OF HOSPITAL STAY.

INTRODUCTION

Antimicrobial chemotherapy choice is a challenge in patients with Chronic Obstructive Pulmonary Disease (COPD), due to both bacterial and viral causes of acute exacerbation. COPD, one important cause of mortality and morbidity worldwide (1), had a hospital in-patient admission rate of 4.70% in Romania in 2017. The most frequent bacteria causing infections in COPD patients are *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Pseudomonas aeruginosa*, but other bacteria such as Enterobacteriaceae and *Chlamydia pneumoni-*

ae might also be involved (2). Acute exacerbations of COPD (AECOPD) need sometimes hospitalizations and have socio-economic impact through severe deterioration of general health status, the progression to complications of disease, and increase use of antibiotic consumption (3-5).

COPD exacerbations require five to seven days of oral antibiotics, according to GOLD recommendations. The initial therapy of AECOPD is with an association of aminopenicillins and clavulanic acid, tetracyclines (doxycycline) or macrolides (azithromycin), in selected patients quinolone (5) and identification of the bacteria and antibiogram are needed. A judicious use of antibiotics administration for AECOPD decreases the risk of treatment failure and early relapse.

There are very few studies on the use of antibiotics in AECOPD in North-East Romania, therefore the aim of our study was to find out the most common used antibiotics in patients with AECOPD admitted in a University Clinical Hospital of Pulmonary Diseases from North-Eastern Romania, from June 2014 to May 2019.

MATERIALS AND METHODS

Study design

This is a descriptive cross-sectional, single-center, retrospective study, conducted in Iasi University Clinical Hospital of Pulmonary Diseases from North-Eastern Romania (340 beds- adult and pediatric pulmonology, thoracic surgery and intensive care). The study received the approval from the Ethics Committee of "Grigore T. Popa" University of Medicine and Pharmacy from Iasi, Romania, and the Ethics Committee of Clinical Hospital of Pulmonary Diseases of Iasi, Romania (approval date 04.06.2020, respectively 22.01.2021).

The inclusion criteria were: 1) Patients of more than 40 years, with diagnosis of COPD, based on spirometry (with the ratio post-bronchodilator forced expiratory volume in one second (FEV1)/ forced vital capacity (FVC) < 0.70),admitted in the hospital, 2) specific J44diagnosis codes of COPD established by International Classification of Diseases 10thRevision (ICD-10): J44.0 - COPD with lower airway acute infection, J44.1 - COPD with acute, nonspecific exacerbation; 3) more than 24 h of hospital length; 4)received at least one antibiotic during hospitalization. There were excluded: patients admitted to the intensive care unit (ICU), other chronic pulmonary diseases (asthma, pulmonary interstitial disease, and pulmonary embolism), any type of cancer disease, tuberculosis under treatment and incomplete data in clinical record file.

There were extracted the following data from electronic and paper medical clinical record files: date of admission and discharge from hospital, length of hospitalization, age, gender, administered antibiotics, bacterial pathogen from antibiogram.

Data Analysis

Results are presented as mean ± standard deviation (SD) for continuous variables and as absolute values and percentages for categorical variables.

RESULTS

A total of 460 admissions in hospital with J44.0 - COPD with lower airway acute infection and J44.1 - COPD with acute, nonspecific exacerbation, were included. They were 354 (77%) admissions for male and 106 (23%) admissions for female. The age of patients varied from 44 years to 88 years, average age was66 ±9 years.

The patients were treated with ceftriaxone, ciprofloxacin, levofloxacin, ceftazidime, amoxicillin + clavulanic acid or cefuroxime according to antibiograms, with a medium of 10 days treatment. In COPD

patients most of the time treatment was started with cephalosporins, rarely with amino-penicillins. Other antibiotic that was recommended in small proportion were clarithromycin, gentamicin, clindamycin, trimethoprim/sulfamethoxazole. The preferred antibiotic for first use was ceftriaxone (fig. 1). Most of the patients received one antibiotic during hospitalization, 23.9% received two antibiotics and 7.6% of patients received 3 antibiotics; the predominant route was intravenous. The predominant bacteria in the sputum were Gram Negative bacteria, followed by *Streptococcus spp.*, while MRSA (methicillin resistant *Staphylococcus aureus*) bacteria was not detected.

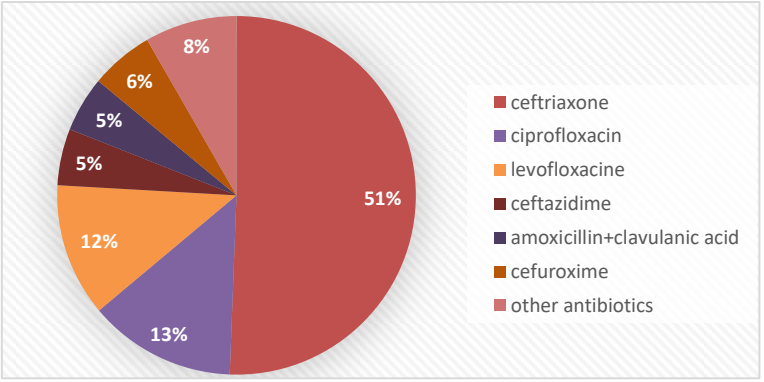

Fig. 1. Patients antibiotic therapy during hospitalization.

Trend of antibiotic use, depending on trimesters and year are depicted in figure 2. There was a higher use of ceftriaxone and ciprofloxacin in the third trimester of 2015.

Hospitalization average length was 11 ± 5 days (fig. 3), the longest duration of hospital stay being of 38 days due to comorbidities. Most of length of hospital stay was in the category of mid-stay: 60 brief-stay (2-6 days), 396 mid-stay (7-30 days) and 4 long-stay (>31 days).

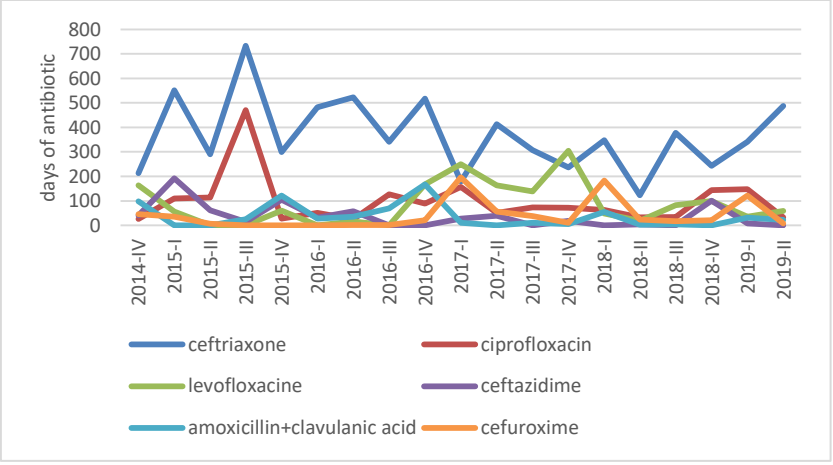

Fig. 2. Trend of antibiotic use (days of antibiotic).

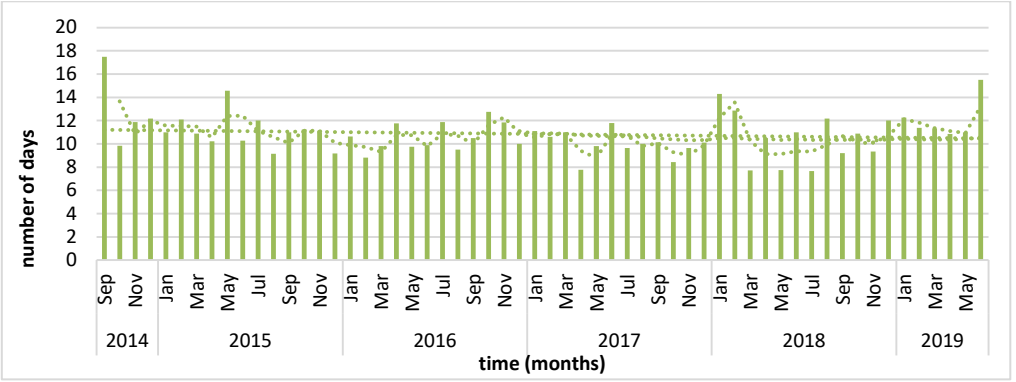

Fig. 3. Average of hospital day length (days)

DISCUSSION

Our findings showed that the preferred antibiotic to be used in COPD patients was ceftriaxone, followed by ciprofloxacin or levofloxacin. According to GOLD recommendations, the preferred route of administration is oral, but the intravenous and the duration of therapy can be longer in COPD exacerbations admitted in hospital. The choice of antibiotic should take into consideration also the local hospital/ region antimicrobial resistance map (5). The European Respiratory Society and the American Thoracic Society guidelines from 2017 recommend beta-lactams in COPD exacerbations to reduce the risk of treatment failure and increase the time between exacerbations according to local hospital guidelines and because the risk of co-infections are frequently reported with the increase in the severity of COPD (5, 6). The use of antibiotics during hospital stay reduce the risk of readmissions and the risk of mortality (7-10).

According to 2020 evaluation of World Health Organization, death due to COPD was on the third place among global death causes (6% of total deaths), due to comorbidities that lead to frequent exacerbations with or without hospitalizations (3). Data obtained from larger cohort might give details on difference on gender or smoking as factors that influence hospitalization length. A recent study on AECOPD inpatients, found that females and males had similar in-hospital and long-term survival and that female smokers had significantly worse outcomes (7).

The use of macrolides in our study was low, even macrolides might be recommended as an adjunctive treatment AECOPD. Since this practice becomes increasingly common, there are studies that found the importance to monitor its benefits on AECOPD, the adverse events and antimicrobial resistance patterns (11).

The average hospital length in our study was 11 days, which is longer in contrast to a cohort study where the mean was 6-7 days in AECOPD patients (12), but among the values from studies that mention a variable average of the length of stay for AECOPD, ranging from 5 to 12 days (13, 14).

Limitations of the study

There are some limitations in our study: it was a single center study with a small number of hospitalized COPD patients; therefore, our findings might not be generalized.

CONCLUSIONS

Ceftriaxone was the preferred drug for AECOPD treatment for hospitalized patients, followed by quinolones (ciprofloxacin or

levofloxacin), while the average hospital length in our study was 11 days. It is difficult to differentiate between bacterial or viral cause of infection; therefore, clinicians are tempted to recommend antibiotics, that might lead to overuse of antibiotics.

CONFLICT OF INTEREST AND FUNDING

The authors declare no conflict of interest.

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