

Evaluation of Antibiotics on Chronic Obstructive Pulmonary Disease Patient in Lung Hospital, West Sumatera, Indonesia

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Abstract:- Chronic Obstructive Pulmonary Disease (COPD) is one of public health problem in Indonesia, which is caused by smoking and air pollution. Treatment with antibiotics prevent COPD exacerbations and improve patient quality of life. Inappropriate use of antibiotics lead to ineffective treatment, decrease patient safety, increase of resistance and treatment cost. This study aims to evaluate the appropriateness use of antibiotics in COPD patients. This is a descriptive retrospective study based on Gyssens method that using patient medical records during the period January-December 2015 in Outpatients Installation of Lung Hospital, West Sumatera. The number of patients who fulfill the inclusion criteria are 86 patients. The results showed that 56,33% antibiotic use was rational, 41,14% antibiotic therapy was not effective, and 2,53% antibiotic therapy was too long.

Keywords:- Evaluation of antibiotic; gyssen method; COPD; rationality.

I. INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a disease in which the airflow in the respiratory tract is gradually obstructed and irreversible, commonly caused by inflammation in the lungs as a response to toxic or harmful particles or gases.^{1,2} The prevalence of COPD is continuously increasing significantly, especially in developing countries, due to the rising number of smokers.³

Acute exacerbations, which involve a deterioration of respiratory symptoms compared to the patient's previous state, can occur in individuals with COPD.¹ These exacerbations are triggered by multiple factors including smoking, viral infections, bacterial infections, and air pollution.⁴ Administering antibiotics has been proven to be beneficial for COPD patients experiencing acute exacerbations, characterized by increased breathlessness, heightened sputum production, and increased sputum purulence.¹ Patients receiving antibiotics demonstrate greater improvement in lung function compared to those who do not receive antibiotics.⁵

Some studies continue to demonstrate the irrationality of antibiotic use in patients with COPD.^{5,6,7} This can have negative consequences for patients, including the development of antibiotic-resistant bacteria, the emergence of diseases caused by superinfections of resistant bacteria, medication toxicity/side effects, longer patient care,

increased treatment costs, and ultimately a decline in healthcare quality.^{2,6,7}

The prudent use of antibiotics can help alleviate the burden of disease and infections, whereas inappropriate use significantly contributes to antibiotic resistance.¹ Resistance leads to a reduced ability of antibiotics to effectively treat infectious diseases. While it cannot be eliminated entirely, resistance can be slowed down through appropriate antibiotic utilization.⁸ The increasing resistance of bacteria responsible for acute exacerbations of COPD is a concerning issue with certain antibiotics used as empirical therapy for COPD.² This leads to decreased treatment efficacy, heightened morbidity and mortality rates among COPD patients.⁸

II. METHODOLOGY

This study employed a retrospective descriptive design, using the Gyssens flowchart to evaluate the utilization of antibiotics. The sampling method used was total sampling, including all patients who met the inclusion criteria. These criteria consisted of outpatients diagnosed with chronic obstructive pulmonary disease (COPD) who received antibiotics at the Lung Hospital, West Sumatera between January and December 2015, with complete medical record data. The data collected encompassed patient characteristics (name, age, gender), clinical data (complaints and diagnosis), and medication usage data (drug name, duration of therapy, dosage, frequency, and route of administration). Data Analysis The demographic data of patients, as well as the patterns and types of antibiotic usage, were analyzed descriptively using tables and diagrams. The evaluation of antibiotic usage was assessed using the Gyssens flowchart, which provided a qualitative assessment. Antibiotic usage was considered rational when falling into category 0, while irrational usage was categorized as I-V. Conclusions were drawn based on the "Diagnosis and Management of COPD" book published by the Indonesian Association of Pulmonologists in 2011.¹

III. RESULTS AND DISCUSSION

The study included a total of 86 patients who met the inclusion criteria, resulting in 158 visits. The demographic characteristics of the patients are presented in Table 1. In Indonesia, COPD tends to have a higher prevalence in males over the age of 30 compared to females, with a prevalence rate of 3.7%.¹⁰ This finding aligns with previous studies that have also reported a higher prevalence of COPD among males.^{5,6,11}

The increasing prevalence of COPD contributes to a significant economic and social burden.¹¹ The high prevalence of COPD is closely linked to the persistently high rates of smoking, which is a major contributing factor to the disease. The relationship between smoking and COPD follows a dose-response pattern, where a higher number of cigarettes smoked per day and a longer duration of smoking increase the risk of developing the disease.¹

The 56-65 age group had the highest number of COPD cases, with 35 patients, while the 25-35 age group had the lowest number, with only one patient (Table 1). These results align with previous studies conducted earlier.^{6,7} The increased prevalence of COPD in older age groups can be attributed to the progressive and chronic nature of the disease. As individuals age, physiological changes contribute to the disease's progression. Those with impaired lung function experience a more significant decline in lung function over time compared to individuals with normal lung function, placing them at a higher risk of developing COPD.^{4,11} This suggests that as people age, their lung function decreases, and this decline is exacerbated by smoking, which acts as a risk factor in increasing the prevalence of COPD.^{3,6}

Table 1: Demographic Characteristics of COPD Patients Receiving Antibiotic Therapy

Demographic characteristics	Frequency (%)
Gender	
Male	80(93.02)
Female	6(6.98)
Age (year)	
25-35	1 (1.1)
36-45	2 (2.3)
46-55	17 (19.8)
56-65	35 (40.7)
>65	31 (36.1)

Out of 86 patients with 158 visits receiving antibiotic therapy, all of them met the inclusion criteria as they had complete and evaluable data. This means that no patients were classified as category VI (0%).⁸ Based on the evaluation of antibiotic use according to the fifth Gyssens category, which refers to antibiotic use without medical indications, there were no visits meeting this criteria (0%). This indicates that antibiotic administration in COPD patients was based on indications to obtain antibiotics.⁹

Drug therapy is considered unnecessary if there are no clear indications in patients. Antibiotics are prescribed when there are clinical symptoms or patient complaints that suggest secondary infection caused by bacteria, with the goal of inhibiting bacterial growth before obtaining microbiological examination results.⁸ From the research data, all patients showed cardinal symptoms such as shortness of breath, productive cough, and accompanying fever.

Category IVA represents the ineffective use of antibiotics. Based on the data obtained, there were 65 visits (41.14%) (as seen in Table II). Two patients with moderate obstructive spirometry results received azithromycin

antibiotics. According to the literature, patients with moderate obstruction should receive fluoroquinolone antibiotics such as ciprofloxacin, levofloxacin, or cotrimoxazole. From the literature, cotrimoxazole (trimethoprim-sulfamethoxazole) is recommended for COPD with mild infections.¹

The use of erythromycin and cephadoxil is not recommended for COPD and is therefore categorized as ineffective use.¹ Erythromycin belongs to the first generation macrolide antibiotics with antimicrobial activity against gram-positive bacteria such as *Staphylococcus aureus*.⁸ Cephadoxil has antibacterial activity against gram-positive bacteria, different from cefixime, which is a third-generation cephalosporin antibiotic that is more active against gram-negative bacteria.⁴ Most patients with exacerbations of COPD have gram-negative bacterial patterns (with a poor prognosis risk), and the use of second and third generation cephalosporin antibiotics is recommended.¹ Ineffective and inappropriate antibiotic use can lead to the spread of resistance, the occurrence of difficult-to-treat superinfections, increased healthcare economic burden, more toxic side effects, and death.¹²

The qualitative evaluation of antibiotics further includes category IVB, with 0 visits (0%) (Table II). This indicates that antibiotic use has taken into account the safety of the patients. It is known that all patients have no history of allergies or comorbidities that would affect drug administration. COPD is a chronic disease that requires long-term medication use.⁵

A total of 0 visits (0%) fall into category IV C (Table II), indicating that the use of antibiotics has taken into consideration the cost of the medication provided to patients. For patients with low to middle-low economic status, the administration of expensive antibiotics would affect the patient's treatment process due to the high cost of medication. Additionally, for hospitalized patients, costly treatment would impact the duration of therapy.^{12,13}

In category IVD, 0 patient visits (0%) were found to receive non-narrow-spectrum antibiotics. Based on the data obtained from medical records, there were no laboratory data such as bacterial culture tests and other incomplete laboratory examinations since they were only conducted during the patient's initial visit. However, patients with COPD at the Lung Hospital, West Sumatera are typically outpatient attendees who have repeated follow-up visits, allowing them to receive antibiotics more than once in their treatment history.

Patients are prescribed antibiotics based on clinical data obtained during their medical visit, including medical history, presence of fever, productive cough with yellow or green sputum, and exertional dyspnea.¹ Typically, multiple bacterial infections, both aerobic and anaerobic, are found in patients. Therefore, broad-spectrum antibiotics that cover both gram-positive and gram-negative bacteria (such as cephalosporins) should be administered as the first-line treatment.⁸

The next category is IIIA (prolonged antibiotic use), with a total of 4 visits (2.53%). The recommended duration of antibiotic treatment for acute exacerbation of COPD is 3-7 days.¹ Prolonged antibiotic use can lead to undesirable effects on patients, such as ineffective treatment and increased resistance, as bacteria that are not killed undergo mutations and become resistant.^{12,14}

There were 0 visits (0%) in category IIIB (insufficient antibiotic use). Using antibiotics for a duration shorter than necessary (too short) can increase the likelihood of resistance as the bacteria in the body are not completely eradicated.^{8,15} Furthermore, there were 0 visits (0%) in category IIA (appropriate dosage). The standard dosage refers to the usual amount of medication given to patients or the minimum amount of medication that produces an effect.⁸ This means that the standard dosage needs to reach 100% for the medication to have a therapeutic effect. In other words, receiving less than 100% of the standard dosage is considered inappropriate dosage use as it does not provide the intended effect.

Similar to the use of antibiotics for too short a duration, inappropriate dosing of antibiotics can also lead to increased resistance.⁸ This is because the dosage falls below the minimum inhibitory concentration of bacteria, rendering the antibiotic ineffective against the bacteria in the body.¹⁶ Under category IIB, which pertains to appropriate interval use, there were 0 patient visits (0%). All prescribed antibiotics had intervals that aligned with the literature. Inappropriate interval use of antibiotics can result in ineffective treatment. For example, amoxicillin is typically administered three times a day or every 8 hours.¹⁷ Therefore, if amoxicillin is only given twice a day, the concentration maintained would not reach the minimum inhibitory concentration, rendering the antibiotic use inappropriate.¹²

Category IIC concerns the appropriate route of antibiotic administration. There were 0 patient visits in this category (0%). All patients were outpatient attendees and received oral administration of antibiotics. For hospitalized patients, intravenous administration is preferred, while oral administration is suitable for outpatient attendees with moderate exacerbation.¹ Oral administration is the easiest, most cost-effective, and safest route, facilitating patient compliance in the treatment of chronic bronchitis.^{1,11}

The use of antibiotics at the appropriate timing falls under category I, with 0 patient visits (0%). Appropriate timing refers to administering antibiotics at the right time to avoid fluctuations in drug levels in the blood.¹⁸ It is difficult to determine whether the timing of antibiotic administration for outpatient attendees is appropriate.

Cefixime is a third-generation beta-lactam cephalosporin antibiotic with better and broader activity against gram-negative bacteria compared to first-generation cephalosporins, and it is bactericidal in nature.¹⁷ Azithromycin belongs to the macrolide group and has a broader spectrum of activity compared to other macrolides. It is usually bacteriostatic but can exhibit bactericidal effects against some organisms at high concentrations.^{17,19}

Erythromycin is also a macrolide with a mechanism of action similar to other macrolides like azithromycin. The combination of azithromycin and cefixime can result in strong bactericidal properties, as cefixime acts on the bacterial cell wall, allowing azithromycin, which inhibits bacterial protein synthesis, to penetrate effectively.¹⁶

In studies related to COPD patients, the administration of azithromycin has been shown to reduce exacerbation frequency and improve patients' quality of life.¹⁹ Another study mentioned that erythromycin use can prevent exacerbations in COPD patients. Azithromycin is also beneficial as a therapy for patients with bronchiectasis and chronic bronchial infection caused by *Pseudomonas aeruginosa*. Long-term use of azithromycin for 12 months significantly reduces the incidence of moderate to mild exacerbations.¹⁴

The final result obtained in the qualitative evaluation of antibiotics is category 0, indicating the prudent, appropriate, and rational use of antibiotics. From the research findings, a total of 89 visits (56.33%) received antibiotics rationally. Antibiotic use is considered appropriate due to proper indication, correct dosage regimen, and observed clinical improvement.⁸

IV. CONCLUSION

Analysis of the appropriateness of drug use according to the Gyssens categories reveals that 56.33% of antibiotic use is appropriate/rational, 41.14% is ineffective, and 2.53% is prolonged use of antibiotics.

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Table 2: Accuracy of Antibiotic Use in COPD Patients based on Gyssens Method at the Outpatient Clinic of Lung Disease Treatment Center in Lubuk Alung

No	Category		Number of Visits	Percentage (%)
1	Incomplete medical records	VI	0	0,00
2	Antibiotic use without indication	V	0	0,00
3	Availability of more effective antibiotics	IVA	65	41,14
4	Use of toxic antibiotics	IVB	0	0,00
5	Use of expensive antibiotics	IVC	0	0,00
6	Availability of other antibiotics with narrower spectrum	IVD	0	0,00
7	Excessive use of antibiotics	IIIA	4	2,53
8	Insufficient use of antibiotics	IIIB	0	0,00
9	Inappropriate antibiotic dosage	IIA	0	0,00
10	Inappropriate antibiotic interval	IIB	0	0,00
11	Inappropriate antibiotic route	IIC	0	0,00
12	Inappropriate antibiotic timing	I	0	0,00
13	Appropriate antibiotic use	0	89	56,33
Total			158	100,00