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Cost-Effectiveness Analysis of Antibiotic Use in Patients with Chronic Obstructive Pulmonary Desease (COPD)
(Study of Dr. M. Djalil Hospital)

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Abstract

Chronic obstructive pulmonary disease (COPD) is a disease with airway limitations that are not completely reversible due to harmful substances or gases. The most common cause of acute exacerbations of COPD is bacterial infection, so treatment that can be done is to use antibiotics. Ineffective drug therapy will affect the effectiveness and costs incurred by patients. The purpose of this study is to find out how cost-effective and antibiotic treatment are in patients with acute exacerbations of COPD. This study uses an observational descriptive method with retrospective data collection based on medical record data and the cost of using antibiotics for Chronic Obstructive Pulmonary Disease (COPD) acute exacerbations of hospitalization at hospitals. Dr. M. Djamil Padang in 2019-2021. The calculation result with the lowest CER was the combination of levofloxacin and ceftriaxone of Rp. 323.6 and an outcome value of 100%. It can be concluded that the most effective use of antibiotic therapy models in COPD patients with acute exacerbations is the combination of levofloxacin and ceftriaxone.

Keywords: Cost-effectiveness, Antibiotics, Acute exacerbation of COPD

Abstrak

Penyakit paru obstruksi kronis (PPOK) adalah penyakit dengan keterbatasan saluran napas yang tidak sepenuhnya reversible dikarenakan bahan yang merugikan atau gas. Penyebab dari PPOK eksaserbasi akut yang paling banyak adalah infeksi bakteri, maka pengobatan yang dapat dilakukan adalah dengan menggunakan antibiotik. Terapi obat yang tidak efektif akan berpengaruh terhadap efektivitas dan biaya yang dikeluarkan pasien. Tujuan dari penelitian ini adalah untuk mengetahui bagaimana efektivitas biaya dan pengobatan antibiotik pada pasien PPOK eksaserbasi akut. Penelitian ini menggunakan metode deskriptif observasional dengan pengambilan data secara retrospektif berdasarkan data rekam medis dan biaya penggunaan antibiotik Penyakit Paru Obstruksi Kronis (PPOK) eksaserbasi akut rawat inap di RSUP. Dr. M. Djamil Padang Tahun 2019-2021. Hasil perhitungan dengan CER terendah

adalah kombinasi levofloxacin dengan ceftriaxon sebesar Rp. 323,6 dan nilai outcome sebesar 100%. Dapat disimpulkan bahwa penggunaan model terapi antibiotik pada pasien PPOK eksaserbasi akut yang paling efektif adalah kombinasi levofloxacin dengan ceftriaxon.

Kata Kunci: *Efektifitas Biaya, Antibiotik, PPOK eksaserbasi akut*

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is one of the diseases that attracts the attention of the world. According to WHO data in 2002, COPD is included in the top 5 deadly diseases around the world. The COPD mortality rate is expected to continue to increase by 30% over the next 10 years if risk factors are not properly managed, especially smoking habits. WHO estimates that in 2020 COPD will be the top 3 leading cause of death (Marta et al., 2014).

The mortality and morbidity of COPD will continue to increase which is related to the worsening of symptoms or commonly referred to as acute exacerbations (Sethi et el, 2002). Acute exacerbation COPD is characterized by an increase in sputum purulence production caused by respiratory tract infections, pollution, temperature changes, allergies and others (Suradi et al., 2012). The most common cause of acute exerbation is bacterial infection (Marta et al., 2014). Based on the cause of COPD with acute exacerbation, treatment that can be done is to use antibiotics (Baharutan et al., 2015).

Antibiotics are a class of drugs that are widely used in the world related to the increasing number of bacterial infections. More than a quarter of hospital budgets are spent on the cost of using antibiotics. The inaccuracy of antibiotic therapy can have a bad impact in the form of the emergence of bacterial resistance to antibiotics so that patient care becomes longer, medical costs become more expensive, and will reduce the quality of hospital services where patients are treated (Okky et al., 2014). The increase in bacterial resistance that causes COPD exacerbations to several antibiotics commonly used by clinicians as empirical therapy will certainly lead to a decrease in the effectiveness of acute COPD exacerbation therapy. This will cause higher morbidity and mortality due to acute COPD exacerbations.

Ineffective drug therapy will affect the costs incurred by patients, hospitals and the government (Andayani, 2013). The cost of health services in Indonesia is increasing so that there is a need for studies on improving the efficiency and effectiveness of health service costs (Handayani et al., 2013). The study of pharmacoeconomics considers two aspects, namely cost and outcome. (Ministry of Health of the Republic of Indonesia, 2013). *Cost Effectiveness Analysis* is one of the pharmacoeconomic methods that aims to compare the cost of treatment with the effectiveness of the therapy provided . In the cost-effectiveness analysis, all costs incurred (both direct and indirect costs) to treat patients will be compared to their effectiveness (Andayani, 2013).

This study was conducted to find out more about the cost-effectiveness and treatment of antibiotics in inpatient chronic obstructive pulmonary disease patients at the Central General Hospital of DR. M. Djamil Padang.

Literature Review

Based on a study conducted by Nalang et al. (2018) regarding the cost-effectiveness analysis of ceftriaxone and cefoctaxem antibiotic therapy in pneumonia patients at Prof. Dr. R. D. Kandou Manado Hospital, the total direct medical cost for ceftriaxone antibiotic therapy showed more cost-effective results than ceflocsim antibiotic therapy. This study uses descriptive analysis using the ACER and ICER calculation formulas. The total medical cost is the result of the calculation of the total length of hospitalization, medical expenses, treatment costs, and laboratory costs. The total cost of patients under five who go home in a recovered state. Patients in the criteria for returning home with a recovered state are patients who no longer show symptoms of pneumonia (Danusantoso, 2000).

The relationship between pharmacists in this problem is that a pharmacist in the hospital is in charge of handing over drugs to patients according to the prescription given by the doctor. Even so, a pharmacist also has an obligation to provide recommendations for the selection of alternative drugs that have the same effectiveness but at a price that is in accordance with the economic ability of the patient, which in this case is a type of antibiotic for community pneumonia patients.

Cost-effectiveness analysis of antibiotic therapy in pneumonia patients can provide alternative therapy options that have a lower cost without reducing the effectiveness of antibiotic drug therapy. The researcher as a pharmacist intends to conduct a research analysis of the cost-effectiveness of antibiotic therapy in pneumonia patients with the aim of obtaining an overview of antibiotic therapy that has a cost-effective value that can provide benefits for patients in the form of efficient and effective antibiotic therapy.

Research Method

a) Types and Design of Research

This type of research is observational using a cross sectional research design according to the perspective of the hospital. The data collection method was carried out retrospectively which was taken from the search of patient medical records and the cost of antibiotics for COPD (Chronic Obstructive Pulmonary Disease) patients with acute exacerbations treated at the hospital. Dr. M. Djamil Padang in 2019-2021.

b) Research Subject and Location

The subjects of the study used were all inpatients with acute exacerbations of COPD (Chronic Obstructive Pulmonary Disease) treated at the hospital. Dr. M. Djamil Padang in 2019-2021, who met the inclusion criteria , namely patients suffering from acute exacerbations of COPD with or without comorbidities who were treated in the inpatient unit of Dr. M. Djamil Padang Central General Hospital In 2019–2021, the patient had a complete medical record and contained basic information needed in the study (antibiotics, laboratory results, age, and gender), Acute exacerbation COPD patients who received antibiotic treatment therapy in treating infections due to exacerbations.

c) Data Collection Methods

The sampling technique used is purposive sampling, where samples that meet the inclusion criteria are directly taken as samples in this study.

d) Research Variables

The variables used in this study are the demographic character of the patients which include age and gender , antibiotic drugs given, comorbidities, length of treatment and direct medical cost.

e) Operational Definition

1) Cost-effectiveness analysis (CEA) is a pharmacoeconomic method that compares two or more treatment interventions that have the same outcome size with the same unit or the same treatment objectives.

2) Cost-effectiveness ratio (CER) is a ratio value obtained by comparing the costs that must be incurred with the average outcome of each antibiotic therapy model.

3) Incremental cost-effectiveness ratio (ICER) is a ratio value obtained by comparing two antibiotic therapy models to determine the additional costs required to achieve an increase in one unit of outcome compared to the comparator.

4) Cost-effectiveness is an analysis to compare the total direct medical costs incurred by patients with acute exacerbation of COPD.

5) Outcome is the ability of an antibiotic therapy model to reduce the number of white blood cells to a normal number (4,000-10,000 mm3) in patients with acute exacerbation of COPD.

6) The antibiotic therapy model is a combination group of antibiotic therapies used by patients with acute exacerbations of COPD during treatment at Dr. M. Djamil Padang Central General Hospital until they show normal white blood cells.

7) Direct medical costs are the costs incurred by patients on the use of antibiotics during hospitalization without taking into account other costs.

f) Research Materials and Materials

The materials and materials in this study are: (1) medical records of patients with acute exacerbation of COPD which are included in the inclusion criteria. (2) data on medical costs during treatment for acute exacerbation of COPD disease in each patient.

g) Result Analysis

1) The data that has been collected is grouped and arranged according to the inclusion criteria in Microsoft Excel for further analysis.

2) Identify and calculate the cost of the antibiotic therapy model given. Other costs that are directly related to medical health services such as hospitalization costs, laboratory examinations, the use of other drugs, medical procedures, and examination costs are not

included in the calculation of direct medical costs because the data analyzed will be smaller and more diverse, so it will be difficult to compare one model with another.

3) Identify and calculate outcomes in the form of evaluation of patients with normal white blood cell counts (4,000-10,000 mm3) in patients with acute exacerbation COPD.

4) Calculate the cost effectiveness ratio (CER) and compare the CER values of each therapy model. The cost-effectiveness analysis was calculated using the Cost Effectiveness Ratio (CER) formula which was calculated based on the amount of antibiotic use costs incurred by COPD patients with acute exacerbations to the results of antibiotic use therapy with the following formula:

$$\text{CER} = \frac{The\ cost\ of\ Antibiotics}{Outcome\ Antibiotics}$$

5) Select the smallest Incremental Cost-Effectiveness Ratio (ICER) value to recommend. The comparison of antibiotic therapy models with other antibiotics was analyzed using the Incremental Cost-Effectiveness Ratio with the following formula:

$$\text{ICER} = \frac{The\ cost\ of\ Antibiotic\ A - The\ cost\ of\ Antibiotics\ B}{Efectiveness\ Antibiotic\ A - Efectiveness\ Antibiotic\ B}$$

6) Select the antibiotic therapy model that has the best therapeutic outcome to be recommended as the highest standard in the treatment of acute exacerbation COPD.

Result and Discussion

Table 1. Characteristics of Acute Exacerbation COPD Patients at DR. M. Djamil Padang Hospital in 2019-2021

Variable	Number of Patients	Percentage (%)
Gender		
Man	23	92%
Woman	2	8%
Age		
46-55	0	0%
56-65	13	52%
>65	12	48%
Total	**25**	**100%**

Based on the data obtained, the number of research samples of acute exacerbation COPD patients at DR. M. Djamil Padang Hospital in 2019-2021 was 25 people. Patient characteristics by gender consisted of 23 male patients (92%) and 2 female patients (8%). The results obtained are in accordance with the research of Veryanti and Wulandari (2020) where from 60 samples it shows that there are 50 male samples and 10 female samples. This is due to the high smoking habit in men compared to women. According to Indreswari, et al. in 2014, the risk factor for the exacerbation of COPD is caused by cigarettes where the largest percentage of active smokers are men.

And the characteristics of patients based on age are the most in the age group of 56-65 years as many as 13 people (52%) and 12 people in the >65 years group (48%) and there are no patients in the 46-55 years group (0%). Characteristics of patients based on age, According to the Ministry of Health of the Republic of Indonesia (2009) the age category of the elderly based on age restrictions is divided into 3, namely the early elderly period of 46-55 years, the late elderly period of 56-65 years, and the elderly period of 65-up to the above (Ramadhan, 2014). The age of the patients in this study was >57 years because the most treated acute exacerbation COPD patients were elderly patients. The results obtained are in accordance with the research of Veryanti and Wulandari (2020), that 90% of COPD sufferers are patients aged 45 years and older because in elderly patients there is a decrease in the strength of the pulmonary muscles and the endurance of the cardiorespiratory system. This is caused by a decrease in the elasticity of the pulmonary parenchyma, causing a decrease in lung function.

Table 2. Antibiotic therapy model in inpatient acute exacerbation COPD patients at Dr. M. Djamil Padang Hospital

No.	Antibiotic Therapy Models	Number of Patients	Percentage (%)
1.	Sefoperazon	1	4%
2.	Azithromycin	2	8%
3.	Ceftriaxone	3	12%
4.	Ampicillin Sulbaktam 3g	3	12%
5.	Levofloxacin	6	24%
6.	Azithromycin + Ampicillin Sulbaktam 1.5g	1	4%
7.	Azitromycin + Levofloxacin	1	4%
8.	Levofloxacin + Ceftriaxone	1	4%
9.	Azitromicin + Ceftriaxone	2	8%
10.	Ampicillin Sulbaktam 1.5g + Levofloxacin	2	8%
11.	Ampicillin Sulbaktam 3g + Levofloxacin	3	12%
Total		25	100 %

In addition, 11 antibiotic therapy models were obtained for patients with acute exacerbations of COPD who were hospitalized at DR. M. Djamil Padang Hospital in 2019-2021. The antibiotic therapy model is a single group and combination of antibiotics used by COPD patients with acute exacerbations during treatment in the hospital until they show normal white blood cells. The antibiotic therapy model that was most widely used by patients was the antibiotic levofloxacin for 6 people (24%), then ceftriaxone, ampicillin sulbactam 3gr and the combination of ampicillin sulbactam 3gr with levofloxacin for 3 people each (12%), then azitromicin, a combination of azithromycin with ceftriaxone and the combination of ampicillin sulbactam 1.5gr with levofloxacin for 2 people each (8%) and cefoperazone, a combination of azithromycin and ampicillin sulbactam 1.5 gr, the combination of azithromycin with levofloxacin, and the combination of levofloxacin with ceftriaxone as much as 1 person each (4%).

In this study, it is necessary to calculate the direct medical cost, the direct medical cost that is researched only in terms of the cost of antibiotics used. Other costs such as hospitalization costs, laboratory examinations, the use of other drugs, medical procedures, and examination costs are not included in the calculation of direct medical costs because the costs used will vary in the medical treatment so it will be difficult to compare one therapy model with another.

Table 3. The results of the CER analysis of the total direct costs of inpatient acute exacerbations of COPD at Dr. M. Djamil Padang Hospital

No.	Antibiotic Therapy Models	Average direct cost (C)	Outcome (E)	CER
1.	Azithromycin + Ampicillin Sulbaktam 1.5g	IDR 154,755	100%	IDR 1,547.5
2.	Azitromycin + Levofloxacin	IDR 102,520	100%	IDR 1,025.2
3.	Levofloxacin + Ceftriaxone	IDR 32,360	100%	IDR 323.6
4.	Ceftriaxon	IDR 38,760	67%	Rp. 578.5
5.	Levofloxacin	IDR 29,600	67%	IDR 441.7
6.	Ampicillin Sulbaktam 3g + Levofloxacin	IDR 277,890	67%	IDR 4,147.6

The outcome of drug therapy is also an assessment in this study as seen from the results of antibiotic therapy used by patients during treatment until the number of white blood cells returns to normal. The normal number of white blood cells (leukocytes) is 4,000-10,000. Leukocytes function to protect the body against the invasion of foreign bodies, including bacteria and viruses. Most leukocyte activity takes place in tissues and in the bloodstream (Sloane, 2004).

The highest therapeutic model outcomes with 100% effectiveness values are the combination of azithromycin + ampicillin sulbactam 1.5gr, the combination of azithromycin + levofloxacin, and the combination of levofloxacin with ceftriaxone. Then the antibiotics ceftriaxone, levofloxacin and the combination of sulbactam ampicillin 3gr + levofloxacin with an outcome of 67%, then the antibiotic azithromycin and the combination of sulbactam ampicillin 1.5gr + levofloxacin with an outcome of 50%, the antibiotic azmpicillin sulbaktam 3gr with an outcome of 33% and the one with an outcome of 0% is the antibiotic sefoperazone and the combination of azithromycin + ceftriaxone. The antibiotic cefoperazone and the combination of azithromycin + ceftriaxone could not be analyzed by the cost-effectiveness analysis method because the outcome was 0%.

Meanwhile, the results of the study showed that patients who received antibiotic drug therapy with a combination of azithromycin + ampicillin sulbactam 3gr, a combination of azithromycin + levofloxacin and a combination of levofloxacin + ceftriaxone each had 1 patient and their leukocytes returned to normal. Patients who used azithromycin and a combination of sulbaktam ampicillin 1.5gr + levofloxacin were 2 patients, each of whom reached the target of normal leukocytes. Then ceftriaxone and the combination of ampicillin

sulbactam 3gr + levofloxacin as many as 3 patients and 2 patients each with leukocytes returned to normal. In the levofloxacin antibiotic with the highest number of patients, namely 6 patients, 4 of them reached the target of normal leukocytes. Antibiotic ampicillin sulbaktam 3gr 3 patients and 2 patients with normal leukocytes. Meanwhile, in the case of cephaloperzone antibiotics, there were 1 patient, azithromycin + ceftriaxone 2 patients and no patients with leukocytes returned to normal.

Table 4. Results of ICER Analysis of the Total Direct Costs in Acute CKD Exacerbation Patients Hospitaled at Dr. M. Djamil Padang Hospital

No.	Antibiotic Therapy Models	Average cost (C)	Outcome (E)	ΔC	ΔE	ICER
1.	Azithromycin + ampicillin sulbaktam 1.5g	IDR 154,755	100	IDR 115,995	33	IDR 3,515
	Ceftriaxon	IDR 38,760	67			
2.	Azithromycin + ampicillin sulbaktam 1.5g	IDR 154,755	100	IDR 125,155	33	IDR 3,792.5
	Levofloxacin	IDR 29,600	67			
3.	Azitromycin + Levofloxacin	IDR 102,520	100	IDR 63,760	33	IDR 1,932.1
	Ceftriaxon	IDR 38,760	67			
4.	Levofloxacin + Ceftriaxone	IDR 32,360	100	IDR 2,760	33	IDR 83.6
	Levofloxacin	IDR 29,600	67			
5.	Azitromycin + Levofloxacin	IDR 102,520	100	IDR 72,920	33	IDR 2,209.6
	Levofloxacin	IDR 29,600	67			

After knowing the outcome of the antibiotic drug therapy model, then a Cost *Effectiveness Ratio* (CER) value was calculated which was useful to describe the total cost of therapy divided by clinical *outcomes*. The CER value of several alternative therapy options that have the same goal is the ratio with the lowest value (Dipiro et al., 2011).

The most effective to less effective antibiotic therapy sequence based on CER calculations is a combination of levofloxacin + ceftriaxone, levofloxacin, ceftriaxone, azithromycin + levofloxacin, azithromycin + sulbactam ampicillin 1.5gr and sulbactam ampicillin 3gr + levofloxacin. Alternative therapies that are more effective in terms of cost and treatment are therapies with lower CER values compared to others (Ministry of Health, 2013). This shows that the combination of levofloxacin + ceftriaxone is a more effective antibiotic therapy option for use by patients with acute exacerbation of COPD at DR. M. Djamil Padang Hospital with the lowest CER value of Rp. 323.6 and an Outcome value of 100%.

After calculating the CER values of several antibiotic therapy models, it is then included in a cost-effectiveness diagram to measure *the Incrumental Cost Effectiveness Ratio* (ICER) to compare 2 or more types of drugs that show additional costs to other options. If this additional cost is low, it means that the drug can be chosen, on the other hand, if the additional cost is very high, the drug is not good to choose (Drummond, 1999; Schulman, 2000).

The calculation of cost-effectiveness analysis using ICER is carried out to provide several alternative options that can be adjusted to the consideration of funds or the availability or absence of these types of alternatives. The order of ICER values from lowest to highest is the combination of levofloxacin + ceftriaxone against levofloxacin with an ICER value of Rp. 83.6, the combination of azithromycin + levofloxacin against ceftriaxone with an ICER value of Rp. 1,932.1, the combination of azithromycin + levofloxacin against levofloxacin with an ICER value of Rp. 2,209.6, the combination of azithromycin + ampicillin sulbactam 1.5gr against ceftriaxone with an ICER value of Rp. 3,515, and the antibiotic combination of azithromycin + ampicillin sulbactam 1.5gr against levofloxacin with an ICER value of Rp. 3,792.5.

Conclusion

Based on the results of the research that has been carried out, it can be concluded that the most effective use of the antibiotic therapy model in patients with acute exacerbation of COPD is a combination of levofloxacin + ceftriaxone with an *outcome* value of 100%, a CER value of Rp. 323.6.

References

Andayani TM. (2013). *Pharmacoeconomics: Principles and Methodologies*. Knowledge Exchange.

Baharutan, Kezia Novita, Fatma Walil, and Adeanne Wullur. 2015. Bacterial Sensitivity Test Isolated from Sputum of Patients with Chronic Bronchitis Undergoing Outpatient Treatment at Prof. Dr. R. D. Kandou Manado Hospital to Antibiotics Ampicillin, Erythromycin, and Ciprofloxacin. *Pharmacon Pharmaceutical Scientific Journal.* Vol 4. No 4.

Danusantoso, H. 2000. Pulmonary Disease Science. Hypocrates. Jakarta.

Dipiro, J et al. 2011. *Pharmacotherapy 8th Edition*. The McGrow-Hill companies, US

Directorate General of Pharmaceutical Development and Medical Devices. (2013). *Guidelines for the Implementation of Pharmacoeconomic Studies.* Ministry of Health of the Republic of Indonesia.

Drummond, M. F. 1999. *An Introduction to Health Economics.* UK: Brookwood Medical Publications. Page 46.

Handayani, F. W., Muhtadi, A., Pharmacy, F., Padjadjaran, U., Dara, T., Manis, K., & Active, S. (2013). *Pharmacoeconomics Studies Underlying Treatment Selection in Indonesia*. Pharmacology, *4*, 1–15.

Ministry of Health, R.I. 2013. *Basic Health Research (RISKESDAS).* Ministry of Health of the Republic of Indonesia.

Marta, N. A., Andrini, F., Saad, A. 2014. *Identification of bakeries in sputum patients with chronic obstructive pulmonary disease acute exacerbations at Arifin Achmad Hospital, Riau Province*. JOM FK. 1;2.

Marta N, Azizman F, Saadetal. 2014. *Identification of Sputum Bacteria in Acute CKD Exacerbation Patients at Arifin Achmad Hospital, Riau Province*. JOM FK. Volume 1 Number 2.

Nalang, A. 2018. ‖Cost-Effectiveness Analysis of Pneumonia Treatment Using Seftriaxone and Sefotaksim Antibiotics at Prof. Dr. RD Kandou Manado Hospital‖. PHARMACON, 7(3). p.322-323

Okky SP, Rizky A, Ivan SP, Cherry R, et al, 2014., *Analysis of minimizing the cost of empiric antibiotic use in patients with sepsis who are sources of respiratory infection.* JFKI. 2014. 3(1): 10-17.

Sethi S, Evans N, Grant BJ, Murphy TF. 2002. *New strain of bacteria and exacerbation of chroic obstructive pulmonary disease*. N engl J Med. Volume 15 Number 7.

Sloane. 2004. *Anatomy and Physiology for Beginners*. Jakarta: EGC. Page 245.

Suradi, Yusup Subagio, Reviono and Harsini. 2012. The *Relationship Between Acute Exacerbation of Chronic Obstructive Pulmonary Disease (COPD) and Sputu, Bacterial Culture Results at Dr. Moewardi Hospital, Surakarta*. Indonesian Respirology: Volume 32 Number 4.

Veryanti, P. R., Wulandari, A. 2020. *Cost-Effective Analysis of Bronchodilator Use Compared to Bronchodilator-Corticosteroid Combination in Patients With Chronic Obstructive Pulmonary Disease (COPD).* Udayana Pharmaceutical Journal, Vol 9, No 1, Year 2020, 13-18.

WHO. (2018). Chronic Respiratory Diseases: Burden of COPD. www.who.int/repiratory/copd/burden/en/