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The Evaluation of Antibiotic Use in Adult Patients With Pneumonia

Indriastuti Cahyaningsih
Department of Clinical Pharmacy, Faculty of Medicine and Health Sciences
Universitas Muhammadiyah Yogyakarta
Yogyakarta, Indonesia
ndree_chy@yahoo.com

Riska Aulia
Department of Clinical Pharmacy, Faculty of Medicine and Health Sciences
Universitas Muhammadiyah Yogyakarta
Yogyakarta, Indonesia
auliaris16@gmail.com

***Abstract*-Pneumonia is one of the most common forms of upper respiratory tract infection. Currently pneumonia is the third leading cause of death in Indonesia and the sixth cause of death in the world. One of the therapies used for pneumonia is antibiotics, but inappropriate use of antibiotics can cause resistance and also less effective treatment. This study aims to evaluate the use of antibiotics in pneumonia patients at the inpatient installation of PKU Muhammadiyah Bantul Hospital based on guidelines from the Association of Indonesian Internal Medicine Specialists in 2010. This research is a descriptive non-experimental observational design with retrospective data collection in the period January - December 2016 and taken in total sampling from 32 medical records of adult pneumonia patients in inpatient care at PKU Muhammadiyah Hospital, Bantul. Data was processed descriptively and compared with the guidelines from Indonesian Internal Medicine Specialist Association. The results showed that there were 32 patients who entered the inclusion criteria with 9 types of antibiotics prescribed with conformity with the Indonesian Internal Medicine Specialist Association guidelines as much as 83.34% (Azithromycin, cefotaxime, ceftazidim, ceftriaxone, ciprofloxacin, gentamicin, levofloxacin). The most widely used single antibiotic therapy in PKU Muhammadiyah Bantul Hospital in 2016 was levofloxacin, 42.85%, and the most widely used combination antibiotic therapy was a combination of azithromycin and ceftriaxone 48.00%. The conclusion is that prescribing antibiotics in pneumonia patients in PKU Muhammadiyah Bantul Hospital is not entirely in accordance with the Indonesian Internal Medicine Specialist Association guidelines.**

Keywords: Pneumonia, Antibiotics, Indonesian Internal Medicine Specialist Association

I. INTRODUCTION

Acute respiratory infections (ARI) cause high morbidity and mortality and lose the work productivity. One of the most common forms of ARI is pneumonia. Pneumonia is defined as an inflammation of the pulmonary parenchyma, distal to the terminal bronchioles which includes the respiratory bronchioles, and alveoli, and results in lung tissue consolidation and disruption of the local gas exchange [1].

The incidence of pneumonia occurs in around 156 million every year worldwide, and 151 million cases occur in developing countries. The highest cases occurred in India 43 million, China 21 million, Pakistan 10 million, and also in Bangladesh 6 million [2]. Whereas according to Basic Health Research (2013) [3] the prevalence of pneumonia in Indonesia reached 2.7%.

Antibiotics become the most widely used drug in infections caused by bacteria. The relatively high intensity of antibiotic use raises various problems and becomes a global threat to health, especially bacterial resistance to antibiotics. Resistance starts from the hospital environment and then spreads to the outside community environment. Antibiotic resistance occurs due to unwise use of antibiotics and the application of incorrect standard precautions in health care facilities.

PKU Muhammadiyah Bantul Hospital is one of the referral hospitals in Yogyakarta, especially the Bantul area. The number of pneumonia patients hospitalized in PKU Muhammadiyah Bantul Hospital in 2016 reached 79 patients. Based on this background, researchers were interested in conducting research on evaluating the use of antibiotics in pneumonia patients using guidelines from Association of Indonesian Internal Medicine Specialists in 2010.

II. METHODS

This research applied a type of non-experimental observational descriptive study. Data were taken retrospectively from January to December 2016 from medical records of pneumonia patients in PKU Muhammadiyah Bantul Hospital. The sampling technique was carried out by using total sampling and obtained a total sample of 79 patients. Data were analyzed descriptively using guidelines from Association of Indonesian Internal Medicine Specialists in 2010.

The research instrument in this study employed medical records of adult pneumonia patients at PKU Muhammadiyah Bantul Hospital in the period January - December 2016. The method of work in this study applied the selection of samples that met the inclusion criteria from medical records of pneumonia patients in PKU Muhammadiyah Bantul Hospital, January - December 2016 that consist of patient who had been given antibiotic therapy and the age of over 18 years. Then, data collection on antibiotic use from medical records was carried out age, gender, antibiotic name, indication, dosage, frequency of administration, duration of administration, and type of use. Furthermore, analyzing the profile of antibiotics, and evaluating the accuracy of antibiotic selection in prescribing based on the guidelines of the

Association of Specialist Doctors in Indonesia in 2010 was finally performed.

III. RESULTS AND DISCUSSION

Data on pneumonia patients were taken entirely and taken with inclusion characteristics (adult patients, diagnosed with pneumonia, receiving antibiotic therapy, and hospitalized). Data that fulfilled the inclusion criteria were 32 medical records.

A. Characteristics of Pneumonia Patients

Characteristics of pneumonia patients were categorized by gender and age-based. Distribution of characteristics of pneumonia patient is explained at table I.

TABLE I. DESCRIPTION OF CHARACTERISTICS OF PNEUMONIA PATIENTS

NO	Characteristics of Patient	Frequency	Percentage (%)
1.	Gender-based		
	Male	18	58
	Female	14	42
2.	Age-based		
	18-49 years	4	12
	50-64 years	11	33
	age ≥ 65 years	17	55

1. Gender-based Characteristics

In this study, male and female patient data were used to determine the relation of sex on patients with pneumonia. The percentage of patients diagnosed with pneumonia in PKU Muhammadiyah Hospital Bantul in 2016 consisted of more male (58%) than female (42%). According to the results of Basic Health Research in 2013 the prevalence of pneumonia in men was higher at 4.8% compared to women at 4.3%. This happened because men tend to smoke. According to the Indonesian Ministry of Health (2005)[4], one of the risk factors that can cause pneumonia is smoking. According to the results of the Global Adult Tobacco Survey (2011)[5]the prevalence of smokers in Indonesia in men reached 67.0% while women only 2.7%, so this is one possibility that men have a higher risk of developing pneumonia than women. In addition, men are more active outside the home so they are easily exposed to air pollution. Air pollution and cigarette smoke contain many chemicals that can become a trigger factor for respiratory infections [6].

2. Age-based Characteristics

Distribution of adult patients based on age can be grouped into three, namely adult patients aged 18-49 years, 50-64 years, and old age ⩾ 65 years [7]. Based on the results of the study there was an increased incidence of pneumonia in each age group. The highest incidence of pneumonia occurred in patients aged ⩾ 65 years or the elderly group exactly 54.6%. According to the Indonesian Ministry of Health (2016)[3] seen from Indonesia's health profile in 2015, populations prone to pneumonia were children aged <2 years, elderly> 65 years, and people who had health problems (malnutrition, immunological disorders).

B. Overview of the Use of Antibiotics

Antibiotics are the most widely used drug in infections caused by bacteria. In the PKU Muhammadiyah Hospital in Bantul in 2016, the antibiotics used for pneumonia included antibiotics in the class of florocuinolone (levofloxacin, ciprofloxacin), macrolide groups (azithromycin), cephalosporin groups (ceftazidim, ceftriaxone, cefotaxime, cefixime), and aminoglycosides (gentamicin). Patients diagnosed with pneumonia got either antibiotic therapy alone or in combination of two or more antibiotics. The description of antibiotic use in pneumonia patients in PKU Muhammadiyah Bantul Hospital is presented in table II.

TABLE II. DESCRIPTION OF SINGLE ANTIBIOTIC USE IN PATIENT

Antibiotic Class	Type of Antibiotic	Frequency	Percentage
Fluorokuinolon	Levofloxacin	3	42.85
Sefalosporin	Ceftazidime	2	28.57
	Ceftriaxone	1	14.29
	Cefoperazone	1	14.29
Total		7	100

TABLE III. DESCRIPTION OF COMBINATION ANTIBIOTICS USE IN PATIENTS PNEUMONIA IN PKU MUHAMMADIYAH BANTUL HOSPITAL IN 2016

Type of Antibiotic	**Frequency**	**Percentage**
Levofloxacin + Cefixime	1	4
Azithromycin + Ceftriaxone	12	48
Levofloxacin + Azithromycin	5	20
Cefixime + Ceftriaxone	3	12
Levofloxacin + Cefotaxime	1	4
Ceftazidime + Ciprofloxacin	1	4
Ceftazidime + Azithromycin	1	4
Total	25	100

Among 32 patients diagnosed with pneumonia, it can be seen that 7 patients received single antibiotic therapy, and 25 patients received combined antibiotic therapy. The most widely used single antibiotic therapy was levofloxacin, which reached 42.85%, while the least used antibiotics were ceftriaxone and cefoperazone, which were 14.29% respectively. Besides, in combined antibiotic therapy, it can be seen that the most commonly used was a combination of azithromycin and ceftriaxone which reached 48.00%, and the most rarely used combination included a combination of levofloxacin and cefixime, levofloxacin, cefoperazone, ceftazidime and ciprofloxacin, and ceftazidim and azithromycin which was only used 4.00%.

The most widely used single antibiotic therapy at PKU Muhammadiyah Bantul Hospital was the fluorocuinolone group antibiotic, levofloxacin. The antibiotic fluorocuinolone

was a broad-spectrum antibiotic and also had a strong activity in inhibiting gram-positive bacteria including penicillin non-perceptible pneumococci and methicillin non-susceptible Staphylococcus aureus (MRSA). This antibiotic was also active in dealing with gram negative bacteria such as Enterobacteriae, Moraxella catarrhalis, producing beta-lactamase H. Influenza, Shigella spp., Salmonella spp., And Nisseria spp [8].

From the results of a study conducted by Nufus (2012)[9], it was stated that levofloxacin became an effective antibiotic in respiratory tract infections, urinary tract infections, and skin infections. Levofloxacin had extensive activities to treat community-acquired and nosocomial infections. Levofloxacin was also available as parenteral preparations that allow widespread use both singly and in combination with other agents. Antimicrobial activity in general included Enterobacteriaceae, P. aeruginosa, srtaphylococci, enterococci, streptococci. It was also stated in the Lee et al. study (2014)[10] that levofloxacin was safe to use in adult patients with special attention to kidney function associated with its limited metabolism and levofloxacin also excreted intact through urine.

Furthermore, antibiotics that were also widely used for the treatment of pneumonia in PKU Muhammadiyah Bantul Hospital were cephalosporin groups, especially third generation of cephalosporins (ceftazidim, ceftriaxone, cefoperazon). Third generation of cephalosporin had a broad spectrum against gram-positive and gram-negative bacteria. This third generation was often used for empirical therapy of various types of infections, so that third generation cephalosporins were widely used to replace penicillin and its class as a first line therapy [11].

Other antibiotics used to treat pneumonia in PKU Muhammadiyah Bantul Hospital were macrolide antibiotics, specifically azithromycin. Azithromycin had a broad spectrum against gram-positive and negative bacteria, making it effective against various pathogenic organisms especially in respiratory tract infections caused by Haemophillus influenzae and also urinary tract infections [12].

Furthermore, aminoglycoside antibiotics (gentamicin) were also used to treat pneumonia in PKU Muhammadiyah Bantul Hospital. According to Carolina (2014)[10] gentamicin was usually used in combination with penicillin to treat infectious diseases such as pneumonia, UTI, and sepsis which often occurred during the study period by gram negative bacteria. Aminoglycoside antibiotics had a broad spectrum and were the antibiotic of choice for treating infectious diseases caused by gram negative bacteria such as E. Coli, Salmonella spp., Shigella spp., Enterobacter spp., Cianobacte spp., Acinetobacter spp., Proteus spp. Klesibella spp., Serratia spp., Morganella spp., Pseudomonas spp., and microbacteria [13].

When comparing between the therapy using combination antibiotics (dual therapy) and single antibiotic therapy (monotherapy), patients who received dual therapy had a relatively shorter treatment period than patients who received monotherapy. Dual therapy used a combination of beta lactam antibiotics with deep macrolides. Initial management of hospitalized pneumonia patients who did not require ICU care could reduce the mortality and length of patient care [14].

At PKU Muhammadiyah Bantul Hospital, the most frequently used dual therapy was azithromycin with ceftriaxone. Combination therapy between azithromycin and ceftriaxone was in accordance with the guidelines for managing patients with pneumonia from the British Thoracic Society (2009) [15]. Therapy recommended by the British Thoracic Society for hospitalized pneumonia patients was antibiotics therapy of beta lactam group combined with macrolide.

3. Evaluation of the Accuracy of Using Antibiotics

Evaluation of the antibiotic use in pneumonia patients in this study referred to the guideline of the Indonesian Internal Medicine Specialist Association in 2010 regarding the diagnosis and treatment of adult pneumonia patients, to examine whether prescribed antibiotics were on the guidelines or not.

TABLE IV. ACCURACY EVALUATION OF THE ANTIBIOTICS USE BASED ON INDONESIAN INTERNAL MEDICINE SPECIALIST ASSOCIATION IN 2010

Type of Antibiotic	Conformity based on Indonesian Medicine Specialist Association	Percentage (%)
Azithromycin	√	25
Cefixime	x	15.27
Cefoperazone	x	1.39
Cefotaxime	√	1.39
Ceftazidim	√	9.72
Ceftriaxone	√	26.38
Ciprofloxacine	√	1.39
Gentamicin	√	1.39
Levofloxacin	√	15.27

Based on the results of the study, the profile of appropriate antibiotic treatment that was based on the guidelines of the Association of Indonesian Internal Medicine Specialists (2010)[1] and were prescribed accordingly reached 83.34%, and 16.66% could be concluded as inappropriate antibiotics. Antibiotics prescribed in PKU Muhammadiyah Bantul Hospital in 2016 that was not contained in the guidelines were third generation cephalosporin antibiotics (cefixime and cefoperazon).

According to The Association of Indonesian Internal Medicine Specialists (2010) [1] the main principle of pneumonia therapy was the administration of certain antibiotics against certain germs in an ARD type both pneumonia and other forms. The treatment of community pneumonia antibiotics used macrolide antibiotics, beta lactam (cefuroxime, high-dose amoxicillin, co-amoxiclav, ceftriaxone, cefotaxime), florokuinolon. On the other hand, nosocomial pneumonia antibiotic therapy used cephalosporin anti pseudomonas group antibiotics (cefepime, ceftazidime), anti-pseudomonas carbapemen, macrolides, aminoglycosides, florocuinolone, vancomycin, and linezolid. When viewed from the lab results and prognosis of pneumonia patients in the inpatient care at PKU Muhammadiyah Bantul Hospital in 2016, patients who received third generation cephalosporin antibiotic therapy (cefixime and cefoperazone) were declared to be improving. In other words, the treatment of pneumonia with antibiotics was successful even though the prescribed antibiotics did

not match those listed on the guidelines of the Association of Indonesian Internal Medicine Specialists.

Pneumonia patients in the inpatient installation of PKU Muhammadiyah Bantul Hospital in 2016 who were successfully treated using antibiotics outside of PAPDI were found in many cephalosporin groups, especially third generation cephalosporins (cefixime and cefoperazone) in PKU Muhammadiyah Bantul Hospital in 2016. This third generation cephalosporin had broad activity (Board Spectrum), which was able to fight infection with gram-positive and gram-negative bacteria. In addition, third generation cephalosporins were active against penicillin non-suspectible S. pneumonia, Haemophilus, Neisseria, and Moraxella Spp [10].

According to Association of Indonesian Internal Medicine Specialists [1], cefoperazone was one of the antibiotics that can be used for empirical therapy in pneumonia, especially for pneumonia caused by the bacterium Pseudomonas aeruginosa. In addition, Cefixime was potent to gram-positive microorganisms such as Streptococcus sp., Streptococcus pneumoniae, Branhamella catarrhalis, Escherichia coli, Proteus sp., and Haemophilus influenza [15], but a journal had not been found stating that cefixime was effective for the treatment of pneumonia.

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