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Research Paper

Profile and Effectiveness of Antibiotics for Adult Pneumoniae Inpatient at Tertiary M. Djamil Hospital in Padang Indonesia

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ABSTRACT: *The effectiveness of antibiotics usage is one of the important responsibilities in pharmaceutical services. The effectiveness of usage antibiotics can be monitored based on body temperature and leukocytes after 2-3 days of using antibiotics. Pneumonia is a respiratory tract infection that uses antibiotics in its treatment. The purpose of this study was to determine the profile and effectiveness of antibiotics in adult pneumonia patients from Respiratory care and Internal Medicine Inpatient Department at M. Djamil tertiary hospital in Padang Indonesia during 2018. This research is a descriptive study using retrospective data. The inclusion criteria were inpatient adult pneumonia patients who received antibiotic therapy without other infectious diseases. The results showed that of the 178 cases studied, only 66 cases met the inclusion criteria for antibiotic use profile analysis, but only 52 cases met the criteria for evaluating the effectiveness of antibiotic use through body temperature and leukocyte examination because there were 14 patients who did not show leukocytosis upon admission to hospital. The most used antibiotics in the treatment of this case is a combination of Ceftazidime and levofloxacin intravenous with a percentage of 34.85%. As many as 48% of patients were not monitored for the effectiveness of using antibiotics through the patient's leukocyte values after 2-3 days of using antibiotics, monitoring only through body temperature for all patients. The percentage of effective antibiotics based on the patient's body temperature and leukocyte values was 73.1%.*

KEYWORDS: *Antibiotic, Body Temperature, Effectiveness, Leukocyte, Pneumonia*

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I. INTRODUCTION

Pneumonia is an acute lower respiratory tract infection in the lung parenchyma affecting the lung tissue (alveoli), caused by microorganisms such as bacteria, viruses, fungi and parasites [1]. Pneumonia can affect anyone, whether children, young adults or the elderly with around 450 million cases each year [2].

The main cause of pneumonia in adults is bacteria. Pneumonia is classified as community pneumonia and nosocomial pneumonia. Community pneumonia is pneumonia that is acquired in the community or outside the hospital, while nosocomial pneumonia is pneumonia that is acquired after 48 hours of hospitalization [2]. Community pneumonia is the most common type of pneumonia that causes death in children, the elderly and people with chronic diseases in developing countries [3]. While nosocomial pneumonia is the most common cause of death in hospital [4]. High pneumonia morbidity and mortality rates in developing countries have resulted in increased hospitalization rates [5].

The 1999 WHO report stated that the highest cause of death from infectious diseases in the world is acute respiratory infections including pneumonia and influenza. From the book SEAMIC Health Statistics 2001, influenza and pneumonia are the sixth leading cause of death in Indonesia [6]. Based on the 2018 Basic Health Research (in Indonesia called RISKESDAS) data, the prevalence of pneumonia based on the diagnosis of health workers increased by around 2% from the previous 1.8% [7]. According to data at M. Djamil tertiary hospital in Padang, pneumonia was ranked second out of the 10 most hospitalized diseases in the 2018 period [8].

Treatment of pneumonia can consist of antibiotics and supportive care [9]. Management of pneumonia caused by bacteria, the same as infections in general, namely by administering antibiotics [10].

Antibiotics are among the most frequently used drugs in the world, especially in developing countries, where the use of antibiotics increased by 36% between 2000 and 2010 [11]. The research by the AMRIN (Antimicrobial Resistance in Indonesia) team, which was conducted in two Indonesian teaching hospitals, found that 84% of inpatients received antibiotic therapy, 67% of antibiotics were used in the internal medicine department [12]. It is estimated that up to one third of inpatients receive antibiotics, and the cost of antibiotics can account for up to 50% of the drug budget in hospitals [13].

Ineffective and excessive use of antibiotics can encourage resistance to certain bacteria. Increased resistance has led to increased morbidity and mortality, thereby increasing patient care costs [14]. Antibiotic resistance is an important problem in health care, because it can lead to treatment failure, prolonged hospitalization, increased costs, and mortality [15]. WHO (World Health Organization) data shows that the high number of antibiotic-resistant bacteria, especially for *Klebsiella* , *Staphylococcus aureus*, and *Streptococcus pneumoniae* [16].

All patients receiving antibiotics should be monitored and evaluated after 2-3 days for improvement in signs or symptoms of infection such as body temperature and white blood cell count [17]. The patient's response to antibiotics should be evaluated after three days of giving antibiotics, if the antibiotics given do not respond then they must be evaluated for possible complications, other sources of infection, or resistance to antibiotics and it is necessary to re-evaluate the patient's clinical diagnosis by discussing it with the PPRA Team (Antibiotic Resistance Control Program) Hospital to find a solution to this problem [18,19].

Monitoring the effectiveness of antibiotics is carried out by doctors, pharmacists and clinical microbiologists every 48-72 hours, taking into account the patient's clinical condition and available supporting data [20]. The effectiveness of antibiotics can be judged by the improvement in signs of infection after 48-72 hours, for example: fever decreases to (36.5-37°C), leukocyte count approaches normal values (5000-10000x10^9 /L) [21]. Therefore, it is very important to monitor the patient's body temperature and leukocyte values after 2-3 days of antibiotic administration as a parameter of the effectiveness of antibiotic use.

In previous studies, an evaluation of the usage antibiotics in pneumonia patients in the internal medicine department at M. Djamil tertiary Hospital in Padang 2017 using the Gyssen method, can be concluded that the use of antibiotics is 51.7% rational [22]. Then, in the same year and hospital an evaluation of the use of antibiotics in pneumonia patients in respiratory care department was carried out and it was concluded that the use of antibiotics was rational 81.81% [23].

II. RESEARCH METHOD

This research was conducted for 6 months (October 2019 to March 2020) at M. Djamil tertiary hospital in Padang, with descriptive research methods. Data was collected retrospectively from patient medical records from Respiratory care and Internal Medicine Inpatient Department for the period 1 January 2018 - 31 December 2018. The sample collection technique was purposive sampling. Inclusion criteria included: All hospitalized adult pneumonia patients who received antibiotic therapy, without other infectious diseases, patients with complete medical record data including patient identity, doctor diagnostic, treatment therapy, body temperature, and laboratory tests, and leukocyte value before and after 2 -3 days of antibiotic usage.

Exclusion criteria included immune compromised patients or patients with complications of immune deficiency diseases such as HIV, AIDS and autoimmune diseases such as lupus (SLE), type 1 diabetes mellitus, chronic liver diseases, and rheumatoid arthritis, did not experience leukocytosis on admission to hospital and patients with long less than 2 days of treatment.

The profile of usage antibiotics was seen through the the most usage antibiotics in this case. Analysis of the effectiveness of using antibiotics was carried out by comparing the patient's body temperature and leukocyte values between before giving antibiotics and after 2-3 days of giving antibiotics.

III. RESULTS AND DISCUSSION

3.1 Antibiotic Usage Profile

There were 178 medical records of patients studied, but only 66 met the inclusion criteria, with 35 male patients (53%) and 31 female patients (47%). There are 13 types of antibiotics used by patients during treatment.

No	Antibiotics Group	Drugs	Total Patients	Percentage
1	Cephalosporin 3th generation + Fluoroquinolone	Ceftazidime IV + Levofloxacin IV	23	34,85%
		Ceftriaxon IV + Levofloxacin IV	14	21,21%
		Ceftriaxon IV + Ciproloxacin IV	2	3,03%

		Ceftazidime IV + Moxifloxacin IV	1	1,51%
2	Carbapenem + Fluoroquinolone	Meropenem IV + Ciprofloxacin IV	1	1,51%
		Meropenem IV + Levofloxacin IV	6	9,09%
3	Cephalosporin 3th generation + macrolide	Ceftriaxone IV + Azythromycin oral	2	3,03%
4	Fluoroquinolone	Levofloxacin IV	1	1,51%
		Levofloxacin oral	1	1,51%
5	Cephalosporin 3th generation	Ceftazidime IV	1	1,51%
		Ceftriaxon IV	12	18,18%
6	Carbapenem	Meropenem IV	1	1,51%

Table 1. Pattern of Antibiotics

From table no. 1, it can be seen that the most widely used antibiotics during the study period were the combination of Ceftazidime and levofloxacin Intravenous (IV) 34.85%, then the combination of ceftriaxone and levofloxacin 21.21%, ranked third most, used a single antibiotic ceftriaxone as much as 18.18%, then meropenem was combined with levofloxacin with a percentage of 9.09%. In general, this pattern of antibiotic use is appropriate according to ATS/IDSA recommendations (2019), as well as the guidelines for the use of antibiotics at M. Djamil tertiary hospital Padang in 2018 where the combination of cephalosporin and Fluoroquinolone class drugs became the main treatment for inpatient pneumonia therapy. [24].

In this study, it can be seen that antibiotics were given intravenously. Only two types of antibiotics are administered orally, namely azythromycin and levofloxacin. According to Cunha (2010) oral antibiotics should be the first choice for infection therapy, but in moderate to severe infections parenteral antibiotics can be considered [25]. Another interesting result was that there were 50 patients (75.74%) using combination antibiotic therapy. Combination drug therapy is performed to treat acute types of infections without a specific diagnosis that require rapid therapy. In this case, usually no or no bacteriological diagnosis has been made. Antibiotic combination therapy is done because although many infections can be cured by a single antibiotic, the right antibiotic is difficult to determine. This strategy can also reduce the possibility of super infection, resistance and toxicity. This is based on the assumption that the desired action of antibiotics can only be obtained by increasing the dose until it approaches the toxic dose, so that if two antibiotics are used, the dose of both types of drugs can be reduced to obtain the same effect [26].

In terms of the type of antibiotics used, the most antibiotics used as first-line therapy in pneumonia patients were 3rd generation cephalosporin antibiotics (ceftriaxone and Ceftazidime). This is because the cephalosporin group is a broad spectrum antibiotic group that can be used as empiric therapy for various types of infections. Increasing the use of this class of antibiotics needs to be followed by monitoring and evaluating the sensitivity and accuracy of use [27].

Fluoroquinolone class of antibiotics are also often used in the treatment of pneumonia, especially in combination with 3rd generation cephalosporin antibiotics. The type of Fluoroquinolone antibiotic that is often used is levofloxacin. Levofloxacin has broad activity for the treatment of community-acquired infections and nosocomial infections. Levofloxacin is also available as a parenteral preparation which allows its widespread use either alone or in combination with other agents [10].

Other antibiotics used in the treatment of pneumonia patients, according to the data obtained, are carbapenems, namely meropenem. Based on the results of the study, 10.6% of meropenem in combination form was used. Meropenem also has a broad spectrum so that this drug also plays a role in empiric therapy because it is active against gram-positive and negative bacteria that produce penicillinase, anaerobic bacteria and Pseudomonas aeruginosa [26].

No.	Culture Result	Total Patient	Percentage
1	*Staphylococcus sp*	3	20 %
2	*Klebsiella sp*	3	20 %
3	*Acinobacter baumannii*	1	6,67 %
4	*Staphylococcus aureus*	1	6,67 %
5	*Staphylococcus haemoliticus*	1	6,67 %
6	*Klebsiella pneumoniae*	2	13,33 %
7	*E. Coli*	1	6,67 %
8	*Candida sp*	2	13,33 %
9	*Candida tropicalis*	1	6,67 %

Table 2. Patient Culture Results

From the data in table 2 which is the result of patient culture, it was found that the most common types of bacteria that cause pneumonia are Staphylococcus sp (20%) and *Klebsiella sp* (20%). These results are similar to the pattern of bacteria from sputum examination at Persahabatan tertiary Hospital in Indonesia 2014 with the order of the top five infectious bacteria, namely *Klebsiella pneumoniae* (25%), Streptococcus viridians (15.5%), *Pseudomonas aeruginosa* (9.4%), *Acinetobacter baumannii* (9. .4%) and Escherichia coli (5.2%). The two most gram-negative bacteria were *Klebsiella pneumoniae* and *Acinetobacter baumannii* [28]. In addition to bacteria, *Candida sp*. (13.33%) was also found in the patient's sputum. Lung infection caused by fungi is still a health problem in Indonesia, because pneumonia caused by this fungus is a disease with a very rare incidence.

In looking at the effectiveness of using antibiotics, actually one method is to look at the results of sputum culture before use and after using antibiotics to see the response of microorganisms. However, the data obtained was only carried out one culture test except for two patients, so the effectiveness of antibiotics could not be seen based on the culture test results.

3.2 Antibiotics effectiveness through body temperature and leukocyte values

Evaluation of the effectiveness of usage antibiotics can be seen from two main things, namely the patient's body temperature and leukocyte values. In this study, the patient's vital examination included body temperature was carried out every day, while the laboratory examination included leukocytes. In data from 178 medical records, 26 patients only had one examination at the start of hospital admission, 24 patients had leukocyte examination before receiving antibiotic therapy and after 1 day of using antibiotics, and 11 patients who were examined before and after more than 3 days of antibiotic use. So that there were only 66 patients who could be monitored for the effectiveness of using antibiotics appropriately based on pharmaceutical service guidelines for antibiotic therapy issued by the Indonesian Ministry of Health and based on other international guidelines.

According to the Guidelines of Usage Antibiotics in M. Djamil tertiary hospital Padang, in the principle section on the use of antibiotics point 7 it is stated that an evaluation of the response to therapy is carried out every 3 days both clinically, laboratory and/or imaging (radiography/ultrasonography). Whenever possible, carry out monitoring with biomarkers (qualitative PCT) [29], But from the medical records that have been observed, there are still many patients who evaluate their response to therapy through laboratory data monitored for more than 3 days and some are even only monitored through laboratory data before using antibiotics, so it is possible that patients with these criteria respond to therapy by observing clinical conditions only.

To analyze the effectiveness of the use of antibiotics, of the 66 patients who met the inclusion criteria, only 52 patients were included in the effectiveness analysis because the other 14 patients did not show leukocytosis from the results of laboratory tests, so the analysis of the effectiveness of antibiotics based on the main parameters of body temperature and leukocyte values could not be continued. for the 14 patients.

The effectiveness of using antibiotics based on vital signs of body temperature shows that the antibiotics given are effective in reducing the patient's body temperature. This is in line with Arifah's 2018 research at Dr. Hasan Sadikin tertiary hospital in Bandung Indonesia, that there is a significant difference between the patient's body temperature before and after antibiotic therapy [30].

Body temperature parameters are carried out routinely every day at M. Djamil tertiary hospital Padang in adult pneumonia patients together with examination of other vital signs, so that the determination of the effectiveness of antibiotics based on body temperature parameters can be observed. The effectiveness of usage antibiotics based on laboratory data on leukocyte values shows a significant decrease in the patient's leukocyte values.

This is in line with Bestari's 2017 study at the Central Java Central tertiary Hospital, where there was a significant difference between the leukocytes of patients before and after therapy [31]. From the data obtained, in general all patients experienced leukocytosis or increased leukocyte values in laboratory tests upon admission to the hospital. Seeing the effectiveness of using antibiotics with leukocyte value parameters is something that is not easy to do in the field, because based on observations, patient leukocyte values are sometimes only done with one examination and many examinations are carried out one day after giving antibiotics or more than three days of using antibiotics. Meanwhile, according to the literature, the effectiveness of using antibiotics is seen 48-72 hours (2-3 days) after using antibiotics, so because of this, many patient data are included in the exclusion criteria.

Percentage of the effectiveness of usage antibiotics based on the main parameters of body temperature and leukocytes. It is said to be effective if there is an improvement in the patient's clinical condition which is marked by a decrease in the patient's body temperature and leukocyte values. It can be concluded that 73.1% of antibiotics are effective in patients. Apart from body temperature and leukocyte values, there are actually other main parameters to assess the effectiveness of antibiotics in adult pneumonia patients such as sputum and chest X-rays of patients before and after treatment. However, this examination is rarely done twice for the treatment

of patients, so this cannot be used as a specific parameter for evaluating the effectiveness of antibiotics in pneumonia patients. Likewise with sputum examination. Almost all patients underwent a single culture test as described in the section on culture and sensitivity test results. Therefore, this cannot be used as a parameter for the effectiveness of usage antibiotics.

IV. CONCLUSION

From the results of the research that has been done, it can be concluded that the most used antibiotics in handling this case were a combination of Ceftazidime and levofloxacin intravenous with a percentage of 34.85%. As many as 48% of patients were not monitored for the effectiveness of using antibiotics through the patient's leukocyte values after 2-3 days of using antibiotics, monitoring only through body temperature for all patients. The percentage of effectiveness antibiotics based on the patient's body temperature and leukocyte values was 73.1%.

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