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Evaluation of Antibiotic Use in Pneumonia Patients with Gyssens Method

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ABSTRACT

Pneumonia has become a disease that threatens human health and life. A bacterial infection can cause pneumonia, making antibiotics the appropriate choice of therapy. Antibiotics must be used appropriately to avoid the development of resistance. This study qualitatively evaluates the use of antibiotics in pneumonia patients. This cross-sectional observational study utilised the medical records of patients from Dumai City General Hospital retrospectively. Evaluation of the use of antibiotics qualitatively using the Gyssens flow chart. All medical record data of pneumonia patients hospitalised in January–December 2021 became the study population. The inclusion criteria were complete medical records of pneumonia patients aged 18-72 years who received antibiotic prescriptions. Patients who died were excluded from the study. This study involved 57 samples that met the inclusion criteria. Qualitatively, antibiotic use fell into the following categories: Category 0 (82.4%), Category II (10.5%), Category III (1.8%), Category IV C (3.5%), and Category IV A (1.8%).

1. Introduction

Pneumonia is a severe infectious disease that causes morbidity and mortality in the community. Despite treatment interventions, medical tests, and preventive measures, pneumonia remains the leading cause of death from infection worldwide (Cilloniz et al., 2016). In 2013, the incidence of pneumonia was found to be 4.0%, and it increased to 4.5% in 2018. In Riau Province, pneumonia was recorded at 3.0% in 2018 (Ministry of Health, 2018). According to the World Health Organization (WHO), deaths worldwide caused by pneumonia in 935,000 people per year or more than 2,500 people per day (WHO, 2014).

Pneumonia is an infectious disease of the respiratory tract that infects parts of the lung tissue or alveoli (Kemenkes, 2018). Pneumonia is caused by the entry of small particles into the lower respiratory tract. The small particles can be in the form of bacteria, viruses, or mycoplasma that cause an infection that causes damage to the lungs (Trimble et al., 2017). Pneumonia is mainly caused by infection with Streptococcus pneumoniae bacteria (Ganaie et al., 2015). Because the primary cause of pneumonia is bacterial infections, antibiotics are one of the correct therapeutic options to overcome these problems (Bestari, 2017).

Antibiotics are effective compounds that can inhibit the growth of microorganisms. Antibiotics are used to prevent and treat various diseases caused by bacterial infections (Kusumawardani et al., 2019). The high rate of use of antibiotics for infectious diseases can increase the risk of inappropriate use of antibiotics. Various studies have found that about 40–62% of antibiotics are misused, among others, for diseases that do not require antibiotics. Inappropriate use of antibiotics can increase the risk of developing resistance, expanding the number of deaths and the economic burden on a country. Deaths due to resistance have reached 700,000 people (Ministry of Health, 2018). The incidence of antibiotic resistance can be reduced by evaluating its use. Evaluation of the use of antibiotics can be held qualitatively and quantitatively (Permenkes, 2015).

A qualitative evaluation of antibiotics by the Gyssens method aims to assess the accuracy of the use of antibiotics, where antibiotics are classified into Category 0 (with rational use) and Category I to VI (with irrational use) (Sukmawati et al., 2020). Evaluation with this method has several advantages, including the form of a flow chart that can evaluate all aspects of prescribing antibiotics, such as considering alternative prescriptions that are more effective, less toxic, cheaper, and have a narrower spectrum (Anggraini et al., 2020).

2. Methods

This study used a retrospective observational method with a cross-sectional design. The study was conducted from January to March 2022 in the medical record room at the Dumai City Hospital with the ethical approval number 0008/KEPK/III/2022. Qualitative evaluation of antibiotics using the Gyssens method. The data was collected from patient medical record data. The population in this study were all medical records of hospitalized pneumonia patients. Medical records of patients diagnosed with pneumonia and receiving antibiotic prescriptions, complete patient medical records, and medical records of adult patients (18-72 years) are classified into inclusion criteria. Medical records of patients who died were excluded from this study. The sample used was 57 medical records. The data is processed using the Microsoft Excel 2019 application. Qualitative evaluation using the Gyssens method of antibiotic use starts from category VI to category 0. The evaluation results of antibiotics that fall into category 0 are antibiotics that do not belong to category VI-I.

3. Results

Demographics of pneumonia patients

Demographic data of pneumonia patients were divided into two categories, namely by gender and age. Patient age data are grouped according to the age categories established by the Indonesian Ministry of Health in 2009 (Kemenkes RI, 2009) (Table 1).

Qualitative evaluation of antibiotic use

The results of the qualitative evaluation, using the Gyssens method to assess the rationality of antibiotic use in pneumonia patients, are presented in Table 3.

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Table 1. Demographic profile of pneumonia patients

Description	Number of samples (n=57)	Percentage
Gender		
Male	33	58%
Female	24	42%
Age		
17 – 25 years	2	3 %
26 – 35 years	7	12 %
36 – 45 years	4	7 %
46 – 55 years	6	11%
56 – 65 years	29	51%
>65 years	9	16 %

Table 2. Profile of pneumonia patient antibiotic use

Types of antibiotics	Group	Total	Percentage
Single-use			
Levofloxacin	Fluroquinolone	30	53%
Ceftriaxone	β-lactam	15	26%
Azithromycin	Macrolide	4	7%
Cefixime	β-lactam	2	4%
Moxifloxacin	Fluoroquinolone	2	3%
Combination use			
Ceftriaxone + Azithromycin	β-lactam + Macrolide	3	5%
Ceftriaxone + Levofloxacin	β-lactam + Fluroquinolone	1	2%
Total		*57*	*100%*

Table 3. Results of qualitative evaluation of antibiotic use

No	Gyssens category	Gyssens criteria	Quantity of antibiotic	Percentage
1	VI	Complete patient data	-	0
2	V	Antibiotics indicated	-	0
3	IV A	There are more effective alternatives	1	1.8%
4	IV B	There are less toxic alternatives	-	0
5	IV C	There are cheaper alternatives	2	3.5%
6	IV D	There is a narrower alternative spectrum	-	0
7	III A	Giving too long	1	1.8%
8	III B	Giving too short	-	0
9	II A	Incorrect dose	6	10.5%
10	II B	Incorrect Interval	-	0
11	II C	Incorrect Route	-	0
12	I	Incorrect Time	-	0
13	0	Rational Use	47	82.4%
			n = 57	100%

4. Discussion

Demographics of pneumonia patients

The results of the demographic study on pneumonia patients by gender are presented in Table 1. The results showed that male patients had a higher frequency than female patients with a percentage of 58 %. This result follows the 2011 Indonesian health profile, which states that most pneumonia sufferers are male (Kemenkes RI, 2012). This phenomenon could be caused because women have an XX chromosome, while men have an XY chromosome. On the X chromosome, there is a role for MicroRNA, which has an essential function for the immune system. Hence, the presence of an X chromosome has a significant influence on immunity. Males' lack of an X chromosome makes their bodies more susceptible to bacterial infections (Pinheiro, 2011). Another factor that can cause male patients to be more vulnerable to pneumonia is environmental factors. Most men have a higher activity outside the home when compared to women. Moreover, the habit of men who often smoke and are exposed to cigarette smoke increases the risk of pneumonia in men (Elfidasari dkk,2013).

The highest number of pneumonia patients is in the age range of 56 – 65 (late elderly), with 51%. These results align with a study conducted by Farida (2017) at one of the referral hospitals in Surakarta, where the highest number of pneumonia patients are 56-65 years old. Increasing age can cause a loss of elasticity and a decrease in lung function due to the degenerative process (aging) and reduce the body's resistance, making it susceptible to infection (Kemenkes RI, 2013). Moreover, changes in anatomy and physiology due to aging have significant consequences on functional lung reserves, increased airway resistance to infection, and decreased body resistance. Late elderly patients are more easily infected with pneumonia due to impaired gag reflex, weakened immunity, impaired temperature regulation response, and various degrees of cardiopulmonary abnormalities (Rizqi, 2014).

Antibiotic use profile

Levofloxacin was the most widely used antibiotic in inpatient pneumonia patients at the Dumai City Hospital in 2020-2021, with a percentage of 53%. The single use of levofloxacin is one of the therapeutic options in pneumonia patients. Levofloxacin is a fluoroquinolone class of antibiotics that inhibits topoisomerase II (DNA gyrase) and topoisomerase IV, which bacteria need for DNA replication (Raini, 2016). Levofloxacin is a new type of fluoroquinolone with a broader spectrum of activity against gram-positive and harmful bacteria and atypical bacteria that cause pneumonia. Levofloxacin has an excellent pharmacokinetic profile, especially its high bioavailability and prolonged elimination half-life time (Ilmi *et al*., 2020).

Qualitative evaluation of antibiotic use

From 57 existing medical record data, only 47 have passed to category 0 (rational use). One medical record is included in Category IV A (alternative options are more effective), and two medical records are included in Category IV C (there is a cheaper alternative). One medical record is included in Category III A (giving antibiotics too long), and six fall into Category II A (inappropriate dose use).

Category IV A (There are alternative options that are more effective)

The results of this study identified one medical record that did not progress to the next category. There are more effective antibiotic options, meaning that there are other antibiotics whose use is more recommended. Category IV A compares the accordance of the therapy with the existing guidelines. In this study, a combination of levofloxacin and ceftriaxone was found. Based on the Association of Indonesian Pulmonary Doctors guidelines (PDPI) (2014), empirical therapy as the first line in treating pneumonia is levofloxacin or β-lactam class antibiotics plus macrolide groups. The combination of ceftriaxone and azithromycin is one of the first-line empiric therapy options recommended because the combination of the two has the same effectiveness as a single administration of levofloxacin (Izadi *et al*., 2018). Thus, a more effective treatment alternative is to change to a single use of levofloxacin or a combination of ceftriaxone plus one of the macrolide class antibiotics (azithromycin).

Category IV C (There are cheaper alternatives)

Two medical records did not make it through to the next category. There are cheaper antibiotics, meaning there are more affordable generic options. Evaluation of this category is carried out by comparing whether there are alternative cheaper prices between antibiotics used in hospitals and the cost of generic drugs in the e-catalog. In this case, it was found that the patient used the branded antibiotic of moxifloxacin for Indonesian Rupiah (IDK) 225,350. Based on the e-catalog 2020, there is generic moxifloxacin at a lower price, IDK 9. 789, that can be chosen as a patient's antibiotic. Furthermore, a cheaper alternative could be assessed by comparing the price of antibiotics used by patients with the antibiotics in the same class. Moxifloxacin and levofloxacin are classes of fluoroquinolone antibiotics but have a significant price gap. The drug

moxifloxacin used in the Dumai City Hospital has a price of IDK 225,350, while levofloxacin has a much lower cost of IDK 10,250. Treatment for pneumonia could be cheaper by replacing the branded drug with a generic drug or switching from moxifloxacin to levofloxacin. This drug substitution can be done because levofloxacin and moxifloxacin are new-generation fluoroquinolone antibiotics with a bioavailability value of around 85-95% and a half-life of 5-83 hours (Raini, 2016). Hence both antibiotics are recommended for pneumonia treatment.

Category III A (Giving too long)

One medical record that did not make it through to the next category. Using antibiotics for too long means that the patient uses antibiotics for more than the recommended duration of antibiotic therapy. The Ministry of Health recommends that the length of treatment given is 3-14 days. Based on the PDPI guidelines, the duration of antibiotics for empiric treatment for community-acquired pneumonia (CAP) is five days, and 3-21 days for Hospital-acquired pneumonia (HAP), with the recommended duration of antibiotics used in HAP, is seven days (PDPI, 2005) (PDPI, 2014). Still, the duration of administration can be longer or faster if there is no clinical improvement in the patient (IDSA, 2016).

In this study, the use of azithromycin for five days did not follow the Indonesian Ministry of Health guidelines (Kemenkes RI, 2021), which states that azithromycin can be consumed for up to a maximum of 3 days. The use of antibiotics for too long can cause these bacteria to become resistant and no longer able to inhibit bacterial growth (Negara, 2014). Prolonged use of antibiotics also leads to prolonged use of empiric therapy. Therefore, it is necessary to do a bacterial culture to see the bacteria that cause the infection. Thus, after the maximum range of empiric therapy has expired, it can be replaced with definitive treatment. Antibiotics should be adjusted according to the results of the bacterial culture test to choose the sensitive antibiotic that could be against the bacteria (Yanuar, 2016).

Category II A (Incorrect dose)

The results of this study found 6 medical records that did not qualify for the next category. In this inappropriate dose category, researchers analyzed the discrepancy between the dose used by the patient and the range of doses in the guidelines. Category II-A is evaluated by comparing the patient's antibiotic dose according to the medical record and the correct dose of antibiotics in the guidelines (Anggraini *et al*., 2021).In this case, the antibiotic ceftriaxone was found, which was given at a dose of 1 gram/day. This dose is not in accordance with the Indonesia Minister of Health (2021), which states that the antibiotic ceftriaxone is given as much as 2-4 grams/day. Based on the Indonesia Ministry of Health (2011), prescribing antibiotics with too low doses will result in not achieving the minimum adequate level. However, if the dose is too high, it is feared that it could cause poisoning, so the six recipes cannot be continued to the next category. Doses of the drugs can be adjusted if patients have special health conditions such as kidney disorders.

Category 0 (Rational use)

This study found 47 medical records that successfully entered category 0 (rational use). Proper use of antibiotics is giving antibiotics that have passed category VI-I. Rational use of antibiotics, namely the use of antibiotics according to the patient's clinical needs, good quality antibiotics at low prices, narrow-spectrum antibiotics, low toxicity antibiotics, indications for the use of antibiotics are sufficient, sufficient doses, appropriate intervals, appropriate duration of administration, correct route and time of administration. Gyssens, 2005). The results obtained were 47 medical records in category 0 because the use of antibiotics was in accordance with predetermined guidelines so all gyssens categorization flow charts were successful. This result aligns with Hardiana (2021), which categorises the use of antibiotics as category 0 if it can pass categories VI to I.

5. Conclusions

The qualitative evaluation of the use of antibiotics using the Gyssens method was obtained as many as 47 medical records (82.4%) were included in category 0 (the use was correct), and 10.5% were included in category II A (use of the wrong dose). Furthermore, one medical record falls into Category III A (taking too long), and two prescriptions (3.5%) fall into Category IV C (there is a cheaper alternative). Moreover, one prescription (1.8%) falls into category IV A (there are more effective alternatives). Further research is needed to regulate the incorrect use of antibiotics in pneumonia patients so that patients receive appropriate and cost-effective treatment

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