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IMPACT OF ANTIMICROBIAL STEWARDSHIP PROGRAM ON THE USE OF ANTIBIOTICS IN PNEUMONIA PATIENTS AT TEACHING HOSPITAL IN SURAKARTA INDONESIA

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ABSTRACT

Objective: Antibiotic resistance is a serious problem worldwide. One cause of antibacterial resistance is the inappropriate use of antibiotics. The study of antibiotic use in hospitals found that 30–80% were not based on indications. Antimicrobial Stewardship Programs (ASP) was developed to control antimicrobial resistance. This study aims to evaluate the impact of ASP in pneumonia patients qualitatively and quantitatively pre-post ASP applied.

Methods: This research is a non-experimental study. Data were taken from the medical records of pneumonia patients and analyzed qualitatively using the Gyssens method and quantitatively using the Defined Daily Dose (DDD) method. Sampling was conducted through purposive sampling and results were described descriptively.

Results: During the study period, 96 samples were obtained with 48 data pre-ASP and 48 data post-ASP. The results of the qualitative analysis using the Gyssens method show an increase in the prudent use of antibiotics from 31.25% to 62.5% pre-post ASP, respectively. Quantitative evaluation shows a decrease of antibiotic use pre-post ASP from 90.84 DDD/100 patients-days to 61.42 DDD/100 patients-days.

Conclusion: The ASP can improve the quality of antibiotic use in pneumonia patients quantitatively and qualitatively.

Keywords: Antimicrobial stewardship program, Gyssens, Pneumonia, Quantitative, Qualitative.

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INTRODUCTION

Antibiotics resistance has become a serious problem worldwide. The acceleration of the discovery of new antibiotics cannot equal the acceleration of bacterial resistance to antibiotics. The cause of bacterial resistance to antibiotics is inappropriate or irrational use of antibiotics [1,2]. About 40–62% found inappropriate use of antibiotics against diseases that should not require antibiotics, whereas in the study of antibiotic use in hospitals it was found that 30–80% were not based on indications [3]. Poor knowledge and misunderstanding of antibiotic treatment are also factors in the increased occurrence of resistance [4].

Efforts to prevent antibiotic resistance have been launched both internationally and nationally. Antimicrobial stewardship program (ASP) in hospitals aims to optimize antimicrobial prescribing to obtain optimal use of antibiotics, prevents the development of antibiotic resistance, improves individual patient care as well as reduce hospital costs, and slows the spread of antimicrobial resistance [5]. Based on Indonesian Health Ministry regulations concerning ASP in hospitals, this program is an attempt to control antimicrobial resistance through preventing selective pressure by applying prudent use of antibiotics and prevents spreading by implementing infection control prevention (Proton Pump Inhibitors) [6]. To find out the effectiveness of the ASP program, it is necessary to evaluate the use of antibiotics in hospitals. Surveillance study of antibiotic use was carried out quantitatively and qualitatively, pre-post ASP.

Indicator of antibiotic use in hospitals quantitatively is through evaluating the reduction in the quantity of antibiotic use. The Defined Daily Dose (DDD)/Anatomical Therapeutic Chemical (ATC) method has been recommended by the WHO for the evaluation of antibiotic use. The advantage of this method is that there is no influence from price changes, dosage forms, and easy for comparison at the institutional to international level [7], while the qualitative indicator used is the Gyssens algorithm. Gyssens algorithm consists of questions that classified to compile and simplify the evaluation process; therefore, it helps in categorizing antibiotic prescribing [8].

One of the infectious diseases with high occurrence and cause of death in Indonesia is pneumonia. The prevalence of death due to pneumonia in Indonesia is around 1.8–4.5% in 2013 [9]. The incidence of pneumonia in Central Java has reached 26.76%. During the past 10 years, there has been an increase in pneumococcal resistance, especially against penicillin. Increased resistance to penicillin is also predicted to have an impact on increasing resistance to several classes of antibiotics such as cephalosporin, macrolide, tetracycline, and cotrimoxazole [10].

METHODS

Study design

This research is a non-experimental study. This study used medical records taken from the teaching hospital. Collected data were analyzed qualitatively using the Gyssens method and quantitatively using the DDD method. DDD is the average daily dose of antibiotic use in adults.

Tools and materials

The tools used in the study are Gyssens diagram, clinical practice guidelines, Guidelines for Diagnosis and Management of Community and Nosocomial Pneumonia in Indonesia at PDPI (Persatuan Dokter Paru Indonesia), Informasi Obat Nasional Indonesia (2017), and the WHO Collaborating Center for Drug Statistics Methodology. Data were obtained from the medical records of pneumonia patients. Before the study was conducted, research approval was obtained from the health research ethics committee, the medical faculty of Universitas Muhammadiyah Surakarta No.1912/B.1/KEPK-FKUMS/II/2019.

Data collection

The data used in this study were secondary data derived from medical records of pneumonia patients. The population of the study was all inpatients with pneumonia at the teaching hospital in Surakarta. The sampling method used purposive sampling following the inclusion and exclusion criteria. Inclusion criteria are hospitalized patients with a diagnosis of pneumonia and receiving antibiotics, while the exclusion criteria are patients with two or more infectious diseases, death, and forced discharge. The sample was taken 3 months' pre-post ASP. Pre-ASP data were collected from October to November 2016 and post-ASP data were collected on June 2018 to August 2018. In February 2017, antimicrobial stewardship committee was formed and March 2018 ASP started to implement. Collecting included medical record number, sex, age, diagnosis, laboratory data (blood test, serum glutamate-pyruvate transaminase, and serum glutamic-oxaloacetic transaminase, SrCr), and supporting examinations such as chest X-ray, culture examination results (if any), antibiotic name, dose, frequency, route, and duration of drug administration, and length of stay (LOS).

Data analysis

Data were analyzed and presented descriptively. The assessment or evaluation of antibiotic use was done qualitatively with the Gyssens algorithm [3]. The assessment of antibiotic use was obtained from the amounts contained in categories 0 and I-VI expressed as a percentage. Category 0 is the appropriate use of antibiotics, Category I is the use of antibiotics in inappropriate time, IIA is the use of antibiotics in incorrect dosage, IIB is the use of antibiotics in inappropriate interval of administration, IIC is the administration of antibiotics in wrong route, IIIA is long duration of antibiotics, IIIB is short duration of antibiotics, IVA is another more effective antibiotic options, IVB is relatively safe or less toxic antibiotic choices, IVC is another cheaper antibiotics options, IVD is another antibiotic choices with narrower spectrum, V is no indication of antibiotic use, and VI is incomplete medical record and cannot be evaluated. Category 0 is appropriate; Category V is unjustified; Category VI is uncategorized because of insufficient of medical records or medical records is not complete; and Categories I, II, III, and IV indicate inappropriate use of antibiotics.

Quantitative data taken include age, sex, type of antibiotic, the strength of the drug, frequency of use, mode of administration, length of administration, and LOS. The data were then tabulated based on the type of antibiotic, drug strength, dosage form, and ATC classification determined by the WHO Collaborating Center for Drug Statistics Methodology. The number of uses was calculated by multiplying the frequency with the LOS of the patient receiving antibiotics, the total strength of the antibiotics used (strength×number of antibiotic use), total per group, and LOS by summing all patient days. Quantitative analysis was performed using the DDD method. Dose (DDD) unit DDD/100 patient-days:

$$\frac{DDD}{100} patient-days = \frac{\begin{matrix} the\,number\,of\,\,grams\,of \\ AB\,used\,by\,the\,patient \end{matrix}}{DDD\,\,WHO\,standard\,\,in\,gram} x \frac{100}{total\,\,LOS}$$

RESULTS

During the study period, a total of 96 patients' medical records data fulfilled the inclusion and exclusion criteria. Forty-eight data were taken pre-ASP and 48 data post-ASP. As for the quantitative evaluation, one data were excluded because it was a pediatric patient. Pediatric patients cannot be combined with adult patients in terms of DDD calculation. Table 1 shows the characteristics of inpatients pneumonia at a teaching hospital in Surakarta.

Based on Table 1, the prevalence of pneumonia pre-post ASP in men is higher (58.3% and 60.4%, respectively) than women (41.7% and 39.6%, respectively). Based on age, pneumonia patients suffered a lot at the age of 18–64 years. There were more CAP patients than HAP patients. According to Howie *et al*., 2016, CAP pneumonia is the most common occurrence. *Streptococcus pneumoniae* is the most common cause of CAP worldwide [11].

The average LOS of pneumonia patient's pre-post ASP was 9.87 days and 10.04 days, respectively. According to Watkins, 2009, the effective duration of antibiotic therapy for pneumonia is 10–14 days [12]. Day of care is calculated from the time the patient enters to leave the hospital with a discharge status or in recovery according to inclusion criteria. LOS is the length of time each patient was hospitalized obtained by dividing the number of days of stay with the number of patients. Decreased LOS is associated with decreased antibiotic use [13].

Antibiotics are the main therapy for pneumonia caused by bacteria, where the initial antibiotic used is broad-spectrum empirical antibiotics while waiting for the results of the cultures. The use of empirical antibiotics is administered in the case of certain bacteria that have not been found. Definitive therapy for antibiotics is the use of antibiotics based on microbiological examination results. After the presence of ASP, antibiotic therapy based on culture testing (definitive) has increased from 29.75% to 64.56%.

The results of the quantitative evaluation of antibiotic use with the DDD method pre-post ASP areshown in Table 2.

The results of the quality of antibiotic use evaluation by the Gyssens method pre-post ASP are shown in Fig. 1.

Table 1: Characteristics of pneumonia inpatients before and after ASP

Characteristics		Pre-ASP (n=48)	Post-ASP (n=48)
Gender	Male	28 (58.3%)	29 (60.4%)
	Female	20 (41.7%)	19 (39.6%)
Age	<18	1 (2.08%)	5 (10.42%)
	18–49	13 (27.08%)	15 (31.25%)
	50–64	20 (41.67%)	11 (22.92%)
	65–79	12 (25%)	13 (27.08%)
	≥80	2 (4.17%)	4 (8.33%)
Pneumonia	CAP	27 (56.25%)	32 (66.67%)
	HAP	20 (41.67%)	15 (31.25%)
	Atopic	1 (2.08%)	1(2.08%)
Length of stay	Patient number	47	47
	Number of care days	464	472
	LOS average	9.87	10.04
Antibiotic therapy	Definitive	21 (43.75%)	17 (35.417%)
	Empiric	27 (56.25%)	31 (64.583%)

CAP: Community-acquired pneumonia, HAP: Hospital-acquired pneumonia

Table 2: Results of the quantity of antibiotic use in pneumonia patients pre-post ASP

	DDD	Antibiotics	Total DDD	DDD/100 patients	Total DDD/100 patients
Before	J01DD04	Ceftriaxone (1000 mg)	6.50	1.40	90.84
		Ceftriaxone (2000 mg)	146	31.47	
	J01DH02	Meropenem (500 mg)	3.75	0.81	
	J01DD02	Ceftazidime (1000 mg)	9	1.94	
	J01MA12	Levofloxacin (750 mg)	135	29.09	
	J01MA02P	Ciprofloxacin (400 mg)	40	8.62	
	J01FA10	Azithromycin (500 mg)	64.17	13.83	
	JO1GB03	Gentamicin (160 mg)	17.07	3.68	
After	J01DD04	Ceftriaxone (2000 mg)	13	2.75	61.42
	J01DH02	Meropenem (500 mg)	9	1.91	
	J01MA12	Levofloxacin (750 mg)	78	16.53	
	J01FA10	Azithromycin (500 mg)	11.67	2.47	
	J01CR01	Ampicillin Sulbactam (1500 mg)	173.25	36.71	
	J01CA01	Ampicillin (1000 mg)	5	1.06	

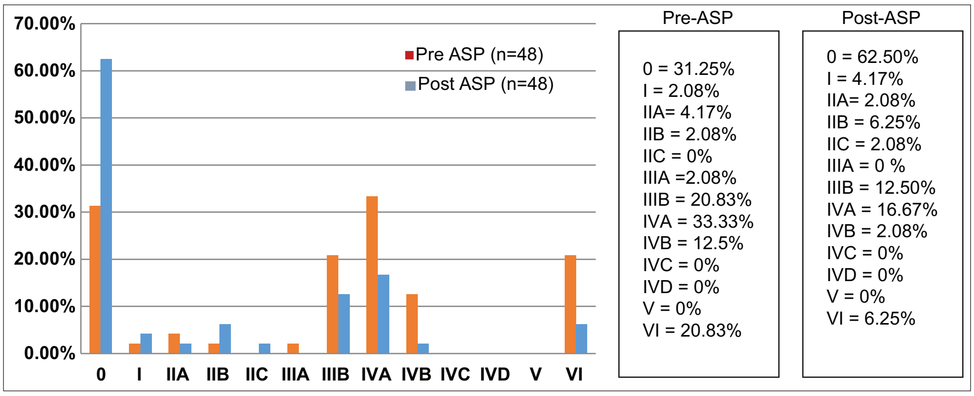

Fig. 1: Classification of Gyssens in pneumonia patients hospitalized in Surakarta teaching hospital before and after ASP

DISCUSSION

Evaluate the use of antibiotics quantitatively

Ceftriaxone is the most widely used antibiotic (31.47 DDD/100 patients-days) before ASP. Based on Moremi's study (2016), 80.6% of *Klebsiella pneumonia* cause pneumonia more resistant to cephalosporins and resistance to third-generation cephalosporins, in which the resistance increased from 26.5% in 2014 to 57.9% in 2015 [14]. Post-ASP, ceftriaxone is not widely used because it has entered the red group under the clinical practice guidelines for the use of antibiotics in Surakarta teaching hospitals. This guideline is classified according to red/reserve, yellow/watch, and green/access. The red group or reserved antibiotic is an antibiotic that should be considered last-resort options and used only in the most severe circumstances when all other alternatives have failed. In this study, there is an improvement in the use of antibiotics that can be seen from the change in the use of antibiotics which used to be more red-type antibiotics, which is ceftriaxone pre-ASP to green-type antibiotics namely Ampicillin Sulbactam post-ASP. Pre-ASP, ceftriaxone (32.87 DDD 100 patients) is the most commonly prescribed antibiotic, while Post-ASP, the most common antibiotic is Ampicillin Sulbactam (36.71 DDD 100 patients). In line with the Newman (2012) study reporting that ceftriaxone use decrease from 72% to 21% after the implementation of clinical practice guidelines and ASP in a tertiary care children's hospital in the city of Kansas, Missouri, USA. Pre-clinical practice guidelines and ASP, ceftriaxone (72%) is the most commonly prescribed antibiotic, followed by ampicillin (13%). Post-clinical practice guidelines, the most common antibiotic is ampicillin (63%) [15].

The number of antibiotic use in the hospital can be calculated using the DDD method with DDD/100 patient-days which illustrates patients who receive the definitive daily dose (DDD). A high DDD value can be influenced by the amount of antibiotic use. The total use of antibiotics in pneumonia patients hospitalized in Surakarta teaching hospital pre-post ASP decreased from 90.84 DDD/100 patient-days to 61.42 DDD/100 patients-days. The greater the total value of DDD/100 patient-days, the higher the level of antibiotic use in 100 days of treatment and vice versa.

Evaluate the use of antibiotics qualitatively

One of the goals of the ASP establishment is to provide optimal antibiotic therapy, the use of the appropriate antibiotics, the correct dosage, which has the least possible resistance and to prevent abuse and excessive use of antibiotics [16]. There is an increase in the prudent use of antibiotics from 31.25% to 62.5% pre-post ASP, respectively. Category 0 (the use of appropriate) pre-post ASP shows 31.25% and 62.5%, respectively. The rational use of antibiotics will have an impact on decreasing antibiotic resistance, increasing the efficacy of antibiotic use, and support patient safety programs. Furthermore, it can also reduce the morbidity and mortality caused by antibiotic resistance [16].

Based on the clinical practice guidelines, inpatients without modification factors, the recommended choice of antibiotic groups is betalactam+antibetalactamase iv or the 2nd or 3rd cephalosporin iv, or fluoroquinolone respiration iv. Inpatients with modification factors, the recommended choices of antibiotic groups are the 2nd or 3rd cephalosporin iv, or fluoroquinolone respiration iv. The atypical bacterial suspect infection can use new macrolides.

In Category IV A (another more effective antibiotic alternatives), it shows a decrease of 33.33% pre-ASP to 14.58% post-ASP. Pre-ASP, several antibiotics were prescribed in combination between cephalosporins (ceftriaxone) and fluoroquinolones (levofloxacin) or cephalosporins with macrolides such as azithromycin so that they are included as IV A. There is also a case; according to the results of the culture examination the patient was resistant to ceftriaxone, but the doctor prescribed ceftriaxone, whereas there are other more effective antibiotic options such as ampicillin or ceftazidime according to the results of a more sensitive culture.

Category VI also shows a decrease in pre-post ASP, from 20.83% to 6.25%. The data included in Category VI are incomplete data such as medical records without a diagnosis, or there is a missing medical record page so it cannot be evaluated. Overall, there is an improvement in the prudent use of antibiotics consist of improving the appropriate use of antibiotics, reducing the incorrect dosage of antibiotics, reducing the incorrect duration of antibiotics, and improving a better antibiotics selection due to higher efficacy and lower toxicity.

Antibiotics stewardship improve antibiotic's prudent use of qualitatively and quantitatively. Antibiotics stewardship commit to always use antibiotics only when they are necessary to treat infection and prevent infection as a prophylactic with the right antibiotics, the right dose, duration, and to administer in the right way. Antibiotics stewardship ensures that every patient gets the maximum benefit from the antibiotic use and avoids unnecessary harm from allergic reactions and side effects, and helps preserve the life-saving potential of antibiotics for the future. Antibiotics stewardship helps improve patients care and shorten hospital stays, thus benefiting patients as well as the hospital. A University of Maryland study showed one antibiotic stewardship program saved a total of USD 17 million over 8 years [17].

Education of the prescriber is important for any successful ASP. The teaching of guidelines and clinical pathways could help to improve antimicrobial prescribing behavior. Adherence to strict prescribing guidelines and a policy of monitoring rational antibiotic use are part of any successful ASP as well [18,19].

Strength and limitation study

This study was conducted on one infectious disease, so it could not find the overall quality profile of antibiotic use in Surakarta teaching hospital. However, focusing only on one infection will find a deeper understanding of the use of antibiotics qualitatively and quantitatively in pneumonia. This research was conducted retrospectively so that the existing medical record data could not be confirmed to the physician who prescribed antibiotics, the researcher could not find out the reason for the doctor regarding antibiotic selection considerations.

CONCLUSION

Based on the conducted research, there are differences in the quality of antibiotic use among pre-and post-ASP in pneumonia patients. Judging from the results of the qualitative analysis using the Gyssens method shows an increase in the antibiotics prudent use from 31.25% pre-ASP to 62.5% post-ASP. In terms of quantity, there is a decrease in total DDD/100 patient-days pre-ASP (90.84 DDD/100 patients-days) and post-ASP (61.42 DDD/100 patients-days). Thus, it shows a decrease in the level of antibiotic use in Surakarta teaching hospitals. In this study, it is also shown from the replacement of a red/reserve group of antibiotics (Ceftriaxone) into a green/access group (Ampicillin Sulbactam).

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CONFLICTS OF INTEREST

All authors have none to declare.

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