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Research Article

ANTIBIOTIC CONSUMPTION AT A PEDIATRIC WARD AT A PUBLIC HOSPITAL IN INDONESIA

FAUNA HERAWATI[1,2]*, MUHAMAD SATRIA MANDALA PUA UPA[1], RIKA YULIA[1], RETNOSARI ANDRAJATI[2]

[1]Department of Clinical and Community Pharmacy, Faculty of Pharmacy, Universitas Surabaya, Jalan Raya Kalirungkut, Surabaya 60293, Indonesia. [2]Department of Pharmacology and Clinical Pharmacy, Faculty of Pharmacy, Universitas Indonesia, Depok, Indonesia. Email: fauna@staff.ubaya.ac.id

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ABSTRACT

Objective: The aims of the study are to describe how antibiotics were used in a pediatric ward and to observe how they were prescribed for infectious diarrheas of bacterial origin indication. Diarrhea or acute gastroenteritis is one of the most common infection diagnoses observed among the hospitalized children. Rehydration therapy is the key treatment for children with diarrhea. With the zinc supplement, the duration of the hospital stay can be reduced. Thus, the decision whether the local or regional health authorities need to provide an antibiotic treatment depends on the etiology of the disease, the patient's nutritional history and immunological status, and eventually, the severity of the disease. Good anamneses and diagnoses are essential to decide whether antibiotic treatment is required.

Methods: The observation in this study consists of two phases. The first-phase observation was taken from the diagnosis and the number of antibiotics used in 2016 retrospectively calculated from each of the patients' medical records. Meanwhile, the second phase descriptive observation was prospectively drawn from the stool culture and the number of antibiotics prescribed to 21 inpatient diarrhea children between May 2017 and December 2017. The amount of antibiotic consumption was administered based on defined daily dose (DDD) and days of therapy (DOT).

Results: In 2016, 56% (828/1476) of the patients received antibiotic prescriptions. On average, the DDD per 100 bed-days was 45.57. In the prospective study, six of 21 patients with diarrhea were prescribed antibiotics intravenously. The DOT was 3.5 days and the DDD for these patients was 12.10/100 bed-days.

Conclusion: There was a high consumption rate of antibiotics which was not indicated in each patient's etiology of diarrhea in the hospital during the period. Thus, the recommendation is to encourage health authorities to judiciously prescribe antibiotics according to the guidelines.

Keywords: Antibiotic prescription, Days of therapy, Defined daily dose, Diarrhea, Pediatrics.

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INTRODUCTION

Children are admitted to hospitals mostly due to diagnoses of either infectious or non-infectious diseases. This study, however, focuses on the diagnoses of infectious diseases among which are urinary tract infection, acute meningitis, community-acquired pneumonia, fever without a localized source, and diarrhea (acute gastroenteritis). These infectious diseases are also the most common indications for antibiotics in hospitalized children [1-3]. Diarrhea or acute gastroenteritis is one of the most common infectious diagnoses seen in hospitalized children. Typically, antibiotics are not for routine use to treat gastroenteritis, except diarrhea triggered by *Shigella*, *Vibrio cholera*, or parasites [4]. The percentage of the patients who receive antibiotics should correlate with the percentage of the diagnoses of the infection. The higher number of antibiotic use could be a predictor of a higher infection prevalence. Unfortunately, there is excessive antibiotic use without any indications of infection [5]. Inappropriate use of antibiotics will increase the incidence of bacterial resistance to antibiotics [6-8]. One of the antimicrobial stewardship programs the goal of the Danish Ministry of Health is to reduce antibiotic consumption by 10% in 4 years' time with the defined daily dose (DDD)/100 bed-days for hospitalized patients [9].

Acute gastroenteritis in the community is usually self-limiting. However, at times, its diagnoses may be complicated and the prescribers may be misled by the diagnoses. Shigellosis infection, for instance, may lead to a life-threatening complication if not correctly diagnosed and quickly treated. Hydration therapy is the key treatment here. Then, antibiotic treatment is also indicated for specific bacterial infection where the identification of an etiological agent by bacterial stool culture is rare [10,11]. Careless use of antibiotics in hospitals can actually trigger another type of diarrhea (antibiotic-associated diarrhea). This type of diarrhea is caused by bacterial species, one of which is *Clostridium difficile*. This situation requires another treatment using different antibiotics since some of the bacterial species are resistant to many of the easily available antibiotics.

The aim of the first phase of the study was to describe the number of antibiotics used in a pediatric ward in 2016. Meanwhile, the aim of the second phase was to closely observe antibiotics used for diarrhea treatment in children between May 2017 and December 2017 preceded with stool tests to confirm the etiology.

METHODS

The study was conducted at Bangil Regional Public Hospital, which is a secondary care hospital with 272 beds. The research method used in the study was a descriptive, observational cross-sectional study. The data were collected based on the two types of medical records. The first type of data was retrospective medical records of the patients in the Pediatric Ward of Bangil Regional Public Hospital in 2016. The second type of data was drawn from the prospective medical records of the patients including microbiology examination and bacteria sensitivity test of the patients admitted to the hospital between May 2017 and December 2017. The study was granted ethical clearance by the Health Research Ethics Committee of Politeknik Kesehatan Kemenkes Surabaya, Ministry of Health No. 025/S/KEPK/V/2017. The antibiotic use was measured as DDD, days of therapy (DOT), and prescribed

daily dose (PDD). The function of the DDD is to estimate the use of antibiotics in hospitals drawn from the total number of grams of each antibiotic dispensed during a period of interest divided by the World Health Organization (WHO) – DDD. DOT is the total number of days during which any unit of a specific antimicrobial agent is administered to a particular patient (numerator) divided by the number of patients (denominator) [12-14]. PDD is the average dose administered based on the total sum of prescriptions. The diagnosis data from medical records and antibiotic use were analyzed descriptively. The equation used to calculate DDD per 100 bed-days was modified from DDD/1000 population/day [15,16] as stated in the following equation:

$$\text{DDD}/1000\ \text{population}/\text{day} = \frac{\text{Amount used in 1 year (mg)} \times 1000}{\text{DDD (mg)} \times \text{population}/365\text{(days)}} \quad (1)$$

Several adjustments were made in terms of the DDD of a specific period and hospital bed-days of care availability derived from the inpatient's days of care to the equation. The DDD was drawn from the assumed average maintenance of dose per day on a drug used for the WHO-based DDD main indication in adults.

The study focused on the analysis of Pearson correlation of the number of patients and the number of antibiotics used. The absolute values of r at 0–0.19 represented very weak, 0.2–0.39 weak, 0.40–0.59 moderate, 0.6–0.79 strong, and 0.8–1 very strong associations or correlations. The significant difference between the average duration of the stay of patients with antibiotics and that of patients without antibiotics was determined by independent t-tests.

RESULTS

More than 65% of the children were admitted to the hospital due to infectious disorders and diarrhea was the second most common disorder. Not all children with infectious disorders were treated with antibiotics. Only 56% of the children admitted to the hospital in 2016 (Table 1) and 29% of the children with diarrhea admitted to the hospital between May and December 2017 were treated with antibiotics (Table 2).

The average DDD per 100 bed-days in 2016 was 45.57 (the result of the difference between 23.18 and 69.95) as shown in Table 3. The Pearson correlation between the number of patients and the DDD per 100 bed-days was weak (0.4). The average DDD for children with diarrhea between May 2017 and December 2017 was 12.1 as shown in Table 4. The DOT for ampicillin of 14 days/4 patients was 3.5 and the DOT for metronidazole of 6 days/2 patients was 3. The PDD for ampicillin of 11.5 g/14 days was 0.8 g and the PDD for metronidazole of 1175 g/6 days was 0.2 g.

The etiology of 48% of the hospitalized children with diarrhea was *Escherichia coli* (Table 5). There were zero *E. coli* isolates sensitive to ampicillin. The average duration of stay of the hospitalized children with diarrhea treated with antibiotics was similar to that of the hospitalized children with diarrhea treated without antibiotics ($p>0.05$).

DISCUSSION

In developing countries, infectious disorders in respiratory and digestive system, predominantly pneumonia, and gastroenteritis ranging between 45% and 80% account for the most frequent reasons for children's hospitalization [17-21]. Antibiotics are indicated particularly for below 5-year-old children with pneumonia, bronchiolitis, and urinary tract infection. Consequently, there is a high DOT of antibiotics prescribed for hospitalized children [22]. The lower DDD per 100 bed-days is attributed to the lower DDD in comparison to the number of patients with diarrhea diagnosis. The DDD is the assumed average maintenance dose per day for a drug mainly prescribed for adults. Apart from its effectiveness, antibiotics also carry a microbial resistance risk. Unnecessary antibiotic prescription is the most common sign of inappropriate antibiotic use [23-27].

Table 1: The number of patients in pediatric ward in 2016

Month	Number of patients		Total (%)
	With antibiotic (%)	Without antibiotic (%)	
January	74 (8.94)	72 (11.11)	146 (9.89)
February	58 (7.01)	57 (8.80)	115 (7.79)
March	70 (8.45)	70 (10.80)	140 (9.49)
April	70 (8.45)	48 (7.41)	118 (7.99)
May	95 (11.48)	90 (13.89)	185 (12.53)
June	79 (9.54)	39 (6.02)	118 (7.99)
July	38 (4.59)	53 (8.18)	91 (6.17)
August	79 (9.54)	66 (10.18)	145 (9.82)
September	51 (6.16)	39 (6.02)	90 (6.10)
October	80 (9.66)	40 (6.17)	120 (8.13)
November	79 (9.54)	34 (5.25)	113 (7.66)
December	55 (6.64)	40 (6.17)	95 (6.44)
Total	828 (56.10)	648 (43.90)	1476 (100)

Table 2: The number of patients in pediatric ward between May 2017 and December 2017

Age (years)	Number of patients		Total (%)
	With antibiotic (%)	Without antibiotic (%)	
<1	4 (19.05)	7 (33.33)	11 (52.38)
1–<5	2 (9.52)	7 (33.33)	9 (42.86)
5–14	-	1 (4.76)	1 (4.76)
Total	6 (28.57)	15 (71.43)	21 (100)

Table 3: Defined daily dose per 100 bed-days in a pediatric ward in 2016

Antibiotic name	ATC code	DDD standard	DDD per 100 bed-days
Oral route of drug administration			
Chloramphenicol	J01BA01	3	1.24
Thiamphenicol	J01BA02	1.5	3.30
Amoxicillin	J01CA04	1	6.79
Amoxicillin/clavulanic acid	J01CR02	1	0.17
Cefadroxil	J01DB05	2	0.68
Cefixime	J01DD08	0.4	2.09
Azithromycin	J01FA10	0.3	2.73
Erythromycin	J01FA01	1	0.72
Spiramycin	J01FA02	3	0.01
Rifampicin	J04AB02	0.6	3.83
Ethambutol	J04AK02	1.2	0.59
Pyrazinamide	J04AK01	1.5	2.65
Total			24.87
Parenteral route of drug administration			
Chloramphenicol	J01BA01	3	2.18
Ampicillin	J01CA01	2	9.09
Amoxicillin	J01CA04	1	1.65
Ampicillin/sulbactam	J01CR01	6	2.04
Cefazolin	J01DB04	3	0.02
Cefuroxime	J01DC02	3	0.02
Cefotaxime	J01DD01	4	0.24
Ceftazidime	J01DD02	4	0.39
Ceftriaxone	J01DD04	2	3.53
Streptomycin	J01GA01	1	0.08
Gentamicin	J01GB03	0.24	0.51
Amikacin	J01GB06	1	0.04
Metronidazole	J01XD01	1.5	0.96
Total			20.77
Total of oral and parenteral routes of drug administration			45.57

DDD: Defined daily dose, ATC: Anatomical therapeutic chemical

Table 4: The prescribed antibiotics for children with diarrhea between May 2017 and December 2017

Patient codes	Antibiotic name	ATC codes	Strength (gram)	Number of units	Duration of therapy (days); prescription (mg)	Duration of stay (days)	DDD standard	DDD patient
A	Ampicillin IV	J01CA01	0.2	23	5; 4×200	6	2	2.3
B	Ampicillin IV	J01CA01	0.2	12	3; 4×200	3	2	1.2
C	Metronidazole IV	J01XD01	0.08	3	1; 1×80	1	1.5	0.16
D	Ampicillin IV	J01CA01	0.3	9	3; 3×300	3	2	1.35
E	Ampicillin IV	J01CA01	0.2	16	3; 4×200	3	2	1.6
F	Metronidazole IV	J01XD01	0.125	15	5; 3×125	5	1.5	1.5
G	–	–	–	–		3	–	–
H	–	–	–	–		2	–	–
I	–	–	–	–		4	–	–
J	–	–	–	–		3	–	–
K	–	–	–	–		4	–	–
L	–	–	–	–		3	–	–
M	–	–	–	–		2	–	–
N	–	–	–	–		4	–	–
O	–	–	–	–		3	–	–
P	–	–	–	–		3	–	–
Q	–	–	–	–		4	–	–
R	–	–	–	–		1	–	–
S	–	–	–	–		3	–	–
T	–	–	–	–		3	–	–
U	–	–	–	–		4	–	–
Total				78	20	67	11	8.11

Daily dose per 100 bed-days: 8.11/67*100=12.10. ATC: Anatomical therapeutic chemical

Table 5: The isolation of bacteria from each patient's stool test between May 2017 and December 2017

Bacteria	Number of isolates in		Total (%)
	Patient with antibiotic (%)	Patient without antibiotic (%)	
Escherichia coli	3 (14.29)	7 (33.33)	10 (47.62)
Serratia odorifera	1 (4.76)	7 (33.33)	8 (38.09)
Burkholderia cepacia	1 (4.76)	1 (4.76)	2 (9.52)
Pseudomonas aeruginosa	1 (4.76)	-	1 (4.77)
Total	6 (28.57)	15 (71.43)	21 (100)

Antibiotics should not be carelessly prescribed for acute gastroenteritis since the misuse of antibiotics contributes to antibiotic resistance, one of which is *Clostridium difficile* infection. According to the Clinical Practice Guidelines of Health Service Facilities (FASYANKES) of the Ministry of Health No. 514/2015, acute gastroenteritis can be treated in the following ways [28]. First, *Shigella* gastroenteritis is treated with ampicillin and trimethoprim-sulfamethoxazole. Then, metronidazole is prescribed if there have been trophozoites of *Entamoeba histolytica* within red blood cells, or if there have been trophozoites or cysts of *Giardia* seen in the feces. Metronidazole can also be considered for persistent diarrhea with blood in the stool when two different antibiotics usually locally effective for *Shigella* have been prescribed without any clinical improvements. Finally, parenteral antibiotic therapy is recommended for bacteremia (systemic infections) triggered by bacterial enteric pathogens [29-31]. Doctors generally refrain from prescribing ciprofloxacin for children though it is effective in the treatment of pathogenic *E. coli* [32,33]. In the study, the etiology of acute diarrhea is *E. coli* (10 specimens; 47.62%), *Serratia odorifera* (eight specimens; 38.09%), *Burkholderia cepacia* (two specimens; 9.52%), and *Pseudomonas aeruginosa* (one specimen; 4.77%). Ampicillin and metronidazole were not recommended for these 21 patients. The sensitivity of *E. coli* to ampicillin is low [34-36]. Interestingly, the average length of the stay of inpatients with antibiotic treatment is similar to that of inpatients without antibiotic treatment.

CONCLUSION AND RECOMMENDATION

Surveillance is mandatory since it is one of the assessment criteria of hospital accreditation and this surveillance extends to the proper use of the antibiotics in the hospital [37,38]. The improper use of antibiotics was, in fact, still detected in the daily routines of the hospital, such as in monitoring drug therapy or medication therapy management using Gyssen flowchart [24]. The average DDD per 100 bed-days was significantly lower than the percentage of the infectious disorder. This study shows that the antibiotic use in children with diarrhea is not appropriate. Meanwhile, ampicillin and metronidazole were not prescribed for the patients due to several reasons. First, infectious diarrhea by *E. coli* is usually self-limiting and has low ampicillin effectiveness against *E. coli*. Second, there were no indications of *Trichomonas vaginalis*, amebiasis, or giardiasis from the stool culture. Further studies of other infectious disorders are recommended to evaluate whether discrepancies between the number of antibiotics prescribed and the number of antibiotics suggested by the therapeutic guidelines exist.

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AUTHORSHIP AND CONTRIBUTORSHIP STATEMENT

FH and MSM collected and calculated the data. FH, MSM, and RY analyzed and interpreted the data. FH, RY, and RA wrote the manuscript. All authors read and approved the final manuscript.

CONFLICTS OF INTEREST STATEMENT

The authors declare that there are no conflicts of interest.

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