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IAI CONFERENCE

RESEARCH ARTICLE

Antibiotic use on paediatric inpatients in a public hospital in Bangil, Indonesia

Ika Norcahyanti[1,2], Malikatur Rosyidah[1], Abdul Kadir Jaelani[3], Antonius N.W. Pratama[1,2]

[1]Department of Clinical and Community Pharmacy, Faculty of Pharmacy, Universitas Jember, East Java, Indonesia

[2]Drug Utilisation Research Group, Faculty of Pharmacy, Universitas Jember, East Java, Indonesia

[3]Bangil Public Hospital, Pasuruan Regency, East Java, Indonesia

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Correspondence
Ika Norcahyanti
Department of Clinical and Community Pharmacy
Faculty of Pharmacy
Universitas Jember
East Java
Indonesia
norcahyanti.farmasi@unej.ac.id

Abstract

Introduction: The importance of antibiotic use in a clinical setting was evaluated in order to support the global action plan to decelerate the spreading speed of antimicrobial resistance. **Aim:** This study aimed to evaluate antibiotic use among pediatric inpatients in Bangil public hospital, East Java, Indonesia. **Methods:** This study used a cross-sectional design. The data were obtained from medical records of pediatric patients admitted to a pediatric ward in 2017. Data were analysed using the anatomical therapeutic chemical classification system (ATC)/defined daily dose (DDD) method in conjunction with data sources from a locally developed bacterial map. **Results:** The results showed the paediatric patients were dominantly male (n=218; 54.2%) and mostly diagnosed with diarrhoea (n=87; 15.3%). Ampicillin-sulbactam was the most commonly used antibiotic (16.3%). The total DDD value was 66.1 DDD/100 bed-days, and ceftriaxone demonstrated the highest DDD value (10.3 DDD/100 bed-days). **Conclusion:** In conclusion, the use of antibiotics in the pediatric ward in Bangil public hospital was comparable to other studies conducted in Indonesia.

Introduction

Infectious diseases are a considerable contributor to morbidity and mortality in developing countries such as Indonesia. Some infectious diseases that are caused by bacteria remain public health concerns; these include pneumonia, urinary tract infections, diarrhoea, and tuberculosis. Antibiotics are used to treat bacterial infections. Antibiotic use in developing countries increased by 36% from 2000 to 2010 (Van Boeckel TP *et al.*, 2014). However, evidence shows that this increase has not been followed by appropriate antibiotic use. The inappropriate use of antibiotics can cause global health threats, especially with the emergence of antibiotic resistance. The notion of inappropriate use of antibiotics may include, but not be limited to, non-optimal prescribing, free use of antibiotics without a prescription, failure to take antibiotics, overuse of antibiotics, and excessive misuse of antibiotics (Ministry of Health of the Republic of Indonesia, 2011).

Among other subpopulations, the use of antibiotics in children is important. Two factors can explain the need for antibiotics in this particular population. Firstly, the immune system in children is not yet fully functioning. Secondly, children tend to be more exposed to pathogens due to their daily patterns of behaviour. However, many antibiotics that have been approved for adult use maybe not suitable for children due to the differences between these two populations, so the extrapolation of clinical data requires careful attention (Shea, Florini & Barlam, 2002).

Some efforts have been initiated to control the inappropriate use of antibiotics. The global campaign of Antibiotic Awareness Week initiated by the World Health Organization (WHO) can act as an example of

this (World Health Organization, 2018a). It is now mandatory that all Indonesian hospitals have an Antimicrobial Resistance Control Committee (PPRA) in clinical settings. The presence and activities of this committee are important factors for the hospital accreditation programme. Evaluating the implementation of antibiotics in the hospital can be carried out to control their usage. This evaluation can be done using a method developed by the WHO's collaborating centre in Norway, which employs the anatomical therapeutic chemical classification system combined with the defined daily dose (commonly known as the ATC/DDD method) (World Health Organization, 2018b). The objective of this study was to evaluate the use of antibiotics in the children population in a Bangil Public Hospital using the ATC/DDD method.

Materials and method

Study design and setting

This study was conducted using a cross-sectional research design in Bangil public hospital, Pasuruan Regency, East Java, Indonesia. Data collection and analysis was conducted from December 2018 to February 2019.

Sample and sampling method

All paediatric inpatients admitted to the Asoka Ward of the hospital from the 1st of January to the 31st of December in 2017 became the target sample. The inclusion criteria used to define the population for this study was hospitalised pediatric patients aged from one month to 14 years with complete patient digital medical record data. The medical record must have contained at least one antibiotic with its ATC code, the patient's identity (name, age, gender, financing status, admission date, discharge date, and diagnosis), and the profile of antibiotics (chemical sub-group, chemical name, dosage regimen, route of administration, and frequency of use). Patients with incomplete data, discharge from the hospital by family's request, and death were excluded from the analysis. This study applied a total sampling method to the patients that met the inclusion criteria.

Data collection and analysis

This study collected primary and secondary data. The primary data was gathered from an interview with a pharmacist involved in the hospital's antimicrobial resistance control programme (PPRA). The secondary data was retrieved from the hospital's Department of Electronic Data Management (PDE), Department of Medical Records, and Department of Infection Prevention and Control (PPI). The secondary data comprised the patient's digital medical record and bacterial sensitivity and resistance pattern. The antibiotics from the patient's data were further calculated based on the ATC/DDD method. The unit for the final calculation that represented the antibiotic use was in DDD/100 bed-days.

Ethical consideration

Ethical approval to conduct the study was granted by the Ethics Committee of the State Polytechnic of Jember number 2536/PL17/LL/2019. Permission to conduct the study was granted by Bangil Public Hospital (Number 445.1/3222/424.202/2018).

Results

This research collected data from 402 pediatric patients that met the inclusion criteria (Table I). Based on the characteristics of the admitted patients, there were more males than females, accounting for 54.2% (n=218) and 45.8% (n=184), respectively. Furthermore, the age group with the largest number of individuals was children aged from one month to two years, consisting of 52.2% (n=210). The top three diagnoses in this study were diarrhoea and gastroenteritis of presumed infectious origin (15.3%; n=87); bronchopneumonia, unspecified (13.5%; n=77); and tuberculosis of lung, without mention of bacteriological or histological confirmation (10%; n=57). Based on the financing status, the most widely used financing method for pediatric patients was the *Badan Penyelenggara Jaminan Sosial* (BPJS) health insurance, accounting for 40.3% (n=162).

A total of 3,730 antibiotic prescriptions were prescribed for 402 pediatric patients and covered nine chemical subgroups and 24 types of antibiotics (Table II). The most widely used antibiotic were penicillins, predominated by an ampicillin-sulbactam combination (16.3%; n=608). The second most used group of antibiotics were cephalosporins, especially cefixime (11.3%; n=422). Meanwhile, across all antibiotics used for pediatric patients, amoxicillin-clavulanic acid (0.1%; n=4) and spiramycin (0.1%; n=4) were rarely prescribed. The evaluation of antibiotic use using the ATC/DDD method in this research showed that the total DDD value of 24 antibiotics was 66.1 DDD/100 bed-days, ranging from 0.04 DDD/100 bed-days (spiramycin, J01FA02) to 10.3 DDD/100 bed-days (ceftriaxone, J01DD04), and the total length of stay (LOS) value was 1,829 days (Table III).

Table I: General characteristics of admitted patients

Characteristics	n	%
Gender		
Male	218	54.2
Female	184	45.8
Age category		
1 month-2 years	210	52.2
2-6 years	113	28.1
6-12 years	65	16.2
12-14 years	14	3.5
Diagnosis (ICD-10)		
Diarrhoea and gastroenteritis of presumed infectious origin	87	15.3
Bronchopneumonia, unspecified	77	13.5
Tuberculosis of lung, without mention of bacteriological or histological confirmation	57	10
Febrile convulsions	48	8.8
Fever, unspecified	33	5.8
Typhoid fever	27	4.7
Septicemia, unspecified	26	4.6
Urinary tract infection, site not specified	20	3.5
Acute upper respiratory infection, unspecified	13	2.3
Nausea and vomiting	11	1.9
Iron deficiency anaemia, unspecified	11	1.9
Septicemia, unspecified	9	1.6
Other diagnoses	149	26.1
Financing status		
BPJS health insurance	162	40.3
The Poor Statement Letter (SPM)	157	39.1
Non-insurance/pocket money	82	20.4
Other insurance	1	0.2

BPJS: *Badan Penyelenggara Jaminan Sosial* or Indonesian Universal Health Coverage, ICD-10: the 10th version of International Classification of Diseases

Table II: Profile of antibiotics used for paediatric inpatients

Chemical sub-group	Chemical name	n	%
Penicillins	Ampicillin-sulbactam	608	16.3
	Ampicillin	479	12.8
	Amoxicillin	204	5.5
	Amoxicillin-Clavulanic acid	4	0.1
Cephalosporins	Cefixime	422	11.3
	Ceftriaxone	378	10.1
	Cefotaxime	127	3.4
	Ceftazidime	9	0.2
	Cefadroxil	5	0.1
Antituberculosis agents	Isoniazide	276	7.4
	Pyrazinamide	224	6.0
	Rifampicin	186	5.0
	Ethambutol	7	0.2
Amphenicols	Chlorampenicol	371	10.0
	Thiamfenicol	88	2.4
Aminoglycosides	Gentamicin	96	2.6
	Streptomycin	60	1.6
	Amikacin	8	0.2
Macrolides	Erytromycin	95	2.5
	Azithromycin	11	0.3
	Spiramycin	4	0.1
Nitromidazole	Metronidazole	46	1.2
Penems	Meropenem	17	0.5
Lincosamide	Clindamycin	5	0.1
Total		**3,730**	**100**

Table III: Profile antibiotic use with ATC/DDD method

ATC code	Name	Standard DDD	Total DDD	DDD/100 bed-days
J01DD04	Ceftriaxone	2	189	10.3
J04AC01	Isoniazide	0.3	158	8.6
J01CR01	Ampicillin-Sulbactam	6	152	8.3
J04AB02	Rifampicin	0.6	110.3	6.0
J01DD08	Cefixime	0.4	120.5	5.6
J01BA01	Chlorampenicol	3	80.4	4.4
J01CA01	Ampicillin	6	79.8	4.4
J04AK01	Pyrazinamide	1.5	74.7	4,1
J01CA04	Amoxicillin	1.5 (PO) 3 (IV)	71.3	3.9
J01FA10	Azithromycin	0.3 (PO) 0.5 (IV)	43	2.3
J01FA01	Erythromycin	1	36.3	1.9
J01DD01	Cefotaxime	4	31.8	1.7
J01BA02	Thiamfenicol	1.5	29.3	1.6
J01GB03	Gentamicin	0.24	16	0.9
J01XD01	Metronidazole	1.5	15.3	0.8
J01GA01	Streptomycin	1	6	0.3
J01DH01	Meropenem	3	5.7	0.3
J04AK02	Ethambutol	1.2	2.9	0.2
J01DD02	Ceftazidime	4	74.7	0.1
J01GB06	Amikacin	1	2	0.1
J01CR02	Amoxicillin + Clavulanic acid	1.5	1.7	0.1
J01DB05	Cefadroxil	2	1.3	0.1
J01FF01	Clindamycin	1.2	1.3	0.1
J01FA02	Spiramycin	3	0.7	0.04
Total				**66.14**

Discussion

In general, the immune responses of T helper 1 (Th1) in the male paediatric population were generally thought to be weaker than those within the female pediatric population, thus making the males more susceptible to some pathogens (Muenchhoff & Goulder, 2014). In addition, behavioural differences between males and females also act as risk factors for infectious diseases. Other studies have also suggested that males in all age groups are more susceptible to airway infections than females. In males, it is likely that airway infections are severe and cause death, especially with pneumonia (Ostapchuk, Roberts & Haddy, 2004). Several reasons can explain why children under the age of six have a higher incidence of infection. Their immune systems are limited and do not yet produce antibodies in a fully functioning manner. This causes children to become prone to bacterial infections, thus requiring antibiotic treatment. When a child begins to grow up, their ability to fight infection will continue to improve, and they become less susceptible to bacterial infections. In

addition to their body's weaker immune system, children under the age of six tend to play in public areas, which increases their risk of being exposed to pathogens, and as a result, this will put them at risk of infectious diseases (Shea, Florini & Barlam, 2002; Simon, Hollander & McMichael, 2015).

High transmission rates of diarrhea disease in children can commonly be caused by poor environmental sanitation, contamination of food or beverages, an impaired immune system, inadequate intestinal flora, and a lack of gastric acidity.

The second most common diagnosis of the disease is unspecified bronchopneumonia, which is pneumonia that attacks the lower respiratory tract. Bronchopneumonia attacks the bronchi within the pulmonary alveolus and causes local inflammation in the pulmonary parenchyma. In Indonesia, basic health research carried out a regular nationwide survey in 2013 that reported that the highest pneumonia cases of pneumonia occurred in children aged one to four years (Ministry of Health of the Republic of Indonesia, 2013a). Pneumonia in children can be associated with several factors, including a disrupted immune system that puts them at risk of exposure to pneumonia-causing bacteria, an imbalanced nutritional intake, and exclusively breastfed as infants.

Tuberculosis (TB) of the lung, without mention of bacteriological or histological confirmation, was the third-largest diagnosis found in this study. Indonesia ranks third in the world for the highest number of TB cases, after China and India. Of the 264 million people in Indonesia (in 2017), the total TB incidence was 842,000, and the total HIV-TB co-infection incidence was 36,000. Because TB is contagious, children are at risk of infection when they live in the same household with a person with active TB, such as parents, or if they study in a school where a person with active TB has phlegm that comes out while speaking, sneezing, and coughing.

Based on the financing status, BPJS is a universal health coverage program run by the Indonesian government with an increasing number of users each year, reaching 171.9 million in 2016. This is due to the cooperation agreement between the hospital and BPJS in the National Health Insurance (JKN) program stated in Presidential Regulation Number 12 of 2013 and Regulation of the Minister of Health Number 71 of 2013 (Government of Indonesia, 2013; Ministry of Health of the Republic of Indonesia, 2013b).

The antibiotic profile results showed that ampicillin-sulbactam was the most commonly used antibiotic. Ampicillin-sulbactam is a broad spectrum β-lactam antibiotic combined with β-lactamase inhibitors that are intended for parenteral administration to overcome ampicillin resistance. Ampicillin-sulbactam works actively against Gram-positive bacteria that generally cause respiratory tract infections, skin infections, intra-abdominal infections, and soft tissue infections such as *Staphylococcus aureus*, *Acinetobacter*, *Enterobacter*, *Haemophilus influenza*, *Escherichia coli*, *Klebsiella*, *Streptococcus pneumonia*, *Streptococcus pyogenes*, and *Streptococcus viridans* (Lacy *et al*., 2009; Adnan *et al*., 2013). This is the first-line therapy used for severe pneumonia in children (≤ 5 years old) (World Health Organization, 2014).

Ampicillin, without sulbactam combination, actively fights bacterial infections caused by *Streptococcus, Pneumococcus*, non-penicillinase producing *Staphylococcus*, Listeria, Meningococcus, *Haemophilus influenza*, Salmonella, Shigella, *Escherichia coli*, Enterobacter, and Klebsiella (Lacy *et al*., 2009). Ampicillin is an alternative treatment for the shigella-induced diarrhoeal disease. It is the first-line therapy for paediatric inpatients aged ≤ 5 years old with severe pneumonia (Ostapchuk, Roberts & Haddy, 2004; Guarino *et al*., 2014; World Health Organization, 2014). This is in accordance with the antibiotic use guidelines formulated by the Bangil public hospital, where this study took place. Ampicillin is also used to treat meningitis and brain abscesses. The third most widely used antibiotic was cefixime. Cefixime is used to treat urinary tract infections, acute media otitis, and respiratory tract infections caused by the bacteria *Staphylococcus pneumonia*, *Staphylococcus pyrogens*, *Haemophilus influenza*, and Enterobacteriaceae (Lacy *et al*., 2009; Bradley *et al*., 2011). Furthermore, cefixime is used as an alternative treatment for diarrhoea caused by *Escherichia coli* and Shigella (Adnan *et al*., 2013; Bruzzese, Giannattasio & Guarino, 2018).

There are several studies similar to those conducted at Bangil public hospital. Research at Kariadi public hospital in Central Java carried out from August to December in 2012 showed a total DDD value of 39.4 DDD/100 bed-days, with ceftriaxone (10.6 DDD/100 bed-days) as the most antibiotic used (Febiana, 2012). Similarly, research at Soebandi Jember hospital during 2016 found a total DDD of 36.93 DDD/100 bed-days, with ceftriaxone (16.9 DDD/100 bed-days) as the most antibiotic used (Fathimatuzzahrah, 2016). In this present research, ceftriaxone also had the highest DDD, and this is thought to be related to the diagnosis of most diseases, namely diarrhoea and bronchopneumonia. Ceftriaxone is effective against Gram-negative bacteria, so it can be used as a treatment for diarrhoea caused by non-typhoidal Salmonella, and Shigella (Shea, Florini & Barlam, 2002; World Health Organization, 2018b). For severe pneumonia, ceftriaxone is a second-line

treatment for children who have failed first-line treatment (World Health Organization, 2014).

Conclusion

This study concluded that the pattern of antibiotic use in the children's patient wards of the Bangil Public Hospital in 2017 was similar to research conducted in several other hospitals in Indonesia, such as the Soebandi Jember hospital and the Kariadi public hospital. In addition, ceftriaxone was found to be the most commonly used antibiotic with the highest DDD value.

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