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Antibiotic rationality on pneumonia treatment to pediatric patients at Sultan Syarif Mohamad Alkadrie hospital Pontianak

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Abstract. In Indonesia, pneumonia is the third cause of death after cardiovascular disease and tuberculosis. Based on data from Health Department in Pontianak, 35% pneumonia cases are from 4000 Respiratory Tract Infections (RTI) patients. This study aimed to evaluate the rationality treatment to pediatric patients with pneumonia in Sultan Syarif Mohamad Alkadrie Hospital Pontianak. The type of this research is an observational study with cross-sectional design and purposive sampling technique, data collections was obtained retrospectively from 20 pediatric patient medical record during 2015. The result highlights class of mostly used antibiotic that is cephalosporin. The result showed that between the variation of administration route and length of stay had a weak relation, but both of administration variation route gave same length of stay. The rationality parameters including appropriate indication 100%, appropriate drug 100%, appropriate dose 95%, and appropriate administration 100%. The conclusions of this study were the treatment of pneumonia for pediatric patients already rational and i.v route is more recommended to be administered rather than i.v followed by oral route.

Keyword: Pneumonia, Pediatrics, Antibiotics Rationality, Length of Stay.

1. Introduction

Respiratory tract infections are a major cause of infectious morbidity and mortality in the world. Nearly four million people die from respiratory infections each year, as much as 98% are caused by lower respiratory tract infections such as pneumonia. The mortality rate is also high in infants, children, and the elderly, In Indonesia, pneumonia becomes the third cause of most death after cardiovascular and tuberculosis. Low socio-economic factors increasing mortality rate. Cases of pneumonia were found to be most prevalent in children under five. According to WHO reports, about 800,000 to 1 million children die each year from pneumonia. In addition, after the smoke haze in West Kalimantan caused an increase of 4,000 patients with respiratory tract infection by 35% based on September 2015 data that published by Pontianak City Health Department[1]. The high prevalence of pneumonia cases and the impact which resulting in high consumption of over-the-counter (such as antiinfluenza, cough medicine, multivitamins) and antibiotics. In fact many antibiotic treatments were prescribed to overcome this infection. Excessive antibiotic prescribing is present in respiratory tract infections especially lower respiratory tract infections such as pneumonia, where most of the causes of this disease are bacterial, viral and mycoplasma (transitional forms between bacteria and viruses), common bacteria are *Streptococcus pneumoniae*, *Staphylococcus aureus*, *Klebsiella* sp, *Pseudomonas* sp[2].

Many treatments received by children are not appropriate which can lead to irrational drug use. Inaccurate diagnosis, selection of antibiotics, indications, dosage, mode of administration, frequency and duration of administration are the cause of inappropriate and inaccurate treatment of infection using antibiotics[3], especially neonates and infants whose liver microsomes enzyme counts for drug metabolism are relatively small, against drugs. The use of antibiotics in children requires special attention because pharmacokinetic factors include the absorption, distribution, metabolism and excretion of drugs can be differences in the therapeutic response or side effects[4].

The use of antibiotics in the health care, especially in pediatric patients diagnosed with pneumonia, requires

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special attention in order to avoid the irrationality of antibiotic use. Therefore, researchers were interested in conducting research on the rationale of the use of antibiotic respiratory infections in hospitalized pediatric patient diagnosed pneumonia at Sultan Syarif Mohamad Alkadrie Hospital Pontianak in 2015.

The main problem in this study is whether the use of antibiotic respiratory infections in pediatric patients diagnosed with pneumonia which includes appropriate indication, appropriate drugs, appropriate doses and appropriate rules of rational use. The purpose of this study is to look at the rationality of antibiotic use of respiratory tract infections in pediatric patients diagnosed pneumonia in terms of appropriate indication, appropriate drugs, appropriate dosage, and appropriate drugs rules. The second purpose is to analyze the relation between variation of administration route and length of stay.

2. Methodology

In this observational research, data collection was conducted retrospectively based on data collection of patient medical records that diagnosed with pneumonia in 2015. The design of this study is descriptive cross-sectional. The tools used in the research are data collection sheets, the notebook equipped with Microsoft Excel and SPSS software.

This research was conducted at Sultan Syarif Mohamad Alkadrie Hospital Pontianak West Kalimantan Province, from June to September 2016. The population in this study were pediatric patients diagnosed with pneumonia and underwent inpatient in year 2015. The samples in this study were all inpatient pediatric patients that meet the inclusion criteria and exclusion criteria. Patients who have medical record data including diagnoses of illness, age (0-12), the name of antibiotics given, dosage, mode of use, rule of use, and length of stay. Sampling technique in this research is a purposive sample that is intentional sampling according to the requirement of the sample which is needed where this sample not taken at random.

Data collection is done by collecting secondary data. The technique of collecting secondary data is done by recording the contents of medical records including patient data (sex, weight, age, disease diagnosis) and antibiotics uses (name of antibiotics, and doses of antibiotics).

The data that has been taken is checked and re-selected based on data that meet the specified inclusion criteria. After that, the data is inserted into the medical records table.

The analyzed data are all data of research result in the form of patient data description which include: Sex, Weight, Age, disease diagnosis, and antibiotic usage include: Name of antibiotics, doses of antibiotics, how to use and rules of use. The data were analyzed historically. The rationale or the absence of antibiotic respiratory infections in pediatric patients diagnosed with pneumonia is determined according to the exact parameters of indication, precise medication, proper dosage, and proper use rules. It is said to be rational if it is appropriate with UKK IDAI (Unit Kerja Koordinasi Ikatan Dokter Anak Indonesia/Coordination Unit of Indonesian Pediatrician) on child's Respirology published by IDAI and Pharmaceutical Care for Respiratory Tract Infection[5]. The data of the research are analyzed descriptively. Qualitative data obtained are presented in the form of tables and graphs/diagrams and percentages

3. Result

Research on the rationale of the use of antibiotic respiratory infections in pediatric patient diagnosed with pneumonia at the inpatient installation of Sultan Syarif Mohammad Alkadri Hospital Pontianak was done by taking data from medical records. The results obtained were 33 pediatric patients diagnosed with pneumonia, but the inclusion criteria were only 20 pediatric patients. Data recorded from the medical record, including medical record number, age, diagnosis, sex, duration of care, patient condition at discharge, and therapy include antibiotic name, dose, antibiotic type, mode of administration, and duration of administration. The medical record contains records and documents on the patient's identity, examination, treatment, other actions and services that have been provided to the patient.

Based on data from the Pontianak City Health Department, in the year 2015, the prevalence of lower respiratory tract infections has increased by 4,000 patients. Data from the Pontianak City Health Department and Sultan Syarif Mohamad Alkadrie Hospital show the difference in the number of very large cases. This is because in this study the researcher specifies only one disease that is patients diagnosed with pneumonia while respiratory infections themselves are divided again based on the anatomical location of ISPA (Upper Respiratory Tract Infection) and ISPB (Lower Respiratory Tract Infection). Acquisition prevalence of respiratory tract infection patient influenced by seasoning factor such as dry season. The dry season that occurred in Pontianak caused smoke haze caused by forest burning, thus increasing the production of pollutants, in the form of dust particles of forest combustion that can enter and attack the respiratory tract and cause respiratory infections.

From the results of the study of respiratory tract infections in pediatric patients diagnosed with pneumonia were male patients (55%) more than women (45%). Several studies have shown different results regarding the sex ratio in pediatric patients with pneumonia-diagnosed respiratory tract infections. In one study conducted in Yogyakarta that based on sex, the

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number of male patients was higher, while other similar studies indicated the number of female patients dominating[6]. The different sex ratios depend on the area in which the study was conducted. Therefore, gender is not one of the determinants of pneumonia in pediatric patients.

Table 1. Patient characteristic

No.	Characteristic	Frequency	%
Gender	Male	11	55.00
	Female	9	45.00
Age	0 – 1 month (Neonates)	1	5.00
	1 month - 2 years (baby/infant)	13	65.00
	2 – 12 years	6	30.00
Duration (days)	4	14	70.00
	5	2	10.00
	6	4	20.00
Antibiotics	*Cefotaxime*	8	40.00
	Cefotaxime-Cefixim	5	25.00
	Ceftriaxone	4	20.00
	Ampisillin	1	5.00
	*Cefotaxime-*Ampisillin	1	5.00
	*Cefotaxime-*Ampisillin-Clavulanic Acid	1	5.00

The total data obtained is grouped the age of pediatric patients diagnosed with pneumonia. Based on the age of pediatrics divided into 3 groups: neonates for pediatric newborn to 1 month, infant or infant for pediatrics aged 1 month to 2 years and children for pediatrics aged 2 years to 12 years. This study proves that the case pneumonia is more common in infants by 65%, while children by 30% and neonates by 5%. The results of this study reinforced with Basic Health Research Results of 2013 which shows the highest pneumonia occurs in the age group 0-2 years[7]. The child has severe pneumonia with symptoms of a cough and difficulty breathing. The immune system of children at that age is also very vulnerable so easily infected by airborne diseases. This becomes a proof that pneumonia was susceptible to children where the immune system was imperfect and the lumen of the airways is narrow, thus infectious. In neonates and small infants, initial therapy of intravenous antibiotics should begin as soon as possible. Because neonates and small infants often have sepsis and meningitis, antibiotics that are supposed to be broad-spectrum antibiotics such as a combination of beta-lactam/clavulanate combined with new intravenous macrolides, or third-generation cephalosporins. If the patient has no fever or the condition has improved and stabilized, antibiotics are replaced with oral antibiotics and medication[8].

Based on the standard of therapy used in this study, the duration of antibiotic use for patients diagnosed with pneumonia is 4-14 days. Table 1 shows the suitability of prolonged use of antibiotics in the treatment of pediatric pneumonia patients with standard therapies used by hospitals.

Antibiotic therapy is given consists of initial treatment can be seen in Table 1. Based on data about antibiotic therapy given, the usage of cefotaxime has highest percentage, that is equal to 40%, followed by a combination of 25% cefotaxime-cefixime antibiotic, ceftriaxone at 20%, ampicillin at 5%, Cefotaxime-ampicillin at 5%, and cefotaxime-ampicillin-Nuvoclav at 5%. Patients who are unable to drink/eat, vomit, seizures, lethargic or unconscious, cyanosis, and severe respiratory distress can be found in very severe pneumonia. From the results of the study known the use of cephalosporin group antibiotics (95%) more than others. Based on the guideline of pneumonia therapy in children, the beta-lactam group was the first choice antibiotic therapy. However, the rapid development of antibiotic resistance results in changes in the use of antibiotics. Bacterial respiratory tract infections such as *Staphylococcus aureus* and *Streptococcus pneumonia* are resistant to penicillin. Resistance occurs due to genetic changes in the body of the bacteria so that genetic mutations occur. For the treatment of bacterial infections with penicillin resistance, cephalosporin is used. The cephalosporins used in this study were the 3rd generation cephalosporins (cefotaxime, cefixime, and ceftriaxone). Selection of antibiotic-type for therapy Respiratory tract infections in pediatric patients diagnosed with pneumonia determines the exact rationale of indication of drugs classified as rational = 100%.

The use of antibiotics is said to be rational if it meets several indicators such as precise indications, proper medication, proper dosage, proper use, and proper use rules. But in this study, only four parameters of rationale are discussed that is a precise indication, proper drug, proper dose and proper use rules. Rational use of drugs is when patients receive treatment in accordance with to their clinical needs, in appropriate doses of need, within a reasonable time period and at an affordable cost.

In this study, the appropriate indication parameter has 100% accuracy percentage is said to be a appropriate indication if there is a match between diagnosis which is upheld by the doctor with accepted treatment. In this study appropriate indications are defined as patients diagnosed with pneumonia and receiving antibiotic therapy such as penicillin-class antibiotics such as ampicillin and amoxicillin and third generation cephalosporin antibiotics such as cefotaxime, cefixime, and ceftriaxone. The results obtained in this study indicate alignment between the diagnosis of the disease and antibiotics given to patients diagnosed with pneumonia. The use of antibiotics given to patients refers to therapy guideline used by hospitals in this study

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that is IDAI Children Respirology,[8] so appropriate indication in this rational research is 100%.

In this study, it is said to be appropriate if the patient is indicated by pneumonia is given antibiotics in accordance with the selection of therapy classes and types of drugs. The use of antibiotics that are inconsistent with the type of disease can lead to irrationality in the use of antibiotics. Early identification of the causative microorganisms can't be performed due to the unavailability of rapid microbiological tests. Therefore, antibiotics were selected based on empirical experience. Generally, the selection of empirical antibiotics is based on the possibility of a causative etiology taking into account the age and clinical state of the patient as well as epidemiological factors. Based on the guidelines used in this study, pneumonia in pediatric patients conducted by parenteral antibiotics as soon as possible, since pneumonia in pediatric patients is generally caused by *S. pneumonia* bacteria where this bacteria is one of the Gram-negative bacteria, therefore, antibiotics given are antibiotics with penicillin groups such as amoxicillin and ampicillin and third generation cephalosporin antibiotics such as cefotaxime, ceftriaxone, and cefixime.

Table 2. Distribution of appropriate antibiotic

No.	Antibiotic	Total patient	Criteria of appropriate drug		Rationality percentage (%)
			Appropriate	Not appropriate	
1.	*Cefotaxime* (IV)	8	8	-	40
2.	*Ceftriaxone* (IV)	4	4	-	20
3.	*Cefotaxime* (IV) *Cefixime* (PO)	6	6	-	30
4.	*Cefotaxime* (IV) Ampicillin (IV)	1	1	-	5
5.	*Cefotaxime* (IV) Ampicillin (IV) *Amoxiclav* (oral)	1	1	-	5
6.	Ampicillin (IV)	1	1	-	5

Table 2 shows the alignment between the therapy guideline used with the results of the study, in which pediatric patients diagnosed with pneumonia received antibiotics based on guideline therapy used in this study. The commonly used antibiotic groups in this study are third generation cephalosporin antibiotics such as cefotaxime, cefixime, and ceftriaxone. Third generation cephalosporins are used because they are much more active against *Enterobacteriacea*e, including penicillinase-producing strains. Cephalosporins are similar to penicillin chemically, to work, and toxicity so they are used as alternatives in case of hypersensitivity to penicillin. In the table, the most widely used antibiotic is cefotaxime (35%) because cefotaxime is more active against Gram-negative bacteria and is active in the cause of *Streptococcus pneumonia* than other cephalosporins. *Streptococcus pneumonia* is the most common bacteria present in children aged 3 weeks 4 years. Parenteral third-generation cephalosporin parenteral administration (Cefotaxime or ceftriaxone) should be prescribed for hospitalized pediatric patients.

In the antibiotic penicillin group used for therapy in the above table, ampicillin is given intravenously and amoxiclav is given orally. Ampicillin is active against certain Gram-positive and Gram-negative organisms but inactivated by penicillinase, including those produced by *S. Aureus* and Gram-negative bacillus which is generally like *E. coli*. The use of ampicillin considered as administration of infection-induced therapy should be by a clear diagnosis of the cause of bacterial infection and associated with antibiotic resistance. In the British Thoracic Society journal, the recommended class of penicillin is amoxicillin[9]. According to some studies that have been done the use of ampicillin has a lot of resistance. However, the use of ampicillin can't be said to be irrational if there are other standards that suggest that the antibiotic may be recommended for pneumonia therapy. According to table 2, there are 2 patients using combined antibiotic therapy, a combination of cephalosporins with penicillin. Antibiotic therapy of the cephalosporin group (cefotaxime) with the penicillin group (ampicillin) is used in the case is considered severe and possibly infected by multiple pathogens (Gram-negative and Gram-positive) because cefotaxime handles more to Gram-negative bacteria while ampicillin is more Gram-positive so combined use can allow increased antimicrobial activity and suppress the growth of infectious pathogens.

There were 6 patients who performed intravenous oral replacement of antibiotics such as cefotaxime and ceftriaxone antibiotic replacement with cefixime antibiotics. This can happen because, during the hospitalization period, the patient was in good condition and requested to go home and must continue the outpatient treatment. Based on the pharmaceutical service guidelines for antibiotic therapy the benefits of antibiotic replacement from intravenous to oral include decreased cost, patient comfort, reduced complications and reduced i.v line infection. There were 3 patients who replaced the dose of antibiotics in one class i.e cefotaxime, replacement of antibiotic doses in one class remained possible with clear evidence of the patient's clinical condition and allowed for the effect of improving the patient's condition on the therapy being undertaken. Except for the use of one group of antibiotics at the same time which can be toxic because of excessive levels in the blood.

The doses administered to pediatric patients are calculated on a dose basis based on body weight which is then matched with standard therapy. The data obtained show that there is one patient who shows underdose in the use of antibiotics (see Table 3). Of these results, the

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number of cases that are not in accordance with the standard of therapy is only 5%, it is influencing therapeutic effect in the therapy process. Underdose in the administration of antibiotics can cause these survived bacteria to regenerate and cause the same repetitive disease, or even have developed themselves resistant to the drug.

Table 3. Distribution of appropriate doses

No	Antibiotics	Weight (Kg)	Dose per day (mg/kg/day)*	Daily dose (terxtbook) (mg)	Daily dose (mg)	Appropriate dose		Rationality (%)	
						yes	no	R	NR
1.	Cefotaxime	13 8 8 13 9,5 8,5 20	50-200 50-200 50-200 50-200 50-200 50-200 50-200	650-2600 850-3400 850-3400 650-2600 475-1900 423-1700 1000-4000	900 1500 1500 1050 750 750 1000	yes yes yes yes yes yes yes		35%	
2.	Ceftriaxone	5,8 8,6 8,6 6,2	50-100 50-100 50-100 50-100	290-580 430-860 430-860 310-620	300 500 500 250	yes yes yes yes		20%	
3.	Cefotaxime (iv) Cefixime (oral)	10 10 11 11 13 12	50-200 (iv) 8-20(oral) 50-200 8-20 50-200 8-20 50-200 8-20 50-200 8-20 50-200 8-20	500-2000 88-220 500-2000 88-220 550-2200 88-220 550-2200 88-220 650-2600 104-260 600-2400 96-240	750 100 750 100 750 100 750 100 1800 225 900 150	yes yes yes yes yes yes yes yes yes yes yes yes		30%	
4.	Cefotaxime Ampicillin	4,2	50-200 100-400	210-840 420-1680	400 800	yes yes		5%	
5.	Cefotaxime Ampicillin Nuvoclav (oral)	7	50-200 100-400 20-90	350-1400 700-2800 140-630	1500 1400 200	yes yes yes		5%	
6.	Ampicillin	6,2	100-400	620-2480	300		no		5%

Table 4. Frequencies of antibiotic use

Antibiotic	Frequency (textbook)	Frequency in hospital (by day)	Conformity		%
			Yes	no	
Cefotaxime (IV)	every 6-8 hours	3x1	8 Patients	-	40
Cefixime (PO)	Every 9-10 hours	2x1	6 Patients	-	30
Ceftriaxone (IV)	every 24 hours	1x1	4 Patients	-	20
Ampicillin (IV)	every 6 hours	4x1	1 Patient	-	10
Amoxi-*Clav* (PO)	every 6 hours	4x1	1 Patient	-	10

Based on the results of research on the frequency of antibiotic use in hospitalized pediatric patients diagnosed pneumonia in Sultan Syarif Mohammad Alkadrie Hospital Pontianak. Therefore, it can be concluded that the accuracy of the rules of use the use of antibiotic patients diagnosed with pneumonia has a percentage of suitability of rules of use of 100%.

This research is retrospective, the limitation of retrospective data is that the researcher can't interact directly with the patient to be able to know the actual condition of the patient so that the patient's condition can

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only be known from the patient's medical record. Additionally the patient's condition after undergoing hospitalization can't be known clearly, and if patients are given antibiotics with outpatient therapy can't be analyzed rationality of its use.

The principle of antibiotic therapy is considered failed if it does not succeed in eliminating clinical symptoms or recurrent infections after therapy is stopped, due to the improper use of antibiotics is very detrimental to the patient. For that antibiotic should be used properly, so that patients are not harmed by the treatment provided. The purpose of treatment is the cure of disease with minimal side effects, then the role of the pharmacist is needed for the achievement of therapeutic goals for preventing and curing the infections.

The data which were comparing administration route (i.v only and i.v followed by oral) to length of stays has a weak correlation but in the same direction for length of stays. So from both administration routes, for the efficiency, can be chosen one of the route which is only i.v. This can be happen because there is no bacterial culture test in the hospital.

4. Conclusion

Based on the results of research on the rationality of the use of antibiotics in pediatric patients diagnosed with pneumonia in RSUD Sultan Syarif Mohammad Alkadrie Pontianak 2015, it can be concluded that the rationality of the antibiotics in the treatment of pediatric patients diagnosed pneumonia from 20 patients, 20 (100%) appropriate medicines, 19 patients (95%) as well as 20 people (100%) of the 20 pediatric patients who were hospitalized in 2015. While from the correlation between administration routes dan lenght of stays has shown a weak relation, so for the efficiency of administration route, only i.v can be chosen.

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