

Inappropriate use of antibiotics in the treatment of acute respiratory infections for the underfive children among general practitioners

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ABSTRACT

Iwan Dwiprahasto - *Inappropriate use of antibiotics in the treatment of acute respiratory infections for the underfive children among general practitioners*

Acute respiratory infection (ARI) is the commonest illness in children and the leading cause of morbidity and mortality in many developing countries. It comprises approximately 50% of all illness in children under five years. Unfortunately, most children are commonly treated inappropriately. A population based study involving all general practitioners (GPs) and pharmacies in Yogyakarta Special Province was carried out in June-July 1992 to provide data on antibiotic utilization for acute respiratory infection (ARI). One hundred and ninety one out of 207 GPs and all pharmacies participated in the study by completing structured form distributed during the study. Ninety three percent of patients with ARI seen by GPs were given antibiotic. Based on WHO criteria on ARI, only 7-14% of all patients were eligible to be given antibiotics. The most frequently used antibiotics for the underfives were ampicillin (38.8%) followed by cotrimoxazole (29.2%), amoxycillin (14.9%), and erythromycin (6.13%). Sixty three per cent of drug cost prescribed for the underfives children were accounted for by antibiotics. It can be concluded that inappropriate use of antibiotics was found in more than 75% patients under 5 years of age. In addition to poor indication for antibiotic use inappropriateness was also found in terms of dose, the length of antibiotic use, drug administration, and drug dosage form.

Key words: ARI - inappropriate use of antibiotics - underfive children - general practitioners - prescribing pattern

ABSTRAK

Iwan Dwiprahasto - *Ketidaktepatan penggunaan antibiotika pada anak balita dengan infeksi saluran pernafasan akut oleh dokter umum*

Infeksi saluran pernafasan akut (ISPA) merupakan salah satu penyakit yang paling sering diderita dan menjadi penyebab utama kematian pada anak di negara sedang berkembang. Namun demikian hampir sebagian besar penderita ternyata diterapi secara tidak adekuat. Suatu studi *cross-sectional* telah dilakukan untuk melihat pola persepsian untuk ISPA, dengan melibatkan seluruh dokter umum dan apotek yang berada di Provinsi DIY, antara bulan Juni hingga Juli 1992. Seratus sembilan puluh satu dokter umum (dari total 207) dan seluruh apotek bersedia untuk ikut serta dalam penelitian. Dokter diminta untuk menulis identitas penderita ISPA pada formulir yang telah disediakan. Berdasarkan formulir tersebut dilacak pola persepsian masing-masing melalui penelusuran resep di apotek-apotek. Antibiotika ternyata diresepkan pada 93% pasien dengan ISPA. Berdasarkan kriteria WHO untuk ISPA, ditemukan bahwa hanya 7-14% pasien yang seharusnya mendapat antibiotika. Antibiotika yang paling sering diresepkan berturut-turut antara lain adalah ampicilin (38%), kotrimoksazol (29,2%), amoksisilin (14,9%), dan eritromisin (6,13%). Dari segi biaya, 63% biaya obat untuk ISPA digunakan untuk antibiotika. Studi ini menyimpulkan bahwa lebih dari 75% persepsian untuk balita tergolong tidak rasional. Di samping tidak jelasnya indikasi pemakaian antibiotika, dosis, cara pemberian, frekuensi dan lama pemberian ternyata juga tidak tepat.

INTRODUCTION

Acute respiratory infection (ARI) is one of the principal causes of illness and death of children in developing countries. In Indonesia this disease is still one of the five major causes of death in children¹. Therefore, it has received special attention and several measures have been taken to overcome this health problem. However, effective treatment of this disease has not yet been appropriately implemented. This is partly due to the lack of information and knowledge related to drug treatment.

Drug utilization studies have not yet been widely implemented in Indonesia. However, the problem of irrational use of drugs has already been detected especially at primary health care level. Previous study conducted by the Ministry of Health of Indonesia in primary health care settings revealed that more than 80% of children suffering from acute respiratory infection were given antibiotics². Amongst those patients who suffered from ARI-78% of under-fives and 65% of over-fives received at least one antibiotic, yet oral antibiotics were prescribed in average quantities of two days' supply. In terms of drug costs, antibiotics account for 54 to 61% of the cost of treating acute respiratory infections³. The problem lies in how to rationalize the use of antibiotics, so that children who may benefit receive them sooner, and to achieve less overprescribing of antibiotics for children who do not need them. This study is, therefore, aimed at detecting inappropriate use of antibiotics in the treatment of acute respiratory infection in underfive children seen by General Practitioners (GPs).

METHODS

Study design

This study was conducted in a cross sectional study design. All GPs in Yogyakarta Special Province involved in this study were admitting only children under 5 years of age with Acute Respiratory Infections. All pharmacies participated in writing down prescriptions for children in their pharmacy over the two-week period.

Selection of study subjects

All GPs were asked to write down data from ARI patients who were under ten years of age encountered in their private practice office within a one-week period (using ARI structured form). Patients' records were collected from 20th to the 26th of July 1992, i.e 6 working days. Informed consent was signed for their willingness to participate in the study.

All children under 5 years of age with ARI attending GPs during the one-week study period were recorded and data were written down on an ARI form by prescribers. Data on date of patient's visit, name, date of birth, age, address, and respiratory rate were recorded on the form.

Eighty-eight pharmacies started to write down prescription data for patients under 5 year old on 20th July and finished by 1st August 1992 on an ARI structured form designed as the pharmacy data record.

Ten research assistants (8 fifth-year students from Department of Anthropology, Faculty of Art, 2 fifth-year students from Faculty of Medicine) went door to door to distribute ARI form to physicians and pharmacies 3 days before the study was commenced. Two pharmacists were also involved in this study and were contacting pharmacies to ask for their participation.

Case definition

The following WHO criteria for Acute Respiratory Infections in children were used to classify patients' diagnosis by age and respiratory rate⁴. The deciding factor for the use of antibiotics in this study is based on WHO criteria for ARI disease in children under 5 years, i.e respiratory 60 per minute or more for young infant (age less than 2 months), 50 per minute or more for the age between 2 months and 1 year, and 40 per minute or more for the age between 1 year to 5 years.

Data Collection

Information on patients with ARI, including the date of visit, name of patient, birth date, age, address, respiratory rate, and name and address of physicians were obtained from prescribers using ARI structured form. Diagnosis listed by physi-

cians were not made on anatomical basis (e.g. tracheobronchitis and bronchiolitis) but were simply listed according to basic WHO criteria. Data on prescriber self-dispensing were also obtained. All of these data were collected at the end of the one-week study period by research assistants.

Data on prescriptions for all children under 5 years attending pharmacies were recorded within a 2-week-period of study using the prescription data form. Data collected from pharmacies included (1) date of prescriptions; (2) name and address of prescribers; (3) name, age, and address of patients; (4) drugs and number of drugs prescribed to the patients, dose, drug administration, dosage form, additional information written in the prescription, prescribed drug's cost; and (5) how many drugs were dispensed to the patients, and how much money was spent by patients to get their drugs.

Data derived from physicians were coded according to the alphabetical order of the name of physicians, regency, and the name, sex, and age of patients from each physicians. Coded data were thereafter used to search for matching prescriptions among the 5,923 prescriptions from pharmacies. All data were validated by the principal investigator and when missing data had been identified, relevant physicians were contacted immediately to get the data completed.

Data analysis

Analysis was performed using EPIINFO 6b statistical programs. This statistical software package was used to calculate summary statistics such as frequencies, means, and percentage to describe the prescription pattern data.

RESULTS

Participants and patient characteristics

During the one-week study period, 191 out of 209 (93.63%) General Practitioners, participated in the study and none of 88 pharmacies refused to participate. As can be seen from TABLE 1, more than 70% of patients reported by physicians were under five years of age. Only 6 patients less than 2 months were seen by GPs in the one week study period. Four hundred and eighty five patients

were recorded by GPs. Comparable number of both sexes are also seen in TABLE 1.

The mean age of male and female reported by GPs were 3.53 and 3.49 year respectively. The mean of respiratory rate of patients recorded by GPs were 25.4 and 24.3 per minute for male and female respectively. The number of patients seen by GPs and the number of antibiotics prescribed are also shown in TABLE 1. More than 90% of patients with ARI treated by GPs were given at least one antibiotic.

TABLE 1. - Patient characteristics

	Sex		Total (%)
	Male	Female	
1. No. of patients with ARI			
- < 2 months	3	3	6 (1.24)
- 2 months - 1 year	42	50	92 (18.97)
- 1 - 5 year	177	210	387 (79.79)
2. Average age (year)	2.53	3.49	
3. Average respiratory rate (x/minute)	25.4	24.3	
4. The use of antibiotics for patients with ARI			
- No. of patients reported		485	
- No. of patients given antibiotics		455	93.81

Patients requiring antibiotics

In relation to the measure of respiratory rate reported by physicians, it can be seen from TABLE 2 that only a small number of patients really need antibiotics. None of the patients who were less than 2 month old had a respiratory rate of 60 or more per minute. Only a few patients between 1 and 5 year old should have been given an antibiotic. Among those three different age groups, the age between 2 months and 1 year has the biggest proportion of patients that needed an antibiotic. However this number does not exceed 11%.

The most frequently used antibiotics for children under 5 years of age with ARI

The use of antibiotics by age is shown in FIGURE 1. The most often prescribed antibiotics by GPs are ampicillin (44.12%), followed by cotrimoxazole (28.86%), amoxicillin (10.93%), erythromycin (4.74%), chloramphenicol (3.05%) with a small proportion of sulfasomydin, penicillin-V, tetracycline, and triple sulfa.

TABLE 2. - Patients eligible for antibiotic use (based on the WHO criteria)

Patients age	No. of patients reported by GPs	Respiratory rate	No. of patients requiring antibiotics	(%)
< 2 months	6	6 or more	0	0.00
2 months-1	92	50 or more	10	10.87
1 year-5 years	387	40 or more	38	9.82

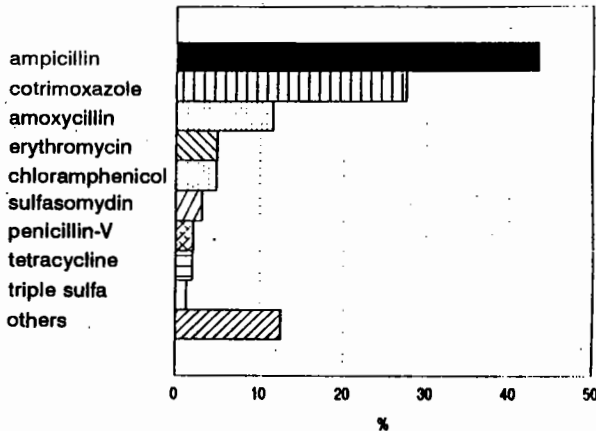


FIGURE 1. - Antibiotic prescribing pattern for ARI patients

Antibiotic dosage

From the total number of 214 patients receiving ampicillin, the average dose of ampicillin for the children aged less than 2 months was 98.65 mg per dose. The average dose of ampicillin prescribed by GPs for the patients aged between 2 months-1 year was 127.16 mg. Greater dose was prescribed for children aged between 1-5 year, i.e. 132.83 mg (TABLE 3). In total, 140 patients reported by GPs received cotrimoxazole in the one week study period. None of the patients under 1 year of age seen by GPs received cotrimoxazole. The average dose of cotrimoxazole prescribed for patients aged between 2 month-1 year and 1 year-5 year were 63.48 and 65.72 mg respectively.

The average dose of amoxycillin prescribed by GPs for different age groups can also be seen in TABLE 3. The total number of patients who received amoxycillin was 53 (10.93%) which makes it the third most often used antibiotic by GPs for children under 5 years of age with ARI. None of patients of less than 2 months was given amoxycillin. The total number of patients who re-

ceived erythromycin for ARI was 23 or 4.74%. The average dose of erythromycin received by the age group of 1-5 years from GPs was 171.88 mg.

The fifth most commonly used antibiotics for children with ARI was chloramphenicol which accounted for 3.05% of the total use of antibiotics. As can be seen in TABLE 3, none of the children age less than 2 months seen by GPs was given chloramphenicol. This TABLE shows that the 1-5 years age group received an average dose of 153.21 mg, which is equal to the 2 months-1 year age group. The average dose of sulfasomydin prescribed for children between 2 months-1 year and 1-5 years were 264.44 and 292.14 respectively.

TABLE 3. - Average dose of antibiotics prescribed for ARI patients

Antibiotics	Average dose (mg)		
	< months	2 months-1 year	1 year - 5 years
Ampicillin	98.65	127.16	132.83
Co-trimoxazole	-	63.48	65.72
Amoxycillin	-	126.39	133.39
Erythromycin	152.14	165.5	171.88
Chloramphenicol	-	153.21	153.21
Sulfasomydin	-	264.44	292.14
Penicillin-V	-	133.93	135.42

The only available oral form of penicillin, i.e. penicillin-V was also prescribed for children with ARI, even though only in 9 patients. GPs prescribed an average of 135.42 mg for the children aged between 1-5 years, which is similar to those age between 2 months-1 year.

Prescribed frequency of administration

Prescribed frequency of administration for children under 5 years with ARI is shown in FIGURE 2. For the total number of 214 children who received ampicillin, most GPs prescribed ampicillin for 3 times/day use, i.e. 81.84%. Seventeen percent of ampicillin prescribed by GPs was given 4 times/day. Even though only a small number, 0.3 percent of patients who received ampicillin were instructed to take the drug either 2 or 6 times a day.

As can be seen in FIGURE 2, among 140 patients who received cotrimoxazole for the treatment of ARI, 53.99% of patients were given

cotrimoxazole for twice daily use and about 40% of patients were given cotrimoxazole 3 times/day. There were also a small number of patients seen by GPs who received cotrimoxazole 4 times/day (2.45%) or even more frequently (4.29%).

In relation to the administration of amoxycillin, it is shown in FIGURE 2 that most GPs prescribed amoxycillin for 3 times/day use (79.71%). About 13 percent of patients seen by GPs received amoxycillin 4 times/day. There is also a small number of patients who received amoxycillin for less than 3 times/day or more than 4 times/day. Altogether they accounted for less than 10% of the total.

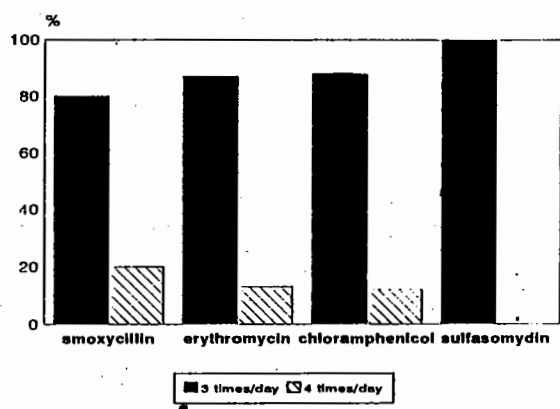


FIGURE 2. - Frequency of antibiotics administration

FIGURE 2 also shows that most GPs prescribed erythromycin for 3 times a day (86.67%). Less than 15% of patients seen by GPs received erythromycin 4 times/day. Among 20 patients with ARI who received chloramphenicol, more than 85% patients were given this antibiotic 3 times/day. Less than 15% of patients who received chloramphenicol from GPs took the drug 4 times/day.

The prescribed length of antibiotic therapy

The prescribed length of antibiotic therapy for the treatment of ARI in children under 5 years is shown in FIGURE 3. Overall, GPs prescribed antibiotic for short courses for all age groups. All young infants were prescribed antibiotics for only 3 days. In addition, GPs prescribed antibiotics for

less than 3 day courses for children age between 2 months-1 year and children between 1 year-5 year (2.97 and 2.82 days mean course duration respectively).

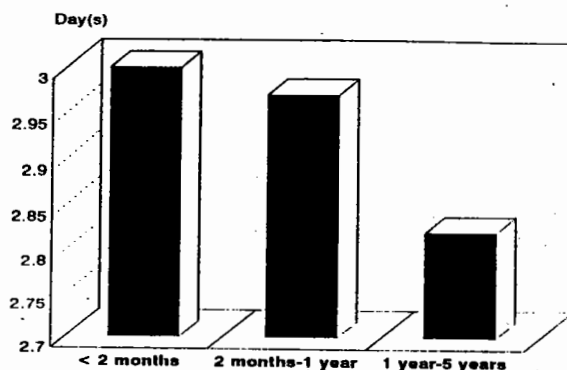


FIGURE 3. - The prescribed length of antibiotic therapy

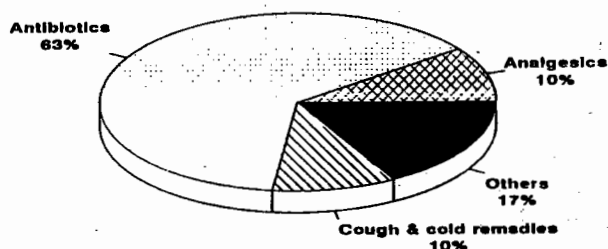


FIGURE 4. - Cost of antibiotics as a proportion of total cost of treatment of ARI

The use of antibiotics for patients requiring them

As shown in TABLE 4 most patients with rapid breathing and presumed pneumonia were given cotrimoxazole. Only a small proportion of patients seen by GPs received an adequate dose of cotrimoxazole, ampicillin, and amoxycillin, i.e 12%, 23.32%, and 18% respectively. Most patients seen by GPs received antibiotics for an inadequate duration of time.

TABLE 4. - Antibiotic use for patients with presumed pneumonia

	Antibiotics*		
	Cotrimoxazole	Ampicillin	Amoxycillin
No. of patients	20	12	6
Average dose prescribed	132.43	152.28	137.42
Proportion of patients receiving an adequate dose	12%	23.32%	18%
Prescribed frequency of administration (times/day)	3	3	3
Average duration of antibiotic course	4.32 days	3.87 days	3.92 days
Proportion of patients treated for adequate length of time	39.20%	42.71%	49.21%

* All the antibiotics were given in powder form (all were given in combination with other non-antibiotic medications)

DISCUSSION

Acute respiratory infection is one of the five major causes of death in children in Indonesia. Epidemiological evidence in the country suggests that more attention should be given to this particular disease especially in relation to treatment. This does not mean that drugs should be given to all patients. Antibiotics should only be prescribed when bacterial infection is strongly suspected.

The findings of this study, if we accept the WHO criteria for defining a patient who requires antibiotics, indicate much inappropriateness of drug use for treating ARI patients. The results show that more than 90% of children under 5 years of age with ARI who visited GPs were given antibiotics. Using WHO criteria for respiratory rates, the data suggest that only 7-14% of children really needed antibiotics. Therefore, more than 75% of children in the study might have taken unnecessary antibiotics during their episode of ARI. This finding is similar to other reports of antibiotic use in children at the primary health care level^{2,3,5} and hospital outpatients^{6,7}

Antibiotic prescribing varied with both the child's age and the prescribers. In particular, the use of ampicillin was more frequent in children seen by GPs. When the WHO guidelines are used to measure inappropriateness of antibiotic use,⁸ the choice of antibiotic by GPs rarely meets this

guideline. Both ampicillin and amoxycillin have similar antibacterial profile and failure to substitute one for the other is not a major therapeutic problem. However, the continued length use of ampicillin shows that WHO and Unicef recommendation are not being followed. The recommended antibiotics of choice for pneumonia are cotrimoxazole, amoxycillin, or procaine penicillin 4. Oral ampicillin has recently been withdrawn from the list of essential drugs by The WHO Expert Committee on the Use of Essential Drugs since November 1989 for several reasons⁹. In addition UNICEF (United Nations Children's Fund) also removed ampicillin tablets, capsules, and suspensions from its catalogue from 1992.

Tetracycline, an antibiotic that has never been recommended for children less than 8 year old due to its side effect of permanent discolouration of the teeth and deposition in bone¹⁰, was still being prescribed for ARI. Sulfasomydin was also prescribed for ARI, even though it is well known that this drug is no longer recommended¹¹. The use of chloramphenicol should also be restricted for ARI patients due to its side effect of bone marrow suppression.

In pediatric practice dose should be calculated according to body weight or surface area. Empirical dosage for any given age group, can frequently lead to underdosage especially for conditions such as otitis media where authorities recommend 50-75 mg/kg/24 hours of ampicillin for adequate levels to be achieved in the middle ear^{12,13}. Underdosage may not be harmful and may be effective in less serious infections where antimicrobial concentrations of antibiotic at the site of infection are adequate. In this study the dose of the recommended antibiotics, amoxycillin for ARI was found to be less in 1-5 years of age group who were seen by GPs (i.e. 133.99 mg) than the minimum recommended dose (i.e. 250 mg)⁴

The pharmacokinetic profile of ampicillin suggests that it should not be taken around meal times. This drug is only well and reliably absorbed from an empty stomach. In addition ampicillin should be taken 4 times a day due to its short elimination half life, i.e. 0.5 hour^{10,11}. However, it is commonly prescribed incorrectly by Physicians. In this study, incorrect prescription of ampicillin occurred in more than 80% of patients seen by GPs. Most children were given am-

picillin 3 times a day, and no other instruction was written on the prescription.

Cotrimoxazole is an effective, less costly, and widely available antibiotic for the treatment of ARI. Its pharmacokinetic profile suggests twice daily administration is sufficient for *Hemophilus influenzae* and *Streptococcus pneumoniae* infection providing a dose of 4 mg Sulfamethoxazole/kg/day is administered. However, more than 45% patients seen by GPs in this study were given cotrimoxazole in inappropriate frequency, i.e. 3 or more times a day.

Antibiotics should only be given (in appropriate dose and administration frequency) to achieve blood concentration estimated to be sufficient for eradicating suspected bacterial infection. This study shows that most GPs prescribed antibiotics for an insufficient duration i.e mostly less than 3 days. In regard to the length of antibiotic use, it has been widely recognized that inappropriate short courses are associated with increasing development of bacterial resistance^{7,14}.

This study shows that all of patients with rapid breathing and presumed pneumonia were given antibiotics. However the findings also indicate that most patients were not treated adequately. Inappropriate use of antibiotics was found not only in terms of inadequate dose, but also inadequate duration of treatment. Most patients seen by GPs were prescribed antibiotics on average for 2.85 days. This study, therefore, indicate that even though all of the eligible patients were prescribed antibiotics, most of them were inadequately treated.

CONCLUSION

Inappropriate use of antibiotics for acute respiratory infection in children aged under five years by general practitioners at their private practices has been presented. Apart from its inadequate dose and frequency of administration, antibiotics had been commonly prescribed in inappropriate duration. This will in turn increase the emergence of bacterial resistance. For the patients who really need antibiotics, they were mostly treated with inadequate dose and duration of treatment. Updated

information on how to use antibiotics appropriately should be taken into consideration as a strategy to improve the quality of treatment.

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