

The use of antibiotics in hospitalized adult typhoid patients in an Indonesian hospital

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Abstrak

Latar belakang: Demam tifoid menduduki peringkat ke tiga dari 10 besar penyakit terbanyak pada pasien rawat inap di rumah sakit (RS) di Indonesia pada tahun 2010. Selain itu terdapat peningkatan resistensi dan kasus-kasus karier, dan relaps. Penelitian ini menyajikan hasil analisis data tentang penggunaan antibiotik pada pasien tifoid dewasa rawat inap di suatu RS di Indonesia.

Metode: Data penelitian diekstrak dari rekam medik pasien tifoid dewasa yang dirawat inap di RS PMI Bogor periode Juli-Desember 2012. Analisis dilakukan dengan kualitatif (DU90%) dan kuantitatif (DDD/shr) dengan menggunakan metode ATC/DDD.

Hasil: Dari 459 pasien tifoid dewasa rawat inap diperoleh DDD/shr pasien tifoid dewasa rawat inap yang menggunakan antibiotik selama dari Juli sampai Desember 2012 sebesar 6,35 DDD/shr. Seftriakson merupakan antibiotika yang dipakai tertinggi yang setara 4,10 DDD/shr; yang berarti bahwa di antara 100 pasien tifoid, 4 pasien memakai seftriakson 2 g setiap hari. Selanjutnya, obat pada segmen 10% lebih banyak dibandingkan pada segmen 90%. Di antara 26 jenis antibiotika, 7 jenis di antaranya termasuk pada segmen DU 90% yaitu seftriakson (64,54%); levofloksasin (13,90%); ciprofloksasin (3,57%); meropenem (2,80%); metronidazol (2,52%); ampicilin-sulbaktam (1,65%); dan sefditoren pivoksil (1,60%).

Kesimpulan: Antibiotik seftriakson yang paling banyak digunakan pada perawatan tifoid pasien dewasa rawat inap di rumah sakit. (*Health Science Indones 2014;1:40-3*)

Kata kunci: antibiotik, tifoid, ATC/DDD, DU 90%

Abstract

Background: Typhoid fever was the third ranked disease among the top 10 diseases in hospitalized patients in Indonesia in 2011. There were increased drug resistance, increased number of carrier, and number of relapse cases. This study aimed to analyze the use of antibiotics in hospitalized adult typhoid patients in a hospital in Indonesia.

Methods: The data were extracted from medical records of drug use in adult typhoid patients hospitalized in the Indonesian Red Cross Hospital in Bogor (West Java) during the period of July to December 2012. The analysis for typhoid was qualitatively (DU90%) and quantitatively (DDD/hbd) using ATC/DDD method.

Results: From 459 typhoid patients, the total use of antibiotics in hospitalized adult typhoid patients during the period of July to December 2012 was 6.35 DDD/hbd. The use of ceftriaxone had the highest DDD/hbd which was equal to 4.10 DDD/hbd. This meant out of 100 typhoid patients, 4 patients received 2 g ceftriaxone per day. Ceftriaxone was given in injection form. Furthermore, there were more drugs in segment 10% than 90% segment. From 26 types of antibiotics, 7 were included in the DU 90% segment which were ceftriaxone (64.54%); levofloxacin (13.90%); ciprofloxacin (3.57%); meropenem (2.80%); metronidazole (2.52%); ampicillin-sulbactam (1.65%); cefditoren pivoxil (1.60%).

Conclusion: Ceftriaxone was the most widely used antibiotics in the treatment of hospitalized adult typhoid patients in a hospital in Indonesia. (*Health Science Indones 2014;1:40-3*)

Key words: antibiotics, typhoid, ATC/DDD, DU 90%

The Indonesian health profile data of 2010 showed that typhoid and paratyphoid fever ranked in the top 10 diseases of hospitalized patients in Indonesia.¹ Case studies at a large hospital in Indonesia showed suspected typhoid cases had been increasing from year to year with an average morbidity of 500/100000 population and 0.6% to 5% mortality.² The 2007 Indonesian Basic Health Research (*Riskesdas*) data showed that the average prevalence of clinical typhoid of 1.6% (range: 0.3% to 3%) nationally.³

At present, problems include, increased resistance to commonly used drugs and increased number of career or relapsed typhoid cases.² At this time, the first line antibiotic for hospitalized adult typhoid patients in Indonesia is ceftriaxone.⁴

A 2004 study a hospital in Yogyakarta (Java) showed that in treating typhoid fever patients there were: 38.7% excessive (over) prescribing, 31.8% under prescribing, 61.875% multiple prescribing, 53.8% incorrect prescribing, and 46.2% extravagant prescribing.⁵ Apart from the effects and side-effects of therapy, the use of inappropriate drugs is a waste and will increase hospital costs and reduce the quality of hospital services.⁶

From these issues, the use of antibiotics in hospitalized adult typhoid patients needed to be qualitatively (Drug Utilization 90% / DU90%) identified to determine the 90% types of drugs most commonly used and also quantitatively identified (Defined Daily Dose/100 days bed or DDD/hbd) to determine the daily maintenance dose which is assumed to be the average for major indications in the treatment of adult patients per hundred patient day using the Anatomical Therapeutic Chemical methods and Defined Daily Dose (ATC/DDD).^{7,8}

This study aimed to evaluate antibiotics use in hospitalized adult typhoid patients qualitatively (DU90%) and quantitatively (DDD/hbd) using ATC/DDD method.

METHODS

The study was conducted at the Indonesia Red Cross Hospital in Bogor (West Java). The data were extracted from all the medical records of hospitalized adult patients diagnosed with typhoid from July to December 2012. There were 459 patients obtained from the medical records.

Medical records of patients with incomplete drug data recording and with severe co-morbidities who

required care in the intensive care unit (ICU) were excluded. Data collected included primary diagnosis of patients and their co-morbid diseases, drug name (either trademarks or generic name), drug dosage form, route of administration, dosage, and the amount of drug administered, total length of stay for typhoid patient in 2012. Samples were patient medical records of hospitalized adult typhoid with complete data on drugs.

Data on drugs were analyzed using the ATC/DDD method to get an overview of drug use. Data on drugs were then traced by name for the active substances then searched for ATC codes and DDD values through the WHO website. Values obtained were then calculated for DDD/hbd and DU 90%.

RESULTS

In general, the total use of antibiotics in hospitalized typhoid patients in the period July to December 2012 amounted to 6.35 DDD/hbd. Table 1 showed that ceftriaxone had the highest DDD/hbd which was 4.10 DDD/hbd. This meant out of 100 typhoid patients, 4 patients received daily ceftriaxone of 2 g per day. The dosage form of ceftriaxone was as an injection.

Table 1. DDD/hbd profile of 10 most widely used antibiotics

Code ATC	Active substance	DDD/shr
J01DD04	Ceftriaxone	4.10
J01MA12	Levofloxacin	0.88
J01MA02	Ciprofloxacin	0.23
J01DH02	Meropenem	0.18
J01XD01	Metronidazol	0.16
J01CR01	Ampicillin-sulbactam	0.10
J01DD16	Cefditoren pivoxil	0.10
J01DD08	Cefixime	0.09
J01DE02	Cefpirom	0.08
J01XX01	Fosfomycin	0.07

Table 2 showed there were more drug items in segment 10% than in segment 90%. From 26 types of antibiotics, 7 types of antibiotics were included in the DU 90% segment namely, ceftriaxone (64.54%); levofloxacin (13.90%); ciprofloxacin (3.57%); meropenem (2.80%); metronidazole (2.52%); ampicillin-sulbactam (1.65%); and cefditoren pivoxil (1.60%).

Table 2. DU 90% profile of antibiotics

ATC Code	Antibiotics	%	% cumulative
J01DD04	Ceftriaxone	64.39	64.39
J01MA12	Levofloxacin	13.87	78.26
J01MA02	Ciprofloxacin	3.56	81.82
J01DH02	Meropenem	2.80	84.61
J01XD01	Metronidazol	2.51	87.12
J01CR01	Ampicillin-Sulbactam	1.65	88.77
J01DD16	Cefditoren pivoxil	1.59	90.36
J01DD08	Cefixime	1.40	91.76
J01DE02	Cefpirom	1.28	93.04
J01XX01	Sodium Fosfomycin	1.08	94.11
J01FA10	Azithromycin	0.93	95.04
J01DE01	Cefepim	0.86	95.90
J01GB03	Gentamycin	0.75	96.65
J01DH51	Imipenem	0.71	97.36
J01DD02	Ceftazidime	0.70	98.06
J01DD12	Sefoperazon	0.63	98.69
J01DD62	Sodium sefoperazon-sulbactam	0.38	99.07
J01GA01	Streptomycin	0.23	99.30
J01CA04	Amoxicillin	0.18	99.47
J01DD01	Cefotaxim	0.15	99.62
J01DB05	Cefadroxil	0.10	99.73
J01CR02	Amoxicillin-clavulanic acid	0.08	99.80
J01EE01	Trimetoprim-sulfamethoxazol	0.08	99.88
J01FA01	Erythromycin	0.05	99.93
J01DB01	Cefalexin	0.04	99.97
J01FA02	Spiramicyn	0.03	100.00

DISCUSSION

From the profile data for DDD/hbd antibiotics obtained, the highest use of ceftriaxone for typhoid was 4.10 DDD/hbd. In 2006, the general use of ceftriaxone in the hospital was 24.627 DDD/hbd for all cases of the disease.⁹ This was consistent with the data obtained in 2011 from the dr. M. Djamil Municipal Hospital in Padang (West Sumatra), where the highest DDD/hbd was for ceftriaxone, with a value of 38.955 DDD/hbd.¹⁰ In 2006, the DU in segment 90% for the treatment of typhoid in the hospital or DDD/hbd ceftriaxone was 24.627 DDD/hbd. Ceftriaxone was used for the treatment of various infectious diseases, the percentage of use for ceftriaxone was 4.10 DDD/hbd for the treatment of typhoid in the hospital which was 16, 65% of the total use of ceftriaxone. The high use of ceftriaxone as antibiotic in the treatment of typhoid was supported by the high incidence of typhoid in the hospital. Therefore, the drug should always be available of in the hospital pharmacy.

There were 7 kinds of antibiotics included in DU 90% segmen from total of 26 kinds of antibiotics. Ceftriaxone had the highest percentage with 64.54%. In 2006, ceftriaxone was also included in the three major segments of DU 90% with the highest percentage of 11.67%.⁹ It showed that the trend for ceftriaxone usage was still high in this hospital. In the Muhammadiyah Hospital Palembang (South Sumatera), ceftriaxone also became the most preferred antibiotic for typhoid (30.77%).¹¹

In the 2013 Indonesian Typhoid Fever Disease Control Guidelines, ceftriaxone was the first-line antibiotics for hospitalized adult patients, while chloramphenicol become first-line therapy for outpatients. Chloramphenicol had disadvantages such as the availability for a sufficient period of time, which can quite often lead to carrier and relapse. While ceftriaxone has the advantages, such as quickly lower body temperature, short duration of administration, can be used as a single dose, and safe enough for children.⁴ A study in 2012 by Juwita *et al* found that in Banjarmasin (South Kalimantan) hospitals, in vitro sensitivity testing of *Salmonella typhi* to antibiotics, showed that *S. Typhi* was still sensitive to chloramphenicol and trimetoprim-sulfamethoxazol, whereas it was resistant to amoxicillin.¹² Each choice of antibiotic use for typhoid should be considered carefully in terms of efficacy, level of sensitivity in each region, price, as well as side effects, and each patient should be evaluated in detail on the factors associated.²

Antibiotics used for treatment of typhoid that were in the 10% DU segment should be replaced by antibiotics that were included in the 90% DU segment. Cefotaxim, ceftazidime, and cefoperazon should be replaced by ceftriaxone, which is still in the same third-generation cephalosporin class. The use of imipenem should be replaced with meropenem which is still in the same carbapenem class, while the use of cefepim could be replaced with cefpirom that is still in the same fourth-generation cephalosporin class. This reduction is expected to be more effectively in terms of cost-effectiveness and the variety of drugs in a hospital formulary can be decreased.

From 26 kinds of antibiotics used for the treatment of typhoid, there were 17 kinds of antibiotics included in the Indonesia National Formulary which is used in the Universal Health Coverage (UHC), including ceftriaxone, levofloxacin, ciprofloxacin, meropenem, metronidazol, cefixime, azithromycin, cefepim, gentamycin, ceftazidime, cefoperazone, streptomycin, cefotaxim, cefadroxil, amoxicillin,

trimetoprim-sulfamethoxazol, and cefalexin. The Indonesian National Formulary is a list of selected drugs which are required and should be available at health facilities.¹³ Ceftriaxone as the first line-therapy for hospitalized typhoid cases has already been included in Indonesian National Formulary.

This study has several limitations, interviews with patients about the symptoms of disease or physicians about the medical consideration on the selection of therapy were not conducted. The bacterial culture results were not check, so diagnosis was taken as stated in the medical records. Data patterns of microbes and microbial resistance patterns of *S. typhi* and *S. paratyphi* were not obtained, so the appropriateness of antibiotics to microbial resistance could not be assessed.

To support the treatment of typhoid, hospitals need to have data pattern on microbes and microbial resistance patterns of typhoid to evaluate the accuracy of the use of antibiotics in the treatment, and avoid the occurrence of microbial resistance. Each antibiotics for typhoid should be considered carefully in terms of efficacy, sensitivity of the bacteria in each region, price, as well as side effects.

In conclusion, antibiotics that are most widely used in the treatment of typhoid in Indonesia Red Cross Hospital in Bogor was ceftriaxone with 4.10 DDD/hbd and DU 90% value of 64.54%. Many variations in the use of third-generation cephalosporin class antibiotics, was less efficient for the hospital.

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