Indonesian Journal of
Tropical and Infectious Disease
Vol. 1. No. 2 May–August 2010

Case Report

Antibiotic Resistance Control Program in Pediatric Hematology and Oncology Patients at Dr. Soetomo Hospital in 2006–2007

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ABSTRACT

Antibiotic resistance has been increasing since the first years of the clinical usage. It caused by inappropriate usage and uncontrol of antibiotic drugs. Therfore an Antibiotic Resistance Control Program (ARCP) is needed to overcome the problem. The purpose of this study is to know microorganism pattern and evaluate antibiotic use. Phase 1 (before ARCP), retrospective study by medical record of pediatric hematology-oncology patients with suspision of infection and admitted at dr Soetomo Hospital from June–August 2006 was carried out. Phase 2 (during ARCP), a prospective observational study was done from November 2006 to January 2007. We were evaluated the isolated microorganism, quantity of antibiotic were determined by Defined Daily Doses (DDD)/100 patients-days, quality of antibiotics usage were assessed with Glyssen classification, and the cost calculation of antibiotic therapy. Twenty seven patients were enrolled in phase 1 and 28 patients in phase 2. Coagulase-negative Staphylococci and Acinetobacter Sp as isolated microorganism was reported. Phase 1, the most sensitive antibiotic was Cefoperazone-Sulbactam and the most resistant was Penicillin G. Phase 2, Meropenem was the most sensitive antibiotic and Cotrimoxazole was the most resistant antibiotic. The use of antibiotics were decreased 6 vs 12 and DDD/100 patients-days were 14.52 vs 45.04. There were improving of Glyssen classification. The cost calculation of antibiotics therapy were decreased. ARCP can improve antibiotic use in pediatric hematology-oncology patients.

Keywords: *pediatric hematology-oncology, antibiotic resistance control program, antibiotic evaluation*

INTRODUCTION

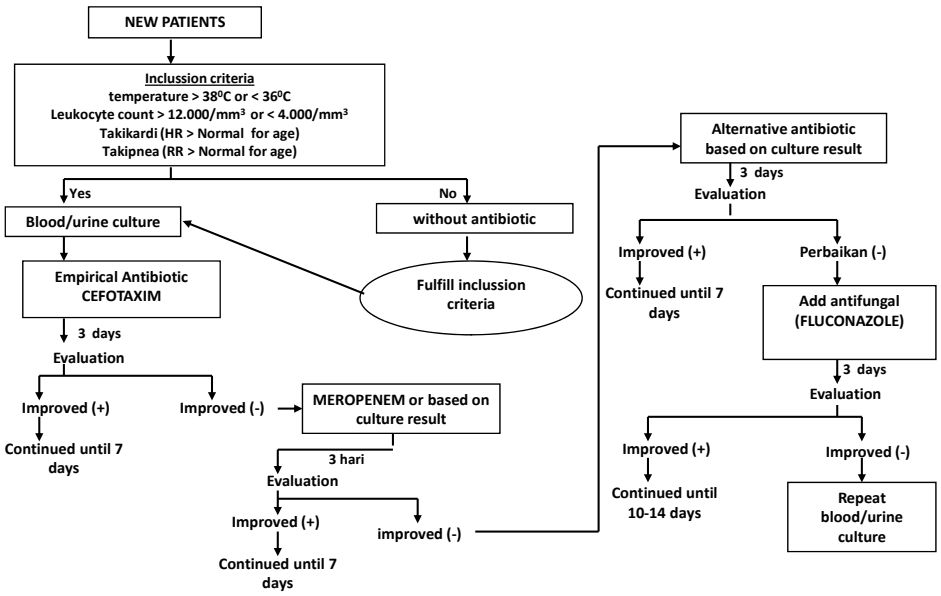
Antibiotic resistance is one of the health problem in the world. Uncontrolled and inappropriate of antibiotic use can increase morbidity and mortality, and also give impact in the quality of health services.[1,2] Antibiotic resistance appear through selection process because of antibiotic overuse and quickly spreading through human contacts.[3] Today, there is many program in the world to overcome antibiotic resistance spreading.[4]

Study of Antimicrobial Resistance in Indonesia (AMRIN study) at Dr. Soetomo hospital was done in 2000–2004. Antibiotic resistance and inappropriate antibiotic use was found, on the other hand infection control has not been done properly.[5] As follow up, Antibiotic Resistency Control Program (ARCP) was performed with Pediatric Hematology Oncology division as a pilot project. The purpose of this study is to know microorganism pattern and evaluate antibiotic use.

METHODS

The study consisted of 2 phase. In phase 1 (before ARCP), retrospective study was done through medical record during June-August 2006. In phase 2 (during ARCP), prospective study was done in November 2006–January 2007. Pediatric hematology oncology patients who were admitted with suspicion of infection were subject of the study. Inclusion criteria were body temperature >38^{o} C or < 36^{o} C, lekocyte count > 12000/cmm or < 4000/cmm, presence of takicardia and/or takipneu. Patients who met the criteria were enrolled the study. In phase 2, will follow antibiotic guidance below (figure 1).

Data study were include patients' characteristic and diagnosis, microorganism isolate from the cultures and result of antibiotic sensitivity tes. Antibiotic usage were evaluated quantitatively with Defined Daily Dose (DDD)/100 patients-days and qualitatively with Gyssen



Fiuture 1. Antibiotic Guideline during Antibiotic resistance Control Program (ARCP)

classification.[6] The DDD represent the average therapeutic dose for an adult for the standard indication. The cost analysis was also evaluated.

RESULTS AND DISCUSSIONS

Twenty seven patients were enrolled in the phase 1, with average age 101,22 (33–108) month-old and average length of stay 29,7 (8–69) days. In phase 2, 28 patients enrolled the study, average age 54,64 (8–69) month-old and average length of stay 29,5 (6–84) days. More than 50% were acute lymphoblastic leukemia patients.

In phase 1, 27 blood cultures was collected, positive results were only found in 17 (37%) cultures. Meanwhile in phase 2, 75 cultures were collected, consisted of 39 blood culture, 19 urine cultures and 7 fecal cultures. Positive results found in 24 (32%) cultures. Similarly study shiwed that positive culture only found in 11 put of 67 patients (16,4%) with febrile neutropenia.[7]

Coagulase-negative Staphylococci was found in 50% blood culture in phase 1 and 44,4% in phase 2. Microorganism isolated in urine cultures were *E coli* ESBL, *Klebsiella pneumoniae*, *Enterobacter aerogenes, Pseudomonas* and *Acinetobacter* sp. *E coli* pathogen serotype 1–11 were found in all of the fecal cultures.

Al-ahwal study showed that 5 out of 11 positive cultures were due to gram-positive microorganism (coagulase-negative *Staphylococci* and *Staphylococcus aureus*), 5 due to gram-negative microorganism (*E coli, Klebsiella* and *P aeruginosa*).[7]

In malignancy patients, the primary anatomic site of infecton is the gastrointestinal tract, where mucosal damage from chemotherapy allows invasion fo microorganism. Damage to the skin from invasive procedures, such as intravascular devices, similarly provides portals of entry for microbes. Bacterial pathogens commonly implicated in neutropenic fever are gram-positive microorganism (*Staphylococcal sp, Streptococcus sp, Enterococcal sp* and *Corynebacterium sp*) and gram-negative microorganism (*E coli, klebsiella sp, Pseudomonas aeruginosa, Enterobacter sp* and *Acinetobacter* sp).[8]

Sensitivity tes was perfomed. In phase 1, sensitive antibiotics were cefoperazone sulbactam, netilmycin and gentamycin. In phase 2, the result were change into meropenem, ciprofloxacin, piperacillin tazobactam and amikacin. Resistent antibiotics in phase 1 were Penicilin G, erithromycin and cotrimoxazole. In phase 2, cotrimoxazole was still resistent followed by cefotaxime and ceftriaxone.

Quantitative and qualitative antibiotic evaluation were done in both phase. Quantity of antibiotics usage were determined by counting DDD/100 patient-days (table 1).

Table 1. Quantitative Antibiotik evaluation

Antibiotics	DDD/100 patient-days	
	Phase 1	Phase 2
Cefotaxime	10.6	7.84
Meropenem	3.6	3.4
Amikacin	2.7	0.5
Ceftazidime	3	0.4
Cloxacillin	7.66	-
Cefepime	0.35	-
Ciprofloxacin	6.3	-
Ceftriaxone	1.34	-
Clindamycin	0.37	-
Cotrimoxazole	7.15	1.5
Gentamycin	0.25	-
Cefoperazone sulb.	1.72	0.88
Total	45.04	14.52

Quantity of antibiotics usage was decreased from 12 to 6 type of antibiotics. DDD/100 patient-days calculation was also decreased from 45,04 (phase 1) to 14,52 (phase 2).

The main problem with DDD is that DDD was made for adults, therefore the result of this study can not be compared with other study in adults.

Table 2. Quality Antibiotic Evaluation

Classification	Phase 1	Phase 2
I (definitely appropriate)	22%	38%
IIA (improper dosage)	0%	0%
IIB (improper dosage interval)	0%	0%
IIC (improper route)	0%	0%
IIIA (excessive length)	46%	30.2%
IIIB (duration too short)	1.6%	1.6%
IVA (more effective alternative agent)	4.7%	11.1%
IVB (less toxic alternative agent)	0%	0%
IVC (less expensive alternative agent)	9.6%	11.1%
IVD (less broad spectrum alternative agent)	11.1%	3.2%
V (unjustified)	5%	4.8%
VI (record insufficient for categorization)	0%	0%

Quality of antibiotic used were assessed with Gyssen clasification (table 2). There was decreased of procentage were found in classification IIIA, IIIB, IVD and V. Increased of procentage was found in clasification I, IVA and IVC.

Similar study by Gyssen in surgery ward showed improvement or quality antibiotics usage. There were increased of category I from 31% to 47% and was decreased of category V form 16% to 8%.[9]

The cost analysis was calculated including cultures and antibiotics usage. This study showed that implementation ARCP could save around Rp 13,135,000 for 27 patients. Gyssen study also found total cost saving of 11% after intervention.[9]

CONCLUSION

From this study we conclude that antibiotic intervention trough ARCP resulted in an improvement of the quantity and quality of antibiotic regimen and in term of costs.

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