ANTIBIOTIC RESISTANCE CONTROL PROGRAM (ARCP) IMPROVING ANTIBIOTIC USE IN PEDIATRIC HEMATOLOGY AND ONCOLOGY PATIENTS AT DR SOETOMO HOSPITAL IN 2006 AND 2008

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ABSTRAK

Resistensi antibiotik terus meningkat secara global sejak beberapa tahun pertama penggunaan klinis. Hal ini terutama didorong oleh tekanan selektif akibat penggunaan obat antibiotik tidak tepat dan tidak terkendali. Tujuan penelitian ini adalah untuk mengetahui mikroorganisme dan pola sensitivitas antibiotik, mengevaluasi penggunaan antibiotik pada pasien hematologi-onkologi anak yang diduga menderita infeksi dan membandingkan hasil ARCP I pada 2006 dan ARCP II pada 2008. Terdapat 28 pasien pada ARCP I dan 23 pasien pada ARCP II. Staphylococcus aureus koagulase negatif adalah mikroorganisme yang paling sering dijumpai pada kedua periode, tersering ditemukan pada kultur darah PPRA I dan II. Pada ARCP I dan II, Meropenem adalah antibiotik yang paling sensitif dan Kotrimoksazol adalah antibiotik yang paling resisten. Meskipun DDD/100 pasien-hari meningkat, tetapi ada perbaikan klasifikasi Glyssen. ARCP dapat meningkatkan penggunaan antibiotik pada pasien hematologi-onkologi anak.

ABSTRACT

Antibiotic resistance is on the rise globally since the first years of the clinical use. It mainly driven by selective pressure imposed by inappropriate use and uncontrol of antibiotic drugs. The purpose of this study is to know microorganism and antibiotic sensitivity pattern, to evaluate antibiotic use in pediatric hematology-oncology patients with suspected suffered from infection and compare the results of ARCP I in 2006 and ARCP II in 2008. Twenty eight patients enrolled ARCP I study, meanwhile 23 patients in ARCP II. Staphylococcus aureus coagulase negative was the most common microorganisme shown in both periods, most frequently found in blood culture PPRA I dan II. In ARCP I and II, Meropenem was the most sensitive antibiotic and Cotrimoxazole was the most resistant antibiotic. Although DDD/100 patients-days increased, but there were improving of Glyssen classification. ARCP can improve antibiotic usage in pediatric hematology-oncology patients.

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

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INTRODUCTION

Antibiotic resistance is one of the health problem in the world and on the rise globally since the first years of the clinical use. It mainly driven by selective pressure imposed by inappropriate use and uncontrol of antibiotic drugs (Nouwen 2006). Antibiotic resistance appear through selection process because of antibiotic overuse and quickly spreading through human contacts. Uncontrolled and inappropriate of antibiotic use can increase morbidity and mortality, and also give impact in the quality of health services (Widodo 2010, Saudimenge et al. 2006; Larson et al. 2007). Antibiotics are the most commonly prescribed drugs in hospital. The major reason that antibiotics are prescribed inappropriately is that there is a lack of knowledge about infectious disease and doctors are afraid not to administered it.

Survey by Larson (2007) in 33 hospital in USA found out that Resistance rates for S aureus, enterococci and K pneumoniae were 52.5%, 18.2% and 16% respectively. This condition advocate the development and implementation of programs for monitoring antibiotic use and resistance and also advocate promoting appropriate antibiotic use and effective infection control.

Antibiotic Resistency Control Programme (ARCP) in Dr Soetomo Hospital was first done in 2006 with Pediatric Hematology Oncology division as a pilot project. This program was evaluated in 2008 based on previous results. Objective of this study is to know microorganism and antibiotic sensitivity pattern and also to evaluate antibiotic use quantitatively and qualitatively.

MATERIALS AND METHODS

Prospective studies were done. ARCP I was conducted in November 2006-January 2007, meanwhile ARCP II was conducted in November 2008-January 2009. Pediatric hematology oncology patients who were hospitalized 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. Patient who met the criteria were enrolled the study and followed antibiotic guidance in Figure 1. Data study were include patients' characteristic, microorganism isolate from the cultures and result of antibiotic sensitivity test. Antibiotic use were evaluated quantitatively with Defined Daily Dose(DDD)/100 patients-days and qualitatively with Gyssen classification.

RESULTS

Twenty eight patients enrolled ARCP I with average age 54.64 (8-69) month-old and average length of stay 29.5 (6-84) days.Twenty three patients were enrolled in ARCP II, with average age 69.6 (6-168) month-old and average length of stay 33.9 (4-155) days. In ARCP I, 75 cultures was collected, consisted of 39 blood culture, 19 urine cultures and 7 fecal cultures and microorganism grew only in 24 (32%) cultures. Meanwhile in ARCP II, 61 cultures was collected, consisted of 24 blood culture, 31 urine cultures and 6 fecal cultures and microorganism grew in 26 (42.6%) cultures.

Staphylococcus coagulase negative was the most frequent microorganism found in blood culture in the ARCP I (44.4%) and also ARCP II (75%). The most frequent microorganism grow in urine culture was E coli ESBL (ARCP I) and Pseudomonas (ARCP II). E coli pathogen serotype 1-11 was found in all of the positive fecal cultures. Sensitivity tes was perfomed. Meropenem, Piperacillin Tazobactam and Amikacin were the most sensitive antibiotics in both periods (figure 2 and 3). Cotrimoxazole was the most resistance antibiotics in ARCP I and ARCP II (figure 4 and 5).
Quantitative and qualitative antibiotic evaluation was done. Quantity of antibiotic use was determined by counting DDD/100 patient-days (table 1). DDD/100 patient-days calculations increased from 14.52 (ARCP I) to 15.47 (ARCP II).

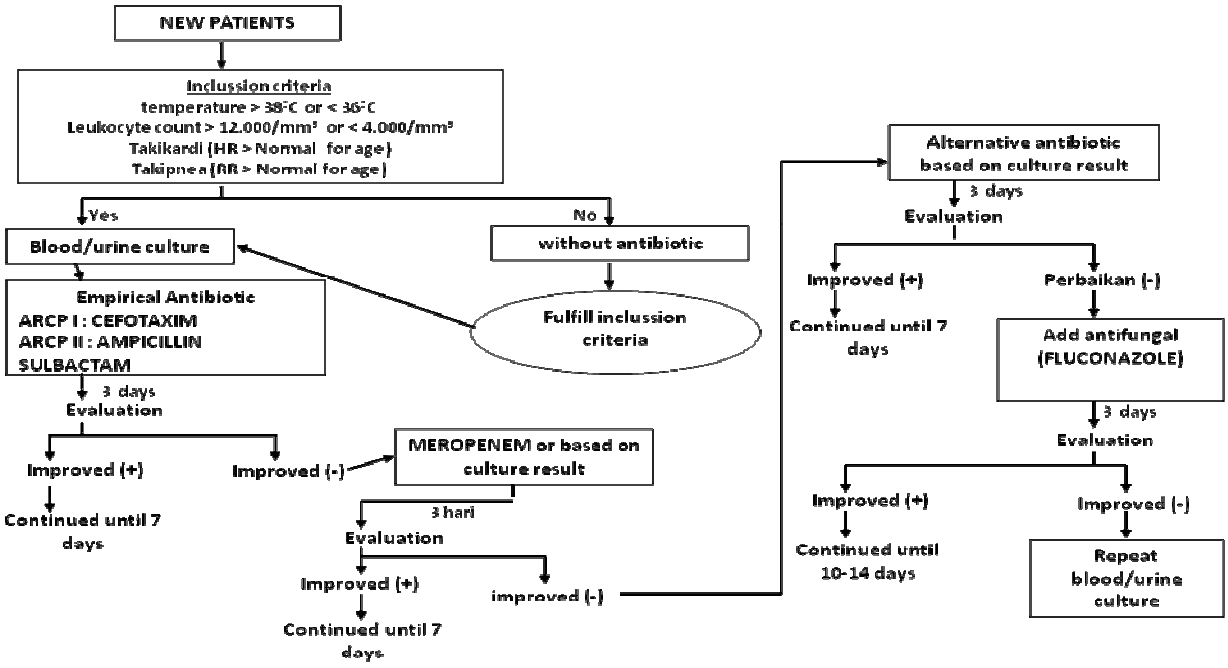

Fig 1. Antibiotic Guideline during Antibiotic resistance Control Program (ARCP)

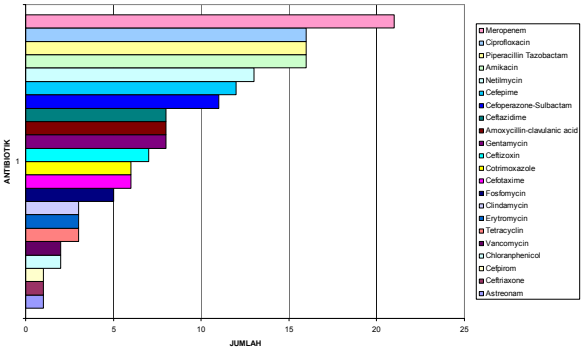

Fig 2. Sensitive antibiotics in ARCP I

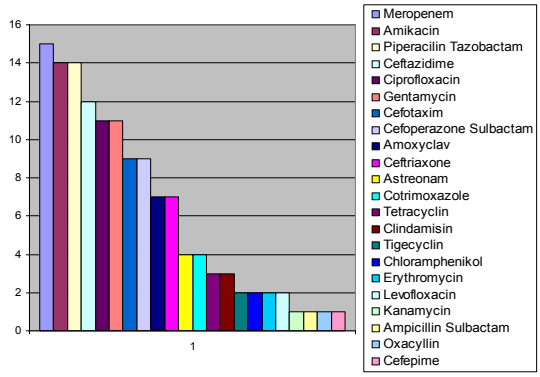

Fig 3. Sensitive antibiotics in ARCP II

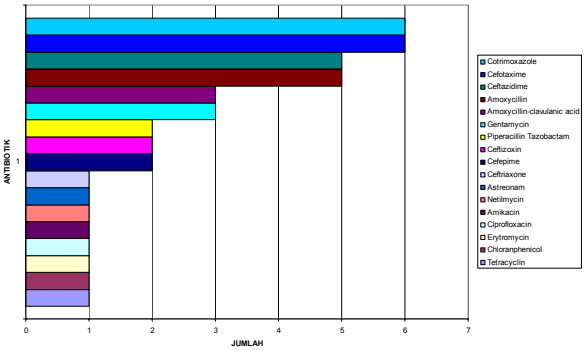

Fig 4. Resistance antibiotics in ARCP I

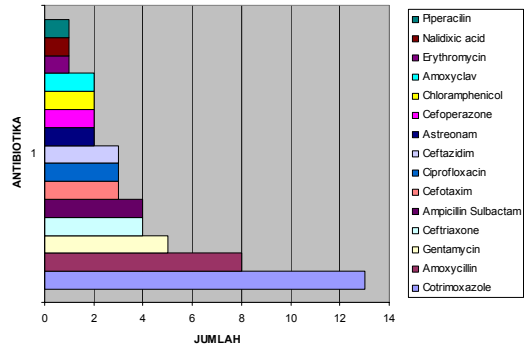

Fig 5. Resistance antibiotics in ARCP II

Table 1. Quantitative Antibiotic evaluation

Antibiotics	DDD/100 patient-days	
	ARCP I	ARCP II
Cefotaxime	7.84	-
Meropenem	3.4	1.3
Amikacin	0.5	0.96
Ceftazidime	0.4	-
Ceftriaxone	-	0.26
Cotrimoxazole	1.5	0.4
Gentamycin	-	1.1
Cefoperaozone sulbactam	0.88	0.84
Ampicilin sulbactam	-	8.09
Amoxycillin clavulanic acid	-	1.5
Total	14.52	15.47

Quality of antibiotic use was assessed with Gyssen clasification (Table 2). There was decreased of prosentage in classification IIIA, IIIB, IVC, IVD and V., on the other and increased of prosentage was found in clasification I, IIA and IIIB.

Table 2. Qualitative Antibiotic Evaluation

Classification	ARCP I	ARCP II
I (definitely appropriate)	38%	55.3%
IIA (improper dosage)	0%	7,9%
IIB (improper dosage interval)	0%	0%
IIC (improper route)	0%	0%
IID (improper time)	0%	0%
IIIA (excessive length)	30.2%	23.6%
IIIB (duration too short)	1.6%	2.6%
IVA (more effective alternative agent)	11.1%	2.6%
IVB (less toxic alternative agent)	0%	0%
IVC (less expensive alternative agent)	11.1%	5.3%
IVD (less broad spectrum alternative agent)	3.2%	0%
V (unjustified)	4.8%	0%
VI (record insufficient for categorization)	0%	0%

DISCUSSION

This study provide result of antibiotics intervention to control antibiotics use through ARCP in 2006 and 2008. This study also provide microorganism and antibiotic sensitivity pattern in pediatric hematology oncology patients. All patients with suspected suffered from infection were enrolled the study and followed the antibiotic guideline. The antibiotic guideline of ARCP I and ARCP II was similar overall, only differed in first empirical antibiotic. In ARCP I, the empirical antibiotic was cefotaxim which was changed into Ampicillin

sulbactam in ARCP II based on the microorganism and antibiotic sentivity pattern of ARCP I.

Microorganism grew in 32% cultures in ARCP I and increased to 42.6% in ARCP II. Study by Al-Ahwal (2005) showed that positive culture only found in 11 out of 67 patients (16.4%) with febrile neutropenia. Increasing of positive blood cultures might be due to the time of cultures was taken. If the cultures was taken before antibiotics was administered, the possibility to have positive culture was higher.

Microorganism pattern in this study showed that Staphylococcus coagulase negative was the most frequent microorganism found in blood culture both in the ARCP I and II. Different patogen was found in urine culture, that was E coli ESBL in ARCP I and Pseudomonas in ARCP II. E coli pathogen serotype 1-11 was found in all of the fecal cultures.

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 and gram-negative microorganism (Kannangara 2006). It was proven by Al-Ahwal (2005) which was shown the most common etiology microorganism was gram-positive microorganism (Staphylococcus coagulase-negative and Staphylococcus aureus).

Meropenem, Piperacillin Tazobactam and Amikacin were the most sensitive antibiotics in both periods. Nevertheless we couldn't use this kind of antibiotics as a first line empirical antibiotic, because initially we have to use antibiotics which was less toxic but still efective enough.

Antibiotics use was evaluated quantitatively and qualitatively. Quantitative antibiotic evaluation was calculated with DDD/100-patient days. In our study, the quantitative increased in ARCP II, it might be due to older patients with heavier body weight. The main problem of using DDD as an evaluation tool is that DDD was made for adult, therefore the result of this study can not be compared with other study in adult. Meanwile in pediatric patients, the dose always be calculated by body weight. Therefore a patient with heavier body weight might have greater DDD.

Quality of antibiotic use was assessed with Gyssen clasification (Gyssen et al. 1992). There was decreased of prosentage in classification IIIA, IIIB, IVC, IVD and V, on the other hand increased of prosentage was found in clasification I, IIA and IIIB. Study by Gyssen (1996) in surgery ward showed improvement or quality antibiotic use. There were increased of category I from 31% to 47% and decreased of category V form 16% to 8%. In this study, although appropriate antibiotics use increased from 38% to 55.3% but there was also increasing improper antibiotic dosage (0% to 7.9%), therefore reguler evaluation and socialization of this program was still needed.

CONCLUSION

This study reveal that microorganism and antibiotic sensitivity pattern was not differ in both periods. Antibiotic controlling through ARCP resulted in an improvement of the quantity and quality of antibiotic regimen. Reguler socialization and evaluation was needed to keep the effectiveness of this program with the goal to prevent antibiotics resistance.

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