EVALUATION OF EDUCATIONAL INTERVENTION PROGRAM ON APPROPRIATE ANTIMICROBIAL USAGE IN DEPARTMENT OF CHILD HEALTH, INDONESIA

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Abstract. Inappropriate use of antimicrobials is one of the factors that accelerate antimicrobial resistance. One of the applicable methods of antimicrobial stewardship program is education of clinicians. An interventional study was carried out to evaluate qualitatively antimicrobial use in the Department of Child Health, Cipto Mangunkusumo Hospital, Jakarta, Indonesia before and after education intervention of medical staff regarding appropriate antimicrobial use. The intervention program consisted of courses and dissemination of empiric antimicrobial therapy guideline cards. Qualitative analysis of antimicrobial use was performed by two independent clinicians using a Gyssens algorithm. Data was obtained from patients medical records during pre-intervention period (December 2015 - February 2016) and post-intervention period (April 2016 - June 2016). Antimicrobial use decreased from 374 to 339 times after intervention education. Appropriate antimicrobial use (Category I) prior-intervention was 58% and significantly increased to 67% post-intervention (p-value = 0.01). Inappropriate antimicrobial use was categorized as insufficient data (Category VI: 2 prior- and 1 post-intervention), no indication (Category V: 24 prior- and 11 post-intervention), inappropriate antimicrobial choice (Category IV: 56 prior- and 43 post-intervention), incorrect duration (Category III: 53 prior- and 32 post-intervention), incorrect dosage (Category IIa: 39 prior- and 29 post-intervention), incorrect dosage interval (Category IIb: 23 prior- and16 post-intervention), and incorrect route of dosing (Category IIc: none). Thus, the educational intervention program has a significant effect on appropriate antimicrobial use by medical staff at the Department of Child Health, Cipto Mangunkusumo Hospital, Jakarta.

Keywords: antimicrobial use, educational intervention program, Gyssens algorithm, medical staff, qualitative analysis.

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INTRODUCTION

Antimicrobial resistance poses a threat and challenge to the global medical world. It increases morbidity, mortality and hospital cost. Appropriate antimicrobial usage, namely, antimicrobial choice,

dosage and treatment duration, through an antimicrobial stewardship program can prevent or delay antimicrobial resistance (Shlaes *et al*, 1997; Dellit *et al*, 2007).

During the past decade, development of new antimicrobials has decreased, with only a few new antimicrobials introduced every year, raising concerns that new antimicrobial development will not be able to cope with the growing antimicrobial resistance (Freire-Moran *et al,* 2011). Efforts to improve infectious disease therapy by using antimicrobial wisely and more selective have been advocated (Chambers, 2001). Studies at Cipto Mangunkusumo Hospital (CMH), Jakarta, Indonesia in 2011 showed antimicrobials were used for 49.2% patients in the Pediatric Intensive Care Unit, with 48.3% deem inappropriate (Yuniar *et al*, 2013).

One method recommended in an antimicrobial stewardship program is providing education on appropriate antimicrobial use (Shlaes *et al*, 1997, Dellit *et al*, 2007). Previous studies showed educational intervention results in improvement in appropriate antimicrobial use (Apisarnthanarak *et al*, 2006, Hadi *et al*, 2008, Thamlikitkul *et al*, 1998). There is still a lack of data on the effectiveness of educational intervention in control and appropriate antimicrobial use at CMH. Thus, a study was conducted to evaluate antimicrobial usage among medical staff of the Department of Child Health, CMH before and after an education intervention program on appropriate antimicrobial use.

MATERIALS AND METHODS

Education intervention program

The education intervention program was conducted by an antimicrobial resistance control program (ARCP) team to medical staff of the Department of Child Health, CMH. The program consisted of lectures, lecture materials and cards containing guidelines on empirical antimicrobial use.

Data collection and analysis

Medical records of in-patients of the Department of Child Health, CMH, Jakarta, Indonesia were retrieved for a period of three months (December 1, 2015 to February 29, 2016) prior to education intervention program and for a period of three months (April 1 to June 30, 2016) following the intervention program. Inclusion criterion was patients 1 month to ≤18 years of age given intravenous antimicrobial. Exclusion criteria were patiens with incomplete medical records, only given oral antimicrobial, or prescribed antimicrobial by attending physician from another department. A qualitative analysis of antimicrobial use was performed using a Gyssens algorithm (Gyssens, 2005) (Fig 1**)** by two independent clinicians.

The study protocol was approved by the Faculty of Medicine, Universitas Indonesia-CMH Research Ethical Committee (239/UN2.F1/ETIK/2016).

RESULTS

Patients meeting the inclusion criterion (n = 343) consisted of 171 in pre-interventional period and 173 in post-interventional period, male:female ratio of 6:4, and mainly between 1 year and 5 years of age; the attending physicians were mainly from the hematology unit (Table 1). Hospitalization duration and clinical outcome were not significantly different pre- and post-education intervention.

Total number of antimicrobial uses was 713 times over the period of the study (Table 2). Major indication of antimicrobial use was respiratory tract

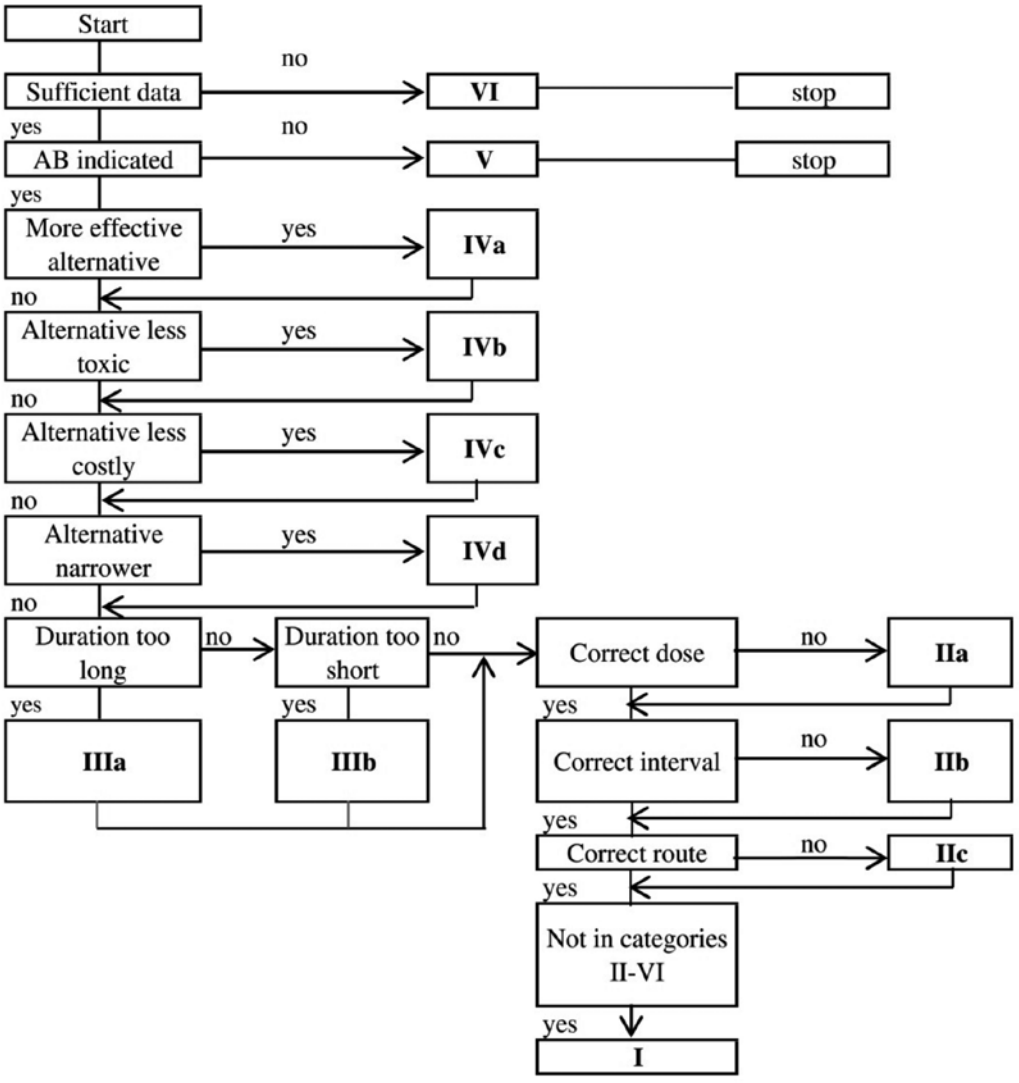

Fig 1-Schematic diagram of Gyssens algorithm (adopted from Gyssens, 2005). Categories are identified by Roman numerals. Category I: Appropriate; Category IIa: Incorrect dose; Category IIb: Incorrect interval; Category IIc: Incorrect route; Category IIIa: Too long duration; Category IIIb: Too short duration; Category IVa: More effective alternatives; Category IVb: Less toxic alternatives; Category IVc: Less costly alternatives, Category IVd: Narrower spectrum alternatives; Category V: No indication; Category VI: Insufficient data.

infection both pre- and post-intervention. Major type of treatment was empirical, and this did change following the education intervention program. Adverse reaction to antimicrobial treatment was ≤0.5%. Appropriate use of antimicrobials (Category I) significantly increased following the education intervention program (Table 3). The major cause of inappropriate antimicrobial use was

Table 1
Characteristics of study subjects at the Department of Child Health, Cipto Mangunkusumo Hospital, Jakarta, Indonesia.

Characteristics	Pre-education intervention program Number (%) (n = 171)	Post-education intervention program Number (%) (n = 172)	p-value
Gender			0.88
Male	106 (62.0)	108 (62.8)	
Female	65 (38.0)	64 (37.2)	
Age group			0.53
1 month - <1 year	8 (22.2)	50 (29.1)	
1 year - <5 years	73 (42.7)	65 (37.8)	
5 years - <10 years	23 (13.5)	21 (12.2)	
>10 years	37 (21.6)	36 (20.9)	
Department of admittance			0.28
Hematology	65 (38.0)	45 (26.2)	
Respirology	30 (17.6)	36 (20.9)	
Gastrohepatology	24 (14.0)	24 (14.0)	
Neurology	19 (11.1)	18 (10.5)	
Nephrology	12 (7.0)	14 (8.1)	
Infection	6 (3.5)	10 (5.8)	
Nutrition and metabolic	5 (2.9)	3 (1.7)	
Cardiology	4 (2.3)	6 (3.5)	
Pediatric emergency	3 (1.8)	9 (5.2)	
Allergy / immunology	3 (1.8)	7 (4.1)	
Hospitalization duration median (range) in days	10 (0-65)	10 (1-66)	0.67
Clinical outcome			0.88
Recovered	151 (88.3)	147 (85.4)	
Worsen / referred	2 (1.2)	2 (1.2)	
Died	17 (9.9)	22 (12.8)	
Discharged	1 (0.6)	1 (0.6)	

incorrect dosage (Category IIa), which did not change following intervention, but there were significant improvements in recognition for antimicrobial therapy (Category V) and appropriate duration of medication (Category IIIb). Based on type of infection as an indicator of antimicrobial use, following intervention appropriate antimicrobial usage significantly increased only for urinary tract infection, and worsened for skin / soft tissue infection (Table 4).

Among the top ten most frequently prescribed antimicrobials, cefotaxime was the most frequently used, followed by ceftazidime, ceftriaxone, amikacin, meropenem, ampicillin-sulbactam, metronidazole, gentamicin, ampicillin,

Table 2
Characteristics of antimicrobial use at the Department of Child Health, Cipto Mangunkusumo Hospital, Jakarta, Indonesia.

Characteristic	Pre-education intervention program Number (%) (n = 374)	Post- education intervention program Number (%) (n = 339)	p-value
Indicator of antimicrobial use			
Respiratory tract infection	87 (23.2)	117 (34.5)	
Urinary tract infection	50 (13.4)	31 (9.1)	
Gastrointestinal tract infection	49 (13.1)	41 (12.1)	
Febrile neutropenia	41 (11.0)	27 (8.0)	
Blood stream infection	40 (10.7)	22 (6.5)	
Skin / soft tissue infection	26 (7.0)	15 (4.4)	
Central nervous system infection	10 (2.7)	4 (1.2)	
Others	51 (13.6)	72 (21.2)	
No indication	14 (3.7)	1 (0.3)	
No infection	6 (1.6)	9 (2.7)	
Choice of therapy			0.6
Empiric	306 (81.8)	287 (84.7)	
Definitive	64 (17.1)	49 (14.4)	
Prophylactic	4 (1.1)	3 (0.9)	
Adverse reaction	2 (0.5)	0 (0)	

and chloramphenicol (Table 5). Following intervention significant increase in apropriateness of antimicrobial use was observed for ceftazidime and marginally significant for ampicillin, while appropriate use of the other eight drugs remained unchanged.

DISCUSSION

One factor contributing to the development of antimicrobial resistance is inappropriate use of these drugs by physicians (Shlaes *et al*, 1997, Dellit *et al,* 2007). This was the first study of an education intervention program for medical staff of the Department of Child Health, CMH to increase appropriate use of antimicrobials. Percent patients prescribed antimicrobials enrolled in the study (89%, data not shown) was lower than a previous study (98%) (Satari *et al*, 2011) as the present study was limited to patients receiving medication intravenously.

There was a modest drop (5%) in use of antimicrobials post-intervention, a lower percent compared to previous studies, *viz* 22% conducted at tertiary care university hospital in Bangkok, Thailand (Thamlikitkul *et al*, 1998), 24% at Thammasart University Hospital, Thailand (Apisarnthanarak *et a*l, 2006) and 17% at Dr Soetomo Hospital, Indonesia (Hadi *et al*, 2008). Appropriate antimicrobial use pre-intervention was higher than that (39.6%) previously reported among pediatric in-patients at CMH (Satari *et al*, 2011). Appropriate antimicrobial

Table 3
Categories of antimicrobial use at the Department of Child Health, Cipto Mangunkusumo Hospital, Jakarta, Indonesia.

Category	Pre-education intervention program Number (%) (n = 374)	Post-education intervention program Number (%) (n = 339)	p-value
Category I			
Appropriate antimicrobial use	218 (58.2)	228 (67.2)	0.01
Category II			
a. Incorrect dose	39 (10.4)	29 (8.5)	0.31
b. Incorrect interval	23 (6.1)	16 (4.7)	0.34
c. Incorrect route	0 (0)	0 (0)	N / A
Category III			
a. Too long duration	32 (8.5)	27 (8.0)	0.67
b. Too short duration	21 (5.6)	5 (1.5)	0.002
Category IV			
a. More effective alternatives	35 (9.3)	23 (6.8)	0.16
b. Less toxic alternatives	1 (0.3)	1 (0.3)	1.00
c. Less costly alternatives	11 (2.9)	13 (3.8)	0.57
d. Narrower spectrum alternatives	9 (2.4)	6 (1.8)	0.51
Category V			
No indication	24 (6.4)	11 (3.2)	0.05
Category VI			
Insufficient data	2 (0.5)	1 (0.3)	1.00

N / A: not applicable.
The percentages in this Table exceed 100 in total because a single antimicrobial usage might be categorized more than once.

post-educational intervention rose 5% (from 218 to 228 times, a modest but significant increase, in agreement with that (9%) reported by Hadi *et al* (2008), but markedly lower increase than that (69%, from 1808 to 566 times) reported by Apisarnthanarak *et al* (2006). These discrepancies were probably due to differences in interventional method applied as well as assessment method.

Significant increases in appropriate antimicrobial use post-intervention were in the categories of recognition for antimicrobial therapy and appropriate duration of medication. This was in line with the study of Yuniar *et al* (2013) conducted at CMH, Indonesia and probably stems from guidelines provided to medical residents who, in general, are in charge of the patients based on available guideliness. Post-intervention improved appropriate antimicrobial usage significantly increased only for urinary tract infection, and worsened for skin / soft tissue infection. This is probably because of the antibiotic guidelines for urine tract infections remain the same based on bacterial pattern, whereas the

Table 4
Appropriate antimicrobial use according to indicator of antimicrobial use at the Department of Child Health, Cipto Mangunkusumo Hospital, Jakarta, Indonesia.

Indication of antimicrobial use	Pre-education intervention program		Post-education intervention program		*p*-value
	Total number	Appropriate Number (%)	Total number	Appropriate Number (%)	
Respiratory tract infection	87	61 (70.1)	117	83 (70.9)	0.90
Urinary tract infection	50	25 (50.0)	31	25 (80.6)	0.01
Gastrointestinal tract infection	49	34 (69.4)	41	30 (732)	0.69
Febrile neutropenia	41	22 (53.6)	27	16 (59.3)	0.65
Blood stream infection	40	25 (62.5)	22	15 (68.2)	0.65
Skin / soft tissue infection	26	16 (61.5)	15	8 (53.3)	0.61
Central nervous system infection	10	6 (60.0)	4	3 (75.0)	1.00
Others	51	29 (56.9)	72	47 (65.3)	0.34
No indication	14	0 (0)	1	0 (0)	NA
No infection	6	0 (0)	9	1 (0.1)	1.00

Table 5
Appropriate use of ten most frequently prescribed antimicrobials at the Department of Child Health, Cipto Mangunkusumo Hospital, Jakarta, Indonesia.

Antimicrobial	Pre-education intervention program		Post-education intervention program		*p*-value
	Total number	Appropriate Number (%)	Total number	Appropriate Number (%)	
Cefotaxime	118	62 (52.5)	125	76 (60.8)	0.19
Ceftazidime	40	23 (57.5)	41	32 (78.0)	0.05
Ceftriaxone	28	13 (46.4)	20	14 (70.0)	0.11
Amikacin	24	15 (62.5)	23	18 (78.3)	0.24
Meropenem	25	19 (76.0)	22	15 (68.2)	0.55
Ampicillin-sulbactam	30	18 (60.0)	12	10 (83.3)	0.28
Metronidazole	16	10 (62.5)	16	8 (50.0)	0.48
Gentamicin	20	16 (80.0)	11	6 (54.5)	0.22
Ampicillin	10	6 (60.0)	15	15 (100.0)	0.06
Chloramphenicol	10	6 (60.0)	16	14 (87.5)	0.12

antibiotic guidelines for skin / soft tissue need to be disseminated more often based on the latest bacterial pattern.

Treatment with meropenem, a third-line antibiotic, requires permission of the ARCP team, which has an evaluation system in the form of periodic meetings at all CMH clinical departments, but the most recent evaluation did not appear to be effective in improving the appropriateness of the use of this antibiotic at the Department of Child Health. Raveh *et al* (2006) at Jerussalem were able to increase appropriate use of meropenem from 82% to 85% after an intervention program consisting of notification of survey results on antimicrobial use prior to the intervention and dissemination of guidelines of appropriate antimicrobial use during a staff meeting post-intervention. Proper usage of meropenem at the Department of Child Health, CMH warrants further attention.

Appropriate usage of cefotaxime, ceftazidime and ceftriaxone before intervention was low. Currently cephalosporin is the most widely used class of antimicrobials because of its wide spectrum of activity, good safety profile, as well as favorable effectiveness (Jyothi and Jagadish Babu, 2012). Antibiogram profiling conducted from July to December 2015 showed reduced bacterial low susceptibillity towards cefotaxime (46.6%) and ceftriaxone (48.2%) (Kumalawati, 2016). However, in the present study intervention resulted in significant increase in appropriate use of ceftazidime and possibly of ampicillin. It should be noted that targets of these two antimicrobials are different; while ceftazidime is administered in gram-negative bacterial infections mostly hospital-based *Pseudomonas*, ampicillin targets gram-positive community-based bacterial infection. Clinicians should pay more attention to the use of cephalosporins to prevent further increase in resistant pathogens. Sustainable education needs to be reinforced to improve selective use of cephalosporins based on the guidelines of empirical antibiotic use. Borde *et al* (2014) reported intervention consisting of revision of guidelines, education, periodic ARCP rounds, intensification of consultations with ARCP team, as well as sharing of feedbacks are effective in reducing inappropriate use of cephalosporins.

In conclusion, the education intervention program on appropriate antimicrobial use conducted with medical staff of the Department of Child Health, Faculty of Medicine, Cipto Mangunkusumo Hospital achieved some improvement but further continual interventions will be needed if the rise in antimicrobial resistance is to be prevented.

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