

The Benefit of Education and Appropriate Antibiotics Use to Reduce Multidrug-Resistant *Acinetobacter baumannii* in a University-Affiliated Intensive Care Unit in Indonesia

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Abstract

Acinetobacter baumannii is an opportunistic pathogen known to cause hospital acquired infection presenting with varying clinical feature from simply to much more severe manifestation. More importantly, widely improper and overuse of antibiotics consumption have caused an endemic of multidrug-resistant-*Acinetobacter baumannii* leading to prolonged hospital stay and poorer prognosis for intensive care patients. A descriptive study of pre- and post-education was conducted at an intensive care setting in Indonesia. The microbiology data were collected to evaluate the benefit of education on hand hygiene and management of antibiotic use to reduce the number of MDR-*Acinetobacter baumannii* infection. Based on the result of previous local susceptibility patterns, Cefoperazone/Sulbactam and Amikacin are favored as the empirical therapy. Chi-square analysis shows the significant reduction of *Acinetobacter baumannii* cases from 70.8% (17/24) to 38% (3/8) with *P*-value 0.006. Similarly, the susceptibility rate significantly increased, from 21% to 100% to Amikacin; from 5% to 89% to Piperacillin/Tazobactam, and from 42% to 89% to Meropenem. Education improving around hand hygiene, appropriate antibiotic prescribing following local hospital guidelines and the result of antibiotic susceptibility has been shown to reduce the transmission of MDR-*Acinetobacter baumannii* in the intensive care in our unit within this Indonesian hospital.

Keywords

Acinetobacter baumannii, Hand Hygiene, Antibiotic Prescribing, Intensive Care

1. Introduction

Acinetobacter spp. is non-fermentative gram-negative coccobacillus which has been increasing recently in accordance with rising cases of multi-drug resistant organisms [1] [2]. The most important characteristics of *Acinetobacter baumannii* are its high survival ability and resistance to wide range of antimicrobials [3] [4]. The clinical feature is ranging from colonization to severe manifestation [1] [2]. This condition is often met in hospitalized patients with severe illness and impaired host defense that needs medical support. The major manifestation of the infection varies from pneumonia, soft tissue infection, urinary tract infection, meningitis, and bacteraemia [5] [6].

Acinetobacter baumannii crude death rate is comparable to other gram-negative bacteria (28% to 32%) [1] [5], and the epidemic of this bacteria has become a global threat [7]. One of the primary causes of this phenomenon is uncontrolled use of antimicrobials in both of the community and hospital [8] [9]. Furthermore, the lack of resources, inadequately trained healthcare workers on education around hand hygiene, good knowledge of antibiotics and microbiology specimens handling supported this problem especially in developing countries [10]. MDR-*Acinetobacter baumannii* can lead to the poorer prognosis of the patients in intensive care and hospital infection control has to be done to prevent transmission among patients and healthcare workers. Therefore, strategy on education and appropriate antibiotics use is essential in order to reduce health care-associated infections. In this study, we sought to evaluate the benefit of hand hygiene promotion on health care worker and appropriate antibiotic use in reducing the number of MDR-*Acinetobacter baumannii* infection among intensive care patients.

2. Materials and Methods

This study was approved by Mochtar Riady Institute for Nanotechnology Ethics Committee (042/MRIN-EC/11/2013). This study was conducted in intensive care unit of a University of Pelita Harapan-affiliated hospital located in Tangerang, Indonesia and consisted of two steps. The first was data of antibiotic susceptibility patterns from June 2012-June 2013. The second step was initiated in September 2013 in the form of education on microbiology specimen handling, hand hygiene and socialization of appropriate antibiotic use to health workers and clinicians. Second data gathering on antibiotic susceptibility patterns was held in October 2013-March 2014. Discussion with clinicians, clinical microbiologists, and clinical pharmacologist with the help of local antibiotic guideline was done to select an appropriate antibiotic therapy.

Clinical samples were inoculated directly onto Columbia blood agar base[®] (Difco[™]) with sheep blood agar 5% and Mac Conkey agar (Difco[™]). Blood samples were cultured using a BD BACTEC[™] blood culture system. All positive blood cultures were sub-cultured onto the same agar. *Acinetobacter baumannii* identification and antimicrobial susceptibility testing was completed using an automated method from VITEK-2 Compact[®] (Biomérieux, France) and CLSI (Clinical Laboratory and Standards Institute) protocols [11]. *Escherichia coli* ATCC[®] 25,922 and *Pseudomonas aeruginosa* ATCC[®] 27,853 were used as control isolate for susceptibility testing.

Isolate distribution data and antibiotic sensitivity were compiled using WHOnet software (WHOnet 5.4) and analyzed with STATA version 10.0. Statistical significance was calculated by using chi-squared analysis. A *P*-value < 0.05 was defined to be statistically significant.

3. Results

Table 1 showed the total number of culture examination during pre-education and post-education. Sputum was the most common cultured specimen in the period of June 2012-June 2013 with total percentage of 84.5% (33/39), followed by blood 13% (3/39) and bronchial secretion 2.5% (1/39). In June 2012-June 2013, a total of 23/39 (60%) patients were suffering from bacterial infection consist of *Acinetobacter baumannii* 17/24 (70.8%), *Acinetobacter iwoffii* 1/24 (4.2%), *Pseudomonas aeruginosa* 2/24 (8.3%), and 16.7% gram positive bacteria isolates (**Figure 1**).

In post-education periode, *Pseudomonas aeruginosa* 4/13 (30.7%) was the most common organism, followed by *Acinetobacter baumannii* 3/13 (23%). *Staphylococcus aureus* and Coagulase negative staphylococci (CoNS) isolates consisted of *Staphylococcus capitis* 1/13 (7.7%), *Staphylococcus hominis* 1/13 (7.7%), *Staphylococcus hemolyticus* 1/13 (7.7%), *Staphylococcus saprophyticus* 1/13 (7.7%) were the highest isolates found in October 2013 to March 2014 (**Figure 1**). Our study also identify 7 cases *Candida* infection before education program dan

8 cases after education program.

Based on the result of antibiotic susceptibility patterns pre-education step, Cefoperazone/Sulbactam and Amikacin were used as empirical therapy (Table 2). Even though Amikacin sensitivity was only 21.4%, this antibiotic was still used as combination therapy for *Acinetobacter baumannii*, *Pseudomonas aeruginosa* and *Klebsiella pneumoniae*. We used local antibiotic usage guideline developed from the existing published guidelines and the result of antibiotic susceptibility testing post-education to assess the appropriateness of antibiotic use.

Almost all of *Acinetobacter baumannii* isolate in this study were multi-drug resistant. The antibiotic susceptibility rate of *Acinetobacter baumannii* to 9 antibiotic regimens is highlighted in Table 3. The outcome of a com-

Table 1. Type of specimen for culture examination during pre-education and post-education.

Type of specimen	Pre-education (n = 39)	Post-education (n = 62)
Urine	0 (0.0%)	2 (3.2%)
Sputum	33 (84.5%)	28 (45.2%)
LCS	0 (0.0%)	1 (1.6%)
Blood	5 (13%)	31 (50%)
Bronchial Secretion	1 (2.5%)	0 (0.0%)

Table 2. Antibiotic use for empirical therapy^a.

Pathogen isolate	Combination therapy	Adult dosage
	Cefoperazone/Sulbactam	Cefoperazone:Sulbactam ratio = 1:1
<i>Acinetobacter baumannii</i>	plus	Mild infection: 1 - 2 gr/IV every 12 hours
<i>Pseudomonas aeruginosa</i>		Severe infection: max 4 gr/IV/day every 12 hours CrCl < 30 ml/min: Sulbactam 2 gr/IV/day
<i>Klebsiella pneumoniae</i>	Amikacin	CrCl < 15 ml/min: Sulbactam 1 gr/IV/day 15 - 20 mg/kg/IV every 24 day 20 - 45 mg/kg/IV every 6 - 12 day
<i>Staphylococcus</i> spp.	Vancomycin	CrCl < 30 ml/min: 10 - 15 mg/kg every 24 jam CrCl < 15 ml/min: 10 - 15 mg/kg every 48 jam

^aAdapted from local antibiotic guideline.

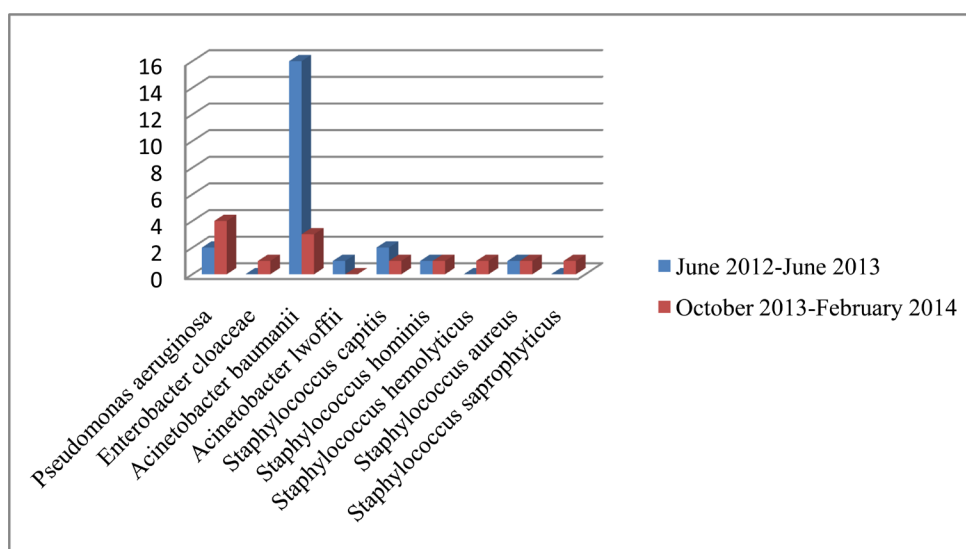


Figure 1. Number of *Acinetobacter baumannii* in June 2012-June 2013 (pre-education) and October 2013-February 2014 (post-education).

Table 3. Antibiotic susceptibility rate of *Acinetobacter baumannii*, June 2012-June 2013 (pre-education) and October 2013-February 2014 (post-education).

Antibiotics	Pre-education (%)	Post-education (%)
Piperacillin/tazobactam	5	89
Cefoperazone/sulbactam	77	89
Ceftazidime	5	67
Cefepime	10	17
Imipenem	16	89
Meropenem	41.6	89
Amikacin	21	100
Levofloxacin	18	67
Tigecycline	35.3	57

bination between education and appropriate use of antibiotics had elicited significant shrinkage of MDR-*A. baumannii* cases compare with non-*A. baumannii* from 70.8% (17/24) in June 2012-June 2013 to 23% (3/13) cases in October 2013-March 2014; *P*-value 0.006.

Education and appropriate use of antibiotics has become a main factor to help prevent the transmission of MDR-*A. baumannii* in ICU in Indonesia where the study conducted (OR 6.4; 95% CI 1.56 - 26.30). **Table 3** showed significant increase of antibiotic susceptibility rate in every antibiotic such as Piperacillin/Tazobactam (89%), Cefoperazone/Sulbactam (89%), Ceftazidime (67%), Imipenem (89%), Meropenem (89%) and Amikacin (100%).

4. Discussion

In this study, MDR-*A. baumannii* is defined as a strain that is resistant to three or more antibiotics such as anti pseudomonalpenicillins or β -lactam, anti pseudomonalcephalosporins, fluoroquinolone, carbapenems, and aminoglycoside [12] [13]. Recently, increasing number of MDR-gram negative cases are followed by increasing number of MDR-*Acinetobacter baumannii* hospital-acquired infections [7] [14] [15]. The decreased number of MDR-*A. baumani* cases in intensive care where this study was held was followed by increasing MDR-*P. aeruginosa* organisms. This finding proved that MDR-*P. aeruginosa* was the most commonly isolated organisms in intensive care patients, contributing 50% (4/8) from all gram negative bacteria. The increasing uses of broad-spectrum antibiotics plays a significant role in associated this phenomenon. Even though the appropriate use of antibiotics therapy and de-escalation of therapy depending on culture and susceptibility testing have been enforced, large numbers of MDR-*P. aeruginosa* cases were still unsolved [12] [16].

MDR-*A. baumannii* is one of many important pathogens causing hospital acquired infection [6] [13] [15]. In this study, all of *A. baumannii* mainly were isolated from lower respiratory tract. These findings are similar with other result where *A. baumannii* were found in 27% patients [17]. Carbapenem resistant *A. baumannii* has endemically emerged globally including in Indonesia [18]. All of isolates before the study was initiated showed that there were no appropriate empirical antibiotic therapies. Aminoglycosides such as Amikacin were not so useful anymore since its sensitivity rate only 21%. This finding is supported by Dent *et al.* [19] who found as much as 58% isolates of *A. baumnaii* are resistant to Imipenem, Amikacin, and Ampicillin-Sulbactam, also similar with study conducted in Turkey that only Amikacin was still sensitive [17]. On the other hand, this problem comparable with increased in appropriate use of Carbapenems and Ciprofloxacin in hospitals [20]-[22].

Appropriate antibiotic use practices still become a challenge with various issue. Several approaches should be implemented before and after prescribing antibiotics such as restricted formulary, comply with local hospital antibiotic guideline, communicate with clinical pharmacologist and clinical microbiologist [23] [24]. Transmission of hospital acquired infection mainly via hands of health care workers, but the compliance of hand hygiene still low around 50%. A study conducted by Allegranzi *et al.* in 2009 showed significant improvement of hand hygiene knowledge and compliance after educational session [25]. Therefore, hand hygiene education is one of the strategies that can be used to prevent the spread of infection in hospitals [10].

The limitation of our observation could not measure the compliance of recommended hand hygiene practice

which may affect the incidence of health care associated infection in our intensive care. The number of positive culture in our study population was of small sample size and specific for intensive care setting, therefore not representative for all other hospital settings.

5. Conclusion

Our study found out that education improving around hand hygiene, appropriate antibiotic prescribing following local hospital guideline and the result of antibiotic sensitivity has been shown to reduce the transmission of MDR-*A. baumannii* in unit in within the Indonesian hospital. This approach was quite easy to apply in developing countries, such as Indonesia.

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Conflict of Interests

The authors declare no conflict of interests.

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