



STUDY REPORT SUMMARY ASTRAZENECA PHARMACEUTICALS

FINISHED PRODUCT: Meronem

ACTIVE INGREDIENT: Meropenem 1g

Study number: **NIS-IVN-DUM-2008/1**

Study title: **An Epidemiological Study on Antimicrobial Treatment of Nosocomial Infections in Clinical Practice**

Developmental phase: IV

Study Completion Date: August 11th, 2011

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BACKGROUND

Hospital-acquired infection is one of the major problems commonly seen in intensive care units (ICU) and is considered as an important factor affecting clinical treatment outcomes of ICU patients. Antibiotics are main determinant for treatment prognosis of hospital-acquired infection. Therefore, antibiotics should be early initiated before findings of bacterial cultures, antibiograms and that way of using antibiotics is so called empiric antibiotic approach. Several evidence showed appropriate antibiotic use has shortened treatment duration and clearly improved clinical outcomes. However, there is still a big gap between the appropriate use and real situation of antibiotic use in current clinical practice. The rate of empiric antibiotic using which is inappropriate to antibiograms is still high.

OBJECTIVES

1. To investigate the situation of appropriate antibiotic use in patients with hospital-acquired infection being treated at ICUs of major hospitals in Vietnam.
2. To explore several factors affecting treatment outcomes of hospital-acquired infection.

METHODS

This is a retrospective cohort study (descriptive observation and review clinical data of subject's treatments at study sites), performed at ICUs of 19 central hospitals with ≥ 400 beds in HCM, Ha Noi and Hai Phong City from 12/2009 to 10/2010. Study subjects are patients at ICUs, who have infectious manifestations within 48 hours after admission, are diagnosed as hospital-acquired infection in accordance with United State's CDC and American Thoracic Society criteria for ventilated pneumonia, and treated with empiric

antibiotics, recommended doses, and results of bacterial culture and antibiograms. Study data is independently analyzed by Statistics Department of University of Medicine – HCMC using SPSS software.

RESULTS

1,100 medical reports were collected. Eligible data for analysis were obtained in 1,063 reports. Subjects consisted of 665 male (63%) and 398 female (37%). Median age was 54 years, with 359 patients whose age \geq 65 years (38%). Majority of patients had underlying diseases, most of those was chronic internal diseases such as heart failure, diabetes and COPD. Most of patients were indicated invasive procedures, majority of them were nasogastric tubes, urinary tubes and mechanical ventilation, within 72 hours before infection initiation. APACHE II Scale was completely recorded in 628 patients (59%) within 24 hours after infection initiation yielding the mean score of 15.8 and SD of 7.6. Median time of ICU staying and total admission time were 18 and 30 days, respectively. 902 cases (85%) were treated with 2 or more antibiotics empirically.

The rate of appropriate antibiotic use in this study was 26% and the inappropriate was 74%. The rate of treatment failure in the inappropriate use group was 63% ($p < 0.001$). The highest rate of treatment failure was seen in hospital-acquired pneumonia with or without mechanical ventilation (72% and 63%, respectively). Negative gram bacteria such as *Acinetobacter*, *Pseudomonas*, *E.coli* and *Klebsiella* were commonly seen in hospital-acquired infection. Of which, *Acinetobacter* and *Pseudomonas* are the two most common with lowest rate of appropriate use of antibiotics (16%). In this study, only 320 cases (30%) have extended-spectrum beta-lactamase (ESBL) results. A total of 301 cases infected with *E.coli* or *Klebsiella* and in which only 163 cases were tested with ESBL (55%). 125 of these 163 cases (77%) has ESBL(+). There still are 138 of total 301 cases with isolated *E.coli* or *Klebsiella* not having ESBL tested. Therefore, the true rate of the ESBL-yielding *E.coli* and *Klebsiella* would be much higher if ESBL test is applied routinely.

Antibiotic resistance in *Acinetobacter* is actually on alarming level because there is a very high rate of bacterial resistance ($>70\%$) in all investigated antibiotics, even with carbapenem group, the resistance rate is also approximately 70%. For *Pseudomonas*, it is slightly better than that of *Acinetobacter*, however, it should be cautioned since the rate of bacterial resistance to the third/fourth generation of cephalosporin and quinolones is over 70%. The sensitive rate is still rather good for meropenem (66%), imipenem (65%) and piperacillin/tazobactam (53%). The situation of antibiotic resistance of *E.coli* and *Klebsiella* is still on relative level. Although, both these bacteria highly resist to almost antibiotics of the third/fourth generation of cephalosporin and quinolones, sensitive rate are still high to antibiotics of carbapenem group (approximately 90%). For antibiotic use by categories of hospital-acquired infection, sensitive rates are high for meropenem (59%) and imipenem (55%) in hospital-acquired pneumonia. Whereas, the most sensitive antibiotics are carbapenem (76-80%), piperacillin/tazobactam (60%) and cefoperazone/sulbactam (53%) in septicemia. Colistin is also investigated in this study yielding a sensitive rate for all four negative-gram bacteria mentioned above is 86% in hospital pneumonia and 72% in septicemia. However, the number of cases using Colistin that was performed antibiograms is not large enough (286 cases), so these results are not confident. The number of cases of Staphylococci-induced hospital-acquired infection using Vancomycin that were performed antibiograms is even smaller (226 cases), so these

findings are not confident enough because of the small number and no MIC results collected, regardless of highly sensitive to Staphylococci (> 90%).

Logistic regression analysis to explore factors related to treatment failure showed that age of ≥ 65 years and ESBL (+) are associated with increasing treatment failure up to 1.5-fold (OR 1.5; 95% CI 1.11 – 2.04; $p=0.009$) and 1.68-fold (OR 1.68; 95% CI 1.06 – 2.64; $p=0.027$), respectively. Meanwhile, the appropriate use of antibiotics is a factor associated with an improvement of treatment failure to 50% (OR 0.54; 95% CI 0.39 – 0.74; $p<0.001$).

In summary, nearly 74% patients with hospital-acquired infection were inappropriately treated with antibiotics and the rate of treatment failure of these cases is 63%. Appropriate use of antibiotics is an important factor associated with an improvement of treatment failure and clinical outcomes.