Journal of Microbiology, Immunology and Infection (2013) 46, 397–398

Available online at www.sciencedirect.com

SciVerse ScienceDirect

journal homepage: www.e-jmii.com

LETTER TO THE EDITOR

Empirical antimicrobial therapy for critically ill patients with *Acinetobacter baumannii* bacteremia: Combination is better

Sir,

Acinetobacter baumannii isolates are resistant to many drugs and can cause severe infections with high mortality rates.[1] The emergence of *A. baumannii* isolates with carbapenem resistance is a matter of great concern. In the October 2012 issue, Huang et al[2] conducted a retrospective study to identify the risk factors and outcomes of patients with carbapenem-resistant *A. baumannii* (CRAB) bacteremia, as compared to carbapenem-susceptible *A. baumannii* bacteremia. This study demonstrated three independent factors of 14-day mortality due to CRAB, i.e., a high Acute Physiology and Chronic Health Evaluation (APACHE) score, the presence of shock, and inappropriate antimicrobial therapy. From Huang's results, two of these risk factors were related to disease severity of bacteremia and were not remediable at the time of diseases onset. However, early appropriate antimicrobial therapy may be able to improve the clinical outcome.

Conversely, inappropriate empirical antimicrobial therapy (IEAT) is a potentially modifiable factor, which has been associated with increased mortality in patients presented with a critical illness.[3] However, the optimal approach for empirical antibiotic therapy in critical patients with *A. baumannii* bacteremia remains controversial. A retrospective cohort study was conducted in a university hospital. The data from 130 patients with bacteremia caused by *A. baumannii*, who presented with critical illness (defined as a Pitt bacteremia score $\geq$4 points) was analyzed. Among this cohort, 27 (20.8%) patients acquired CRAB bacteremia, 94 (72.3%) individuals acquired multidrug-resistant bacteremia, and 51 (39.2%) patients received IEAT. The 30-day crude mortality rate was statistically higher among patients receiving IEAT than that of those initially treated by appropriate (*in vitro* active) antibiotic regimens (32/63, 50.8% vs. 21/67, 31.3%; $p = 0.032$). Moreover, empirical combination regimens directed against *A. baumannii* (i.e., a carbapenem plus sulbactam or an aminoglycoside) were less likely to be inappropriate than monotherapy (8/33, 24.2% vs. 44/97, 45.4%; $p = 0.003$). A survival analysis of Cox regression model was applied, after adjusting for age, gender, and underlying disease (McCabe classification), and found that patients with empirical combination therapy had a lower mortality rate (adjusted odds ratio = 0.31; 95% confidence interval: 0.15–0.72; $p = 0.006$) (Fig. 1).

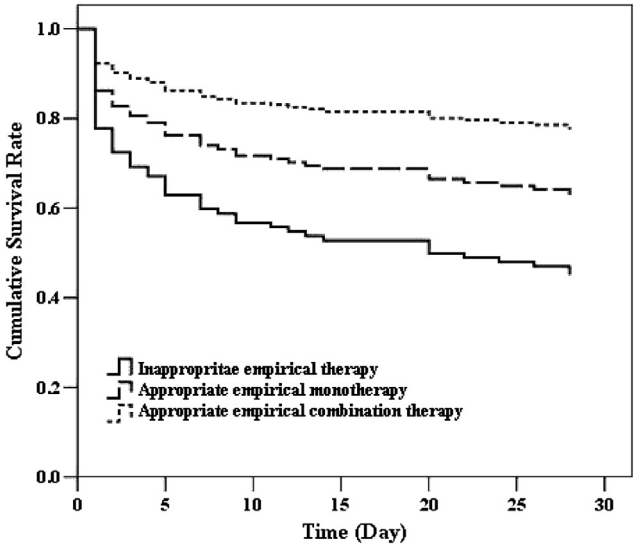

Figure 1. Survival curves for critically ill patients with *Acinetobacter baumannii* bacteremia (Cox model), adjusted for age, gender, underlying disease (McCabe classification), and appropriateness of antimicrobial therapy. Patients receiving empirical combination therapy were associated with a lower mortality rate ($p = 0.006$).

http://dx.doi.org/10.1016/j.jmii.2013.03.004

Expected benefits of empirical combination therapy for bacteremia caused by resistant organisms, are based on the following rationale: to broaden coverage providing at least one appropriate activity,[4] or to exploit the synergy activity.[5] Our study suggests that the use of empirical combination antimicrobial therapy will be associated with more appropriateness for patients with critical illness due to *A. baumannii* bacteremia and with a favorable outcome. Therefore, it appears reasonable to initiate empirical combination antimicrobial therapy directed against *A. baumannii* bacteremia in critically ill patients. This recommendation may be seriously considered for critical patients at risk of *A. baumannii* infections, or in the clinical settings of the presence of endemic multidrug-resistant *A. baumannii* in healthcare facilities. However, the optimal empirical combination regimens directed against *A. baumannii* infections, should be based on local antimicrobial susceptibility patterns.

References

1. Lee NY, Lee HC, Ko NY, Chang CM, Shih HI, Wu CJ, et al. Clinical and economic impact of multidrug resistance in nosocomial *Acinetobacter baumannii* bacteremia. *Infect Control Hosp Epidemiol* 2007;**28**:713—9.
2. Huang ST, Chiang MC, Kuo SC, Lee YT, Chiang TH, Yang SP, et al. Risk factors and clinical outcomes of patients with carbapenem-resistant *Acinetobacter baumannii* bacteremia. *J Microbiol Immunol Infect* 2012;**45**:356—62.
3. Micek ST, Welch EC, Khan J, Pervez M, Doherty JA, Reichley RM, et al. Empiric combination antibiotic therapy is associated with improved outcome against sepsis due to gram-negative bacteria: a retrospective analysis. *Antimicrob Agents Chemother* 2010;**54**:1742—8.
4. Tamma PD, Cosgrove SE, Maragakis LL. Combination therapy for treatment of infections with gram-negative bacteria. *Clin Microbiol Rev* 2012;**25**:450—70.
5. Lee NY, Wang CL, Chuang YC, Yu WL, Lee HC, Chang CM, et al. Combination carbapenem-sulbactam therapy for critically ill patients with multidrug-resistant *Acinetobacter baumannii* bacteremia: four case reports and an *in vitro* combination synergy study. *Pharmacotherapy* 2007;**27**:1506—11.

Nan-Yao Lee
Jen-Chieh Lee
Ming-Chi Li
Chia-Wen Li
Wen-Chien Ko*
Department of Internal Medicine, National Cheng Kung University Medical College and Hospital, Tainan, Taiwan

*Corresponding author. Division of Infectious Disease, Department of Internal Medicine, National Cheng Kung University Hospital, Number 138, Sheng Li Road, 704 Tainan, Taiwan.
E-mail address: winston3415@gmail.com (W.-C. Ko)

11 March 2013