Hsin-I Shih
Hsiang-Chin Hsu
Chih-Hsien Chi
Wen-Chien Ko

**Macrolide combination
antibiotic therapy should
be prudently considered
in complicated CAP cases
and in regions with low
macrolide susceptibility**

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Dear Editor,

In response to the article by Martin-Loeches et al. [1] regarding improved survival in intubated patients with community-acquired pneumonia treated with combination antibiotic therapy with macrolides, we would like to address several points regarding macrolide resistance and study population.

In the recent decade, susceptibility of pneumococcus to macrolides in Asia has been very low. Erythromycin susceptibility is <20% in Taiwan and Korea, and about 25% in Hong Kong and China [2]. Macrolide-resistant strains (*ermB* and *mefA*) are widely circulating in Asia. Low susceptibility of pneumococci to macrolides is difficult to deny. According to a study in Taiwan, macrolide susceptibility of pneumococci remains low, even though macrolide usage has been decreasing for many years. The rate of erythromycin resistance in streptococcal pneumonia showed an increasing trend, from 80.2% in 1999 to 92% in 2003 [3, 4]. The 2007 ATS/IDSA guidelines for community-acquired pneumonia (CAP) were based on epidemiology studies in the USA.

In the USA and Europe, appropriate therapies, in which a macrolide would be combined with a beta-lactam, showed that macrolides may be effective in treating bacteremic pneumococcal pneumonia, CAP, severe sepsis, and septic shock due to CAP [1, 5]. However, synergic effects of macrolides and beta-lactams in treating invasive pneumococcal pneumonia in Asia may not be as good as in the USA and Europe. Macrolides may be used only to empirically cover atypical pathogens such as *Legionella* or *Mycoplasma*.

Moreover, in this article, Martin-Loeches et al. did not indicate such detailed characteristics as underlying diseases, pathogens, disease severity, or number of days of intensive care unit (ICU) stay for the empirical antimicrobial therapy group that was treated with a macrolide or for the empirical antimicrobial therapy group treated with fluoroquinolones. The authors only indicated ICU mortality and that overall mortality in the macrolide group was lower than in the fluoroquinolones group. Furthermore, according to the 2007 ATS/IDSA guidelines for CAP, subjects who were suggested to be treated by a fluoroquinolone and a beta-lactam combination were those with possible *Pseudomonas* infection. In this study, compared with the macrolide and beta-lactam combination group, cases receiving fluoroquinolone and beta-lactam combination had lower proportions receiving third-generation cephalosporins and higher proportions receiving fourth-generation cephalosporins, carbapenem, and piperacillin/tazobactam. Therefore, cases receiving fluoroquinolone and beta-lactam combinations may have more complicated conditions than those receiving macrolide and beta-lactam combinations. Since cases receiving a fluoroquinolone tended to have more complicated predisposing factors, we could not expect that they would have better short- and long-term prognosis.

Accordingly, prudent antibiotic use remains essential in complicated cases with severe CAP in regions with low macrolide susceptibility.

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H.-I. Shih (✉) · H.-C. Hsu · C.-H. Chi
Department of Emergency Medicine,
National Cheng Kung University Hospital,
No. 138 Sheng Li Road,
Tainan City 704, Taiwan
e-mail: n506594@mail.hosp.ncku.edu.tw;
hshihnckutw@gmail.com

W.-C. Ko
Division of Infectious Diseases,
Department of Internal Medicine,
National Cheng Kung University Hospital,
Tainan City, Taiwan