Use of Cephalexin Plus Trimethoprim/Sulfamethoxazole vs Cephalexin Alone for Treatment of Uncomplicated Cellulitis

To the Editor—We read with much interest the article by Pallin et al [1], which presents the data from the double-blind, randomized, placebo-controlled trial that compared the clinical effectiveness of trimethoprim/sulfamethoxazole plus cephalexin vs cephalexin alone in treatment of cellulitis without abscess in the outpatient setting where community-associated methicillin-resistant Staphylococcus aureus (CA-MRSA) is reportedly endemic. The authors concluded that addition of trimethoprim/sulfamethoxazole to cephalexin provided no statistically significant clinical benefit compared to cephalexin alone. Although the authors claimed that the findings supported the Infectious Diseases Society of America (IDSA) recommendations against use of antibiotics targeting CA-MRSA for most cases of cellulitis, several concerns should be taken into account in interpreting the study results.

The study was designed as a superiority trial, for which the sample size was estimated based on the assumption that the clinical effectiveness in the subjects who received trimethoprim/sulfamethoxazole plus cephalexin would be better than those who received cephalexin alone, with a response rate difference of 13%. However, the study failed to demonstrate the difference. With the difference of 3% between the 2 treatment regimens as is shown in this study, the sample size would be much greater than that estimated if the study had been designed to demonstrate the equivalence or noninferiority between the 2 regimens. Using the results available in this study, the power of the study would be <10%, if the sample size is 144 and the α value is .05. In this study, the case number of cellulitis due to CA-MRSA is small, which will further preclude the study from demonstrating the role of adding trimethoprim/sulfamethoxazole to cephalexin. In the retrospective study that was conducted by Szumowski and colleagues among patients with skin and soft-tissue infection due to CA-MRSA at an ambulatory clinic in Boston [2], only 0.5% of the 216 MRSA isolates were resistant to trimethoprim/sulfamethoxazole,
and clinical resolution of infection on empirical therapy was highly associated with use of empirical antibiotics that were active against the isolates after controlling for incision and drainage and human immunodeficiency virus (HIV) status in multivariate analysis (odds ratio, 5.91; 95% confidence interval, 3.14–11.13).

In this study, a large number of subjects were screened but a significant proportion (6338/6491; 97.6%) were excluded from enrollment. Of note, diabetic patients who have been found to be associated with a higher rate of MRSA colonization are excluded from participating in the study [3, 4], which will significantly limit the applicability and generalizability of the study results.

Therefore, the conclusion in this study that the results could provide experimental support for IDSA recommendations against antibiotics targeting CA-MRSA for cellulitis should be questioned. We need to see more multicenter studies enrolling patients with microbiologically confirmed cellulitis before we really know it.

Note

Potential conflicts of interest. All authors: No reported conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

Yu-Ju Chou,1 Kuan-Yeh Lee,1 Mao-Song Tsai,2 Hsin-Yun Sun,2 and Chien-Ching Hung2,3,4
1Department of Internal Medicine, National Taiwan University Hospital, Hsin-Chu Branch; 2Department of Internal Medicine, National Taiwan University Hospital and National Taiwan University College of Medicine, Taipei; 3Department of Medical Research, China Medical University Hospital, Taichung; and 4China Medical University, Taichung, Taiwan

References


