Questionable Superiority of Linezolid for Methicillin-Resistant Staphylococcus aureus Nosocomial Pneumonia: Watch Where You Step

TO THE EDITOR—In their recent article, Wunderink et al [1] claim that linezolid is superior to vancomycin for treatment of methicillin-resistant Staphylococcus aureus (MRSA) nosocomial pneumonia. The accompanying commentary suggests that this should influence nosocomial pneumonia treatment guidelines [2]. I disagree with both conclusions because of concerns about data validity, the questionable clinical applicability of the findings, and potential author and editorial conflicts of interest.

First, medical comorbidities were unequally distributed between subjects who received linezolid and those who received vancomycin; compared with vancomycin recipients, linezolid recipients had 15% less diabetes mellitus and 24% less kidney disease, they required 10% less mechanical ventilation, and they exhibited fully 52% less bacteremia. Unequal distribution of subject medical comorbidities could explain some or all of the marginally significant 11% difference in clinical cure between linezolid and vancomycin recipients. Unequal distribution of cardiac, renal, and diabetic comorbidities also undermined 2003 and 2004 studies by Wunderink et al in which they claimed linezolid superiority over vancomycin among overlapping MRSA pneumonia cohorts [3,4]. In addition to citing concerns about unequal subject allocation, others decried these studies’ overlapping subject cohorts and overinterpretation of subgroup analyses [5–7]. By contrast, earlier studies by Wunderink et al without reported unequal distribution of medical comorbidities showed that linezolid and vancomycin were equivalently effective [8,9]. Read alone and in historical context, this study leaves real doubt regarding the purported superiority of linezolid.

The clinical applicability of the findings is also questionable. Most patients with nosocomial pneumonia are treated before pathogen identification, and in many cases, the pathogen is never identified. Thus, the authors’ findings only pertain to the minority of patients who have proven MRSA nosocomial pneumonia. Furthermore, although linezolid was associated with superior clinical cure in the 28.4% of subjects in the per-protocol population, 60-day mortality was equivalent among linezolid and vancomycin recipients. Because clinical cure was a subjective outcome (“resolution of clinical signs and symptoms of pneumonia compared with baseline, improvement or lack of progression in chest imaging, and no requirement for additional antibacterial treatment”), the major question is whether an impact on this subjective multipartite outcome among a minority of patients without a mortality benefit justifies the fiscal and other costs of linezolid. The presented data do not resolve this question.

Enthusiasm for these findings should be tempered by potential conflicts of
interest. Linezolid’s maker, Pfizer, funded the study, provided editorial support for the manuscript, and furnished every author with consultants’ fees, speakers’ fees, grants, and/or full-time employment. The author of the accompanying editorial also is the recipient of a research grant from Pfizer. Although industry collaborations are valuable and respectable, the reader must consider whether Pfizer funding created a conflict of interest for study authors or the editors. Medical journals should protect editorial objectivity by selecting editors not funded by the company that also funded the study being discussed.

Because of these concerns, it is premature to change nosocomial pneumonia treatment guidelines.

Note

Potential conflicts of interest. Author certifies no potential conflicts of interest.

The author has 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.

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References