Methicillin-Resistant *Staphylococcus aureus* Pneumonia Treatment

Do Not Confuse Pharmacokinetics and Pharmodynamics

To the Editor:

We have read with great interest the article in a recent issue of CHEST (October 2006) by Jeffres et al., which suggested that aggressive dosing strategies for vancomycin (eg, trough concentrations > 15 mg/L) may not offer any advantage over traditional dosing targets (range, 5 to 15 mg/L) in patients with methicillin-resistant *Staphylococcus aureus* (MRSA) health-care-associated pneumonia. A lack of response to treatment with vancomycin in patients infected with MRSA, and in patients infected with vancomycin intermediate-resistant *S aureus* (VISA) and heterogeneous VISA (hVISA), has been increasingly reported despite apparent in vitro susceptibility (minimum inhibitory concentration [MIC], 2 mg/L). Moreover, MRSA isolates that show reduced susceptibility to vancomycin (MIC, 2 mg/L) are highly prevalent among strains that cause invasive infections.

In the study by Jeffres et al., the tested staphylococci exhibited a mean vancomycin zone diameter > 14 mm and would therefore be considered fully susceptible. Nevertheless, disk diffusion is not an acceptable method for testing of the vancomycin susceptibility of *S aureus*, specifically for the detection of VISA or hVISA. Thus, the authors may not have excluded the idea that a lack of response to treatment was not associated with a high vancomycin MIC for MRSA (2 mg/L) or VISA/hVISA.

Unbound trough serum concentrations of vancomycin that are four to five times the MIC or 24-h area under the curve/MIC ratio of 400 were shown to be the pharmacodynamic parameters that best correlated with a successful clinical outcome. Considering that vancomycin is 50% protein-bound in serum and that lung concentrations will not protein-bound in serum and that lung concentrations will not exceed 20 to 30% of the serum concentrations, a trough serum concentration level of 15 to 25 mg/L may be adequate for the treatment of MRSA with a MIC at the breakpoint for susceptibility (2 mg/L), with a concentration of 30 to 40 mg/L being required for the treatment of VISA/hVISA pneumonia. Unfortunately, Jeffres et al. did not consider the potential impact of variations in MRSA MICs on differences in outcome. Thus, it still seems appropriate to continue monitoring vancomycin serum levels in order to ensure effective therapeutic concentrations until the results of well-designed prospective clinical studies, including vancomycin MIC determinations, become available.

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**References**


Appropriate Pharmacokinetic Index for Outcome in *Staphylococcus aureus* Pneumonia

To the Editor:

We read with interest the study by Jeffres and colleagues (October 2006) investigating the relationship between vancomycin pharmacokinetic (PK) indices and outcome in patients with confirmed *Staphylococcus aureus* pneumonia. This study did not find a correlation between vancomycin area under the curve (AUC) ≥ 400 μg/h/mL and hospital mortality in patients with *S aureus* pneumonia. While the authors acknowledge that previous clinical studies show an association between vancomycin PK indices and patient outcomes, they do not further clarify that the AUC/minimum inhibitory concentration (MIC) ratio and not AUC alone, as evaluated in the current study, has correlated better with patient outcomes in those studies. Although this correlation is not evidenced in all studies evaluating this relationship, the AUC/MIC ratio is the best parameter predicting...