REFERENCES


Vancomycin Dosing for Methicillin-Resistant Staphylococcus aureus Nosocomial Pneumonia

To the Editor:

We read the study by Jeffries and colleagues1 (October 2006) with interest and were intrigued with the conclusion that trough concentrations >15 μg/mL may not offer any advantage over traditional targets. This retrospective study was not adequately powered to detect differences between traditional and aggressive trough concentrations. Therefore, a statistically insignificant result is only inconclusive and not a negative finding.

With substantial imbalances between nonsurvivors and survivors, assessments of the variable in question in both analyses are impossible. Nonsurvivors were older with higher APACHE (acute physiology and chronic health evaluation)-II scores and had greater frequencies of bacteremia, end-stage renal disease, mechanical ventilation, and vasopressors. The trough concentration ≥15 μg/mL group had higher APACHE-II scores and more patients receiving mechanical ventilation and vasopressors (a factor significantly associated with mortality in the multivariate analysis). Is it plausible that sicker patients receiving trough concentration ≥15 μg/mL have the same risk of death as less ill patients receiving lower vancomycin trough concentrations?

The unavailability of minimum inhibitory concentrations made it impossible to calculate the area under the inhibitory curve values, although the accompanying editorial2 stated these were calculated. Disk diffusion does not adequately identify Staphylococcus aureus with reduced vancomycin susceptibility.3 While most isolates likely had an minimum inhibitory concentration ≤0.5 μg/mL, we will never know for certain. Therefore, pharmacodynamic target attainment rates cannot be compared.

While vancomycin may not display pharmacokinetic qualities of the optimal agent for methicillin-resistant S aureus pneumonia, prospective, randomized trials comparing vancomycin target concentrations will hopefully provide some definitive answers to the role of aggressive vancomycin dosing for this disease. The major issue is that vancomycin has not had a fair comparison. Unfortunately, this study had the worst possible result, as it did not definitively conclude anything.1 However, this study and the accompanying editorial suggest that the time for optimizing vancomycin dosing is over and clinicians should use “better” agents.

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Methicillin-Resistant Staphylococcus aureus Pneumonia Treatment

Do Not Confuse Pharmacokinetics and Pharmacodynamics

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).1 Moreover, MRSA isolates that show reduced susceptibility to vancomycin (MIC, 2 mg/L) are highly prevalent among strains that cause invasive infections.2

In the study by Jeffres et al,1 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.3 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.3 Considering that vancomycin is 50% protein-bound in serum and that lung concentrations will not exceed 20 to 30% of the serum concentrations,3 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 al1 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.2,3 Although this correlation is not evidenced in all studies4–5 evaluating this relationship, the AUC/MIC ratio is the best parameter predicting...