Vancomycin Therapeutic Guidelines: Closer Examination of Neonatal Pharmacokinetics

To the Editor—We read with interest the recent paper of Patel et al describing the pharmacokinetic and pharmacodynamic profile of the vancomycin regimens according to the recently published vancomycin guidelines [1]. It has been recommended that a value ≥400 for the ratio of the 24-hour area under the serum concentration-versus-time curve (AUC$_{24}$)
to the minimum inhibitory concentration (MIC) is essential to obtain adequate vancomycin efficacy [2]. We fully agree with the statement of Patel et al that regimens producing trough values in excess of 15 mg/L are not always necessary to provide an AUC$_{24}$/MIC $\geq$400, especially if the MIC is $\leq$1 mg/L. Minimizing the vancomycin trough concentrations needed to achieve the desired AUC value may diminish the risk of nephrotoxicity [3].

The guidelines are valid only for adults. No recommendation for dosing of neonates based on AUC$_{24}$/MIC is available. We want to report about vancomycin peak and trough concentrations measured during routine patient care of neonates recently hospitalized in our neonatology unit. We have calculated the steady-state AUC$_{24}$ with maximum a posteriori Bayesian estimation (MW/PHARM 3.60, Medware) [4] using both the measured peak and trough concentrations. The results are shown in the Table.

As can be seen, AUC$_{24}$ $\geq$400 is found in all patients. The trough concentrations are within the usual reference range for neonates (5–10 mg/L) [5, 6]. According to routine automated susceptibility testing (BD Phoenix) of strains (Staphylococcus aureus or coagulase-negative staphylococci [CoNS]) isolated from blood cultures from our neonates, MIC values of $\leq$1 were found.

These results indicate that if the MIC is $\leq$1, AUC$_{24}$/MIC $\geq$400 can be reached with trough concentrations in the usual range and existing dosing schemes for vancomycin treatment of neonates.

Table. Pharmacokinetic Parameters of Neonates Exposed to Vancomycin

<table>
<thead>
<tr>
<th>Neonates n = 8</th>
<th>Postnatal age (days)</th>
<th>Weight (kg)</th>
<th>AUC$_{0-24}$ (mg/L h)</th>
<th>C$_{\text{min, steady state}}$ (mg/L)</th>
<th>C$_{\text{max, steady state}}$ (mg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean $\pm$ SD (range)</td>
<td>24 $\pm$ 9 (12–35)</td>
<td>1.3 $\pm$ 0.5 (0.7–2.0)</td>
<td>429 $\pm$ 36 (404–609)</td>
<td>7.8 $\pm$ 0.8 (6.8–9.4)</td>
<td>33.7 $\pm$ 4.9 (28.4–43.0)</td>
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</table>

Abbreviations: SD, standard deviation; AUC, area under the curve for serum concentration versus time; Cmin, minimum vancomycin concentration; Cmax, maximum vancomycin concentration.

Note

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

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