Vancomycin AUC Dosing: Is One Concentration in the Hand Worth Two in the Bush?

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Abstract

Background

• A pre-specified trough range of 15 to 20 mcg/mL is a poor surrogate for targeting a 24-hour area-under-the-curve to minimum inhibitory concentration (AUC/MIC) ratio of 400 to 600 mg*h/L and has been associated with an increased risk of nephrotoxicity1,5

• Revised guidelines recommend a transition to AUC/MIC therapeutic drug monitoring (TDM) to optimize vancomycin exposure for serious invasive methillin-resistant Staphylococcus aureus (MRSA) infections while minimizing toxicity based on limited data without high quality evidence and limitations in strength5

• AUC/MIC TDM requires substantial clinical and operational resources when the majority of prescribed vancomycin is empiric and not required beyond a few days with implementation of rapid diagnostics and antimicrobial stewardship initiatives

• There is sparse published data comparing the accuracy of single- to two-level AUC/MIC estimations with a suggested –8% (AUC peak- trough/AUC full ratio: 0.86 vs AUC trough/AUC full: 0.78) difference in accuracy as described by Neely, et al10

Methods

• Prospective cohort analysis of hospitalized adult patients with stable renal function prescribed vancomycin who required TDM from 10/2020 to 12/2020

• Two appropriate vancomycin concentrations were obtained at steady-state during a single dosing interval for each patient

• AUC was calculated by two methods:

  - Trapezoidal equations utilizing peak and trough concentrations (P/T)
  - Trough (T)-only concentration combined with a population volume of distribution

• Estimation of population volume of distribution (Vd):
  - Body mass index (BMI) ≤ 25: total body weight (kg) multiplied by 0.7
  - BMI > 25: total body weight (kg) multiplied by 0.5

• Trapezoidal method equations per Pai MP, et al8

• Accuracy of the AUC TDM estimation method was analyzed by comparing the percent and actual AUC difference calculated between the P/T and T-only AUC for each patient

• Clinical application patient level review was independently conducted by two clinical pharmacists to evaluate if a change in dosing would have been made according to AUC estimation methodology

Results

• Greatest variance between calculated T-only and P/T AUC was seen in a 158 kg patient (17% difference) and patients with CrCl <150 mL/min (> 10% difference)

• Both methods resulted in the same modification to the vancomycin regimen based on patient level chart review

Table 1. Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>(N=31)</th>
<th>Value</th>
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</thead>
<tbody>
<tr>
<td>Age (median)</td>
<td>59 years</td>
<td>21 (17.9)</td>
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<tr>
<td>Sex, male (%)</td>
<td></td>
<td>58%</td>
</tr>
<tr>
<td>Weight (kg), median (IQR)</td>
<td>70.75 (63.1 to 93.9)</td>
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<tr>
<td>BMI kg/m2, median (IQR)</td>
<td>27.25 (23.3 to 34.5)</td>
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<tr>
<td>Serum creatinine mg/dL, median (IQR)</td>
<td>1.10 (0.75 to 1.07)</td>
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Table 2. Comparison of Calculated AUC

<table>
<thead>
<tr>
<th>Parameter</th>
<th>(N=31)</th>
<th>T-only vs P/T</th>
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</thead>
<tbody>
<tr>
<td>Peak % difference in AUC (SD)</td>
<td>7.45% (7.2)</td>
<td></td>
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<tr>
<td>Median % difference in AUC (IQR)</td>
<td>0.65% (-3.8 to 9.2)</td>
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<tr>
<td>Mean absolute difference in AUC (SD)</td>
<td>20.85 mg*h/L (14.4)</td>
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<tr>
<td>Median absolute difference in AUC (IQR)</td>
<td>25.86 mg*h/L (14.7 to 42.2)</td>
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<tr>
<td>Trough values, mean (SD)</td>
<td>14.3 mg/L (5.5)</td>
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Figure 1. Percent Difference between P/T and T-only Methods with apparent normal distribution, p<0.04 by Shapiro's test

Conclusions

• T-only AUC method performed similarly to the more laborious trapezoidal P/T AUC method resulting in no dose adjustment differences between groups

• Trapezoidal P/T method should be considered for patients with body weight >150kg, significant body mass index (BMI) ≥ 25, and CrCl <150 mL/min (> 10% difference)

• Both methods resulted in the same modification to the vancomycin regimen based on patient level chart review

References: