Comparison of initial vancomycin costs between trough- and area under the time-concentration curve-guided dosing

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Abstract

Background: Vancomycin is the drug-of-choice for treatment of most invasive infections due to methicillin-resistant Staphylococcus aureus (MRSA). Trough-guided vancomycin dosing is the current standard, dosing based on area under the curve in 24-hour trough-concentration-time curve (AU_{24h}) to minimum inhibitory concentration (MIC) ratio best practice clinical efficacy while often reducing trough concentrations associated with increased risk of nephrotoxicity. However, several barriers exist in widespread adoption of AU_{24h}-guided dosing, including the potential impact of drug costs. The purpose of our study was to determine the relative cost of vancomycin therapy when initial dosing is guided by AU_{24h} compared to current practices. We also sought to describe the current dosing practice relative to attainment of targeted vancomycin exposures.

Methods: A retrospective, single-center study was performed on patients hospitalized at Duke University Hospital (Duke) in calendar year 2017 with suspected or confirmed invasive MRSA infection and stable renal function. For the primary outcome measure, a cost-minimization analysis (CMA) was performed on 200 randomly-selected patients utilizing DUH wholesale vancomycin acquisition cost within the first 48 hours of therapy determined from actual (trough and AUC) and AU_{24h} dosing utilizing a historical computer model. Secondary analyses described dosing practices and attainment of goal trough or AU_{24h} vancomycin exposures.

Results: In the 200 enrolled subjects, the median (IQR) difference between AU_{24h} and trough-guided (reference) was 88 (0; 150). Duke vancomycin troughs were timed and labeled correctly in only 54% of samples, while 20.7% exceeded two hours of the next scheduled dose. Mean loading doses among trough- and AU_{24h}-guided cohorts were 21.9 mg/kg and 24.8 mg/kg, respectively. Initial dosing was predicted to achieve an AU_{24h} within 400-600 mg/L in 65.5% and 100%, respectively. Initial measured serum trough concentration means of 15.20 mg/L were observed in only 22% of subjects. Predicted troughs > 15 mg/L (a known risk factor for nephrotoxicity) would be avoided in 27.1% of patients if executed by AU_{24h}-guided dosing.

Conclusion: Vancomycin acquisition cost was comparable between dosing methods. Opportunities identified include dosing and monitoring modifications to improve target attainment.

Introduction

- Trough-guided vancomycin dosing continues to be a common practice with improved efficacy and safety of AU_{24h}-guided dosing.1,4
- Several logistic barriers exist to widespread implementation of AU_{24h}-guided dosing, including cost.

Objectives

- To compare the initial (48hr) acquisition cost of vancomycin using either trough- or AU_{24h}-guided dosing in hospitalized patients with suspected or confirmed invasive MRSA infection and stable renal function
- To describe the number of measured or calculated steady-state serum vancomycin trough concentrations ≥ 15 mg/L between dosing methods
- To describe the practice of trough-guided dosing at DUH in terms of the following: loading doses, timing, labeling and attainment of targeted steady-state serum concentrations

Methods

- Study design: retrospective, single center, parallel design
- Inclusion
- Age ≥ 18 years of age admitted to DUH 11/1/17 to 12/31/17
- Total body weight ≤ 110 kg
- Inpatient initiation and receipt of IV vancomycin for suspected or confirmed invasive MRSA for ≥ 96 hours
- Absence of unstable renal function as evidenced by: baseline SCR < 2 mg/dL or CrCl > 50 mL/min (utilizing modified Cockcroft-Gault equation see Table 1)
- Exclusion
- History of any renal replacement therapy or use within 96 hours of vancomycin initiation
- Incomplete medical records

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Primary Analyses

- Endpoint
  - AU_{24h} acquisition cost of vancomycin within the first 48 hours of therapy
- Analysis
  - Cost-minimization perspective of dosing at hours 00:00 and 48:00

Secondary Analyses

- Endpoints
  - Results of calculated or measured steady-state serum vancomycin trough concentrations
  - Loading doses (mg/kg)
  - Descriptive statistics among dosing cohorts and for endpoints describing dosing practices

- AU_{24h} acquisition costs determined for each dosing method
- AU_{24h}-guided initial dosing of vancomycin determined for each patient utilizing BestDose™ (V1.126, University of Southern California):
  - goal AU_{24h} > 400 mg/L
  - loading doses capped at 3 g: maintenance doses capped at 2 g
  - CrCl estimated utilizing modified Cockcroft-Gault formula (see footnote Table 1)
- Preference to regimens with least frequent administration

Results

Figure 1. Patient Screening and Enrollment* Encounters screened n = 844

Table 1. Patient demographics and clinical characteristics (n=200)

<table>
<thead>
<tr>
<th>Age at arrival, yrs, median (range)</th>
<th>Gender, male, n (%)</th>
<th>Race, n (%)</th>
<th>Caucasian/white</th>
<th>African American/black</th>
<th>Other</th>
<th>Baseline CrCl mL/min, median (IQR)</th>
<th>Vancomycin indication, n (%)</th>
<th>Nephrotoxicity, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>57 (18-87)</td>
<td>124 (62)</td>
<td>140 (70)</td>
<td>50 (26)</td>
<td>19 (9)</td>
<td>90.6 (67.3-121.4)</td>
<td>9.6 (74.1)</td>
<td>23 (11.5)</td>
<td>32 (16.0)</td>
</tr>
</tbody>
</table>

Discussion

- Conservative dosing practices in the trough-guided cohort (including suboptimal loading doses in 33%) likely minimized differences in acquisition cost between dosing methods.
- Predicted troughs > 15 mg/L (a known risk factor for nephrotoxicity) would be avoided in 27.1% of patients if executed by AU_{24h}-guided dosing.
- While AU_{24h}-guided dosing will require 2 samples (obtained in only 18% of trough-guided cohorts within 96 hrs), this will likely improve timely patient-specific pharmacokinetic modeling and likely reduce the number of regimen changes.

Limitations

- AU_{24h}-guided dosing limited by retrospective data and dependent upon creatinine clearance estimation
- Cost minimization analysis limited to drug cost only and assumes equivalent efficacy

Conclusions

- Compared to trough-guided dosing, Bayesian AU_{24h}-guided vancomycin dosing was associated with comparable median costs and therapy while potentially improving the attainment of targeted AU_{24h} exposures.
- Lab reports describing trough vancomycin concentrations were accurate in only 54% of samples.
- Initial (measured) attainment of target concentrations utilizing trough-guided dosing occurred in only 22.1% of patients, likely due to suboptimal loading doses in patients with higher drug clearance than many hospitalized patients (as evidenced by normal and/or stable renal function).

References


Disclosures

Authors have nothing to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation.

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