Introduction

• Vancomycin is an antibiotic that has been utilized clinically for nearly 60 years against serious, life-threatening, gram-positive infections.
• Studies have linked low vancomycin levels (<10 mg/L) to therapeutic failure and the emergence of resistance.
• A 2009 IDSA consensus guideline paper proposed that serum vancomycin trough concentrations of 15-20 mg/L be targeted for serious infections and that loading doses be administered in order to rapidly attain these serum vancomycin trough levels.
• Empirical vancomycin dosing nomograms have been developed to aid clinicians and they are 52-70% predictive for the 15-20 mg/L target trough range.
• These nomograms take into account patient age, gender, weight, and serum creatinine levels to provide an empiric loading dose, maintenance dose, and initial dosing frequency in the period before the first steady-state vancomycin trough level is obtained (usually prior to 3rd dose).
• Island Health has a published nomogram, however, anecdotal observation suggests that the nomogram is used infrequently.

Uniqueness of Research

• Analysis of health information databases can aid in refining clinical practice.
• Laboratory and pharmacists' resources were combined to create an electronic database to evaluate the effectiveness of a clinical dosing tool.

Study Objectives

1st Objective: to evaluate the adherence to the Island Health empirical vancomycin dosing nomogram

Outcome measure:
• proportion of vancomycin orders that adhere to the nomogram in terms of dose and frequency given patient age, weight, and serum creatinine

2nd Objective: to characterize the performance of adherent orders

Outcome measure:
• determine the proportion of first serum vancomycin troughs that fall within the target range of 15-20 mg/L with empirically dosed vancomycin orders.

Methods

Design

• Retrospective, observational, clinical informatics study spanning Island Health

Study population

Inclusion
• Age ≥ 18 years
• Acute, inpatient at Island Health
• Received IV vancomycin for at least 48 hours

Exclusion
• Data created before January 1, 2009
• Cases outside nomogram parameters
• Incomplete data sets

Data Management

1. Island Health Carrier Database
2. Laboratory Parameters Database
3. Pharmacy Orders Database
4. Combined Datasets (n = 2,333)
5. Reviewed Cases (n = 5,640 (n = 1,880))
6. Maintenance Order Cases (n = 4,794 (n = 1,598))
7. Loading Dose Cases (n = 646 (n = 202))

Query limited to pharmacy orders and laboratory parameters entered into the database between Jan 1, 2009 to Dec 31, 2014.

Pharmacy orders limited to IV vancomycin. Laboratory parameters limited to: serum creatinine, any vancomycin level, (N = row of data).

Pharmacy orders and laboratory parameters emerged. Laboratory parameters limited to: 7 days of vancomycin orders. Multiple laboratory parameters associated with each order.

Datasets temporarily grouped into order cases (n) consisting of a vancomycin order, patient age, and 3 linked clinical parameters: (1) serum creatinine level, (1) measured weight, and (1) vancomycin trough level. Each order case = 3 rows

Manual inspection and review of each order case in order cases only. Each order case corresponds to one empirical vancomycin order.

Multiple orders per PNA with different dosing regimens being entered at different times (≥14 days).

Adherent, non-adherent, and non-load orders are shown in Table 1.

Results

Table 3: Characteristics of adherent and non-adherent order cases. (n = 1,880)  

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Adherent (n = 71%)</th>
<th>Non-Adherent (n = 29%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years), median (IQR) (range)</td>
<td>66 (25) (20-89)</td>
<td>65 (24) (20-89)</td>
</tr>
<tr>
<td>Sex, no. (%) male</td>
<td>145 (45.5%)</td>
<td>447 (57.3%)</td>
</tr>
<tr>
<td>Weight (kg), mean ± SD</td>
<td>69 ± 14</td>
<td>76 ± 14</td>
</tr>
<tr>
<td>Initial serum creatinine (μmol/L), median (IQR)</td>
<td>70 (30)</td>
<td>79 (43)</td>
</tr>
<tr>
<td>Vancomycin dose (mg/kg), mean ± SD</td>
<td>16.1 ± 1.3</td>
<td>14.3 ± 3.3</td>
</tr>
</tbody>
</table>

Table 4: Proportion of levels among adherent and non-adherent order cases in ranges of interest. (n = 1,880)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Adherent (n = 71%)</th>
<th>Non-Adherent (n = 29%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial vancomycin level (mg/L)</td>
<td>6.17 (7.4)</td>
<td>11.7 (8.1)</td>
</tr>
<tr>
<td>Level 1</td>
<td>32%</td>
<td>39%</td>
</tr>
<tr>
<td>Level 2</td>
<td>42%</td>
<td>36%</td>
</tr>
<tr>
<td>Level 3</td>
<td>26%</td>
<td>25%</td>
</tr>
</tbody>
</table>

Table 5: Proportion of load order cases. (n = 1,880)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Adherent (n = 71%)</th>
<th>Non-Adherent (n = 29%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Load ordered</td>
<td>93%</td>
<td>91%</td>
</tr>
<tr>
<td>Not loaded</td>
<td>6%</td>
<td>10%</td>
</tr>
</tbody>
</table>

Discussion

Findings
• Overall, 19% of all maintenance orders analyzed were in the target range of 15-20 mg/L, median (IQR) trough concentration of 11.9 (8.1) mg/L.
• 1st Outcome Measure
• 29% of assessed orders adhered to the suggested nomogram dose and frequency.
• 16% of assessed cases received a loading dose and 6% were loaded and adherent to the dosing nomogram.
• 2nd Outcome Measure
• Adherence led to a non-statistically significant (NIS) proportion of vancomycin trough levels in the range of 15-20 mg/L: 20% vs 19%.

Limitations
• The sample of orders studied is reflective of only orders with complete electronic footprints (only a small fraction of vancomycin orders).
• Limits of clinical informatics data: e.g. order entry is not permanently updated on a 24hr basis potentially leading to timing discrepancies.

Conclusion

• Adherence to the empiric vancomycin dosing nomogram is limited.
• Target troughs of 15-20 mg/L are not attained >80% of the time when vancomycin is empirically dosed at Island Health.
• Adherence to the nomogram does not appear to improve the proportion of trough levels in the 15-20 mg/L range – a discrepancy seeing as previous studies have demonstrated the nomogram to be 52-70% predictive.

A Retrospective Clinical Informatics Study: Improving and validating the use of a VANCOMycin nomogram (ID-VAHC).

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Island Health.