**Evaluation of Vancomycin Dosing Practices and Attainment of Target Pre-Dialysis Trough Levels in Hemodialysis Patients**

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**Background**
Vancomycin is a bacterioidal glycopeptide antibiotic that was first introduced in 1956. (1) It is commonly used in the treatment of infections caused by methicillin-resistant Staphylococcus aureus (MRSA). (2) A steady rise in the number of infections caused by this organism since the early 1980s has led to an increase in the use of this antibiotic. (2)

In 2003, a consensus review was issued jointly by the American Society of Health-System Pharmacists, the Infectious Disease Society of America, and the Society of Infectious Diseases Pharmacists to guide the use and therapeutic monitoring of this antibiotic. (3) It is agreed that trough serum concentrations are the most accurate and practical method for monitoring the effectiveness of this drug.

To avoid the development of resistant organisms, current recommendations suggest monitoring trough serum vancomycin concentrations above 10 mg/L. (2) For complicated infections such as bacteriaemia, endocarditis, osteomyelitis, meningitis, and hospital-acquired pneumonia, higher trough serum vancomycin concentrations of 15-20 mg/L are recommended. (3)

In hemodialysis patients, infection is the second leading cause of death, accounting for 12.5-36% of the mortality that occurs in this population. (4,5) Septicemia is the cause in three out of every four deaths caused by infectious etiology. (4,5) There is a fair amount of data in the literature discussing therapeutic drug monitoring for vancomycin; however, dosing information in the hemodialysis population to achieve specific levels is limited. (1)

In 2007, the Clinical Pharmacotherapist of the Fraser Health Renal Program devised a set of weight based vancomycin dosing guidelines for patients undergoing hemodialysis who weigh at least 50 kg. For a patient weighing 50-75 kg, a single loading dose of 1000 mg given over the last 60 minutes of dialysis, followed by maintenance dose of 500 mg given over the last 60 minutes of each subsequent dialysis run. (6) For patients weighing over 75 kg, a single loading dose of 1500 mg given over the last 90 minutes of dialysis is suggested, followed by a maintenance dose of 750 mg given over the last 45 minutes of each subsequent dialysis run. (6) In the Fraser Health Renal Program, these dosing guidelines are provided as a tool to prescribers; however, physicians and pharmacists are free to prescribe the vancomycin regimens as they see fit for each patient and need not follow these dosing suggestions.

**Aim of This Study**
This was a retrospective chart review conducted at Surrey Memorial Hospital.

- The primary aim of this study was to evaluate how well our current vancomycin dosing strategies have been working in terms of achieving specified target trough pre-hemodialysis serum concentrations.
- The secondary aim of this study was to assess whether the aforementioned vancomycin dosing guidelines have been adopted by our practitioners.

**Methods: Project Design**
To identify patients who met the inclusion criteria, drug usage reports were generated through the BC Provincial Agency’s Patient Records and Outcome Management Information System (PRAMIS) and Meditech, our hospital’s medication dispensing software. All episodes of care where a patient on hemodialysis received vancomycin at our hospital during the period of January 1, 2008 through December 31, 2012, inclusive, were identified.

- Patients were included if they had stage 5D chronic kidney disease and were receiving conventional high-flux intermittent hemodialysis treatments at Surrey Memorial Hospital, were prescribed intravenous vancomycin therapy during the time that they were on hemodialysis, and had at least one pre-hemodialysis vancomycin level drawn during their course of therapy. It was required that the pre-dialysis vancomycin level was drawn, at earliest, immediately prior to the second hemodialysis run where a dose of vancomycin was to be given.
- Patients were excluded if they were pregnant or breastfeeding, if it was determined that the serum vancomycin level drawn was not drawn immediately prior to the commencement of a hemodialysis session, if vancomycin doses were not given as prescribed prior to collection of the pre-hemodialysis level, or if the patient was admitted to the intensive care unit.

**Methods: Outcomes & Statistics**

**Table 1: Patient Demographics**

<table>
<thead>
<tr>
<th>Type of Infection</th>
<th>Number of courses of vancomycin in patients meeting inclusion criteria</th>
<th>Number of patients</th>
<th>Vancomycin initiated as outpatient, n (%)</th>
<th>Vancomycin initiated as inpatient, n (%)</th>
<th>Mean age, years ± SD</th>
<th>Mean dry weight, kg ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary infection</td>
<td>68</td>
<td>58</td>
<td>33 (49)</td>
<td>35 (52)</td>
<td>63 ± 17</td>
<td>73.5 ± 18.7</td>
</tr>
<tr>
<td>Secondary infection</td>
<td>30</td>
<td>26</td>
<td>20 (77)</td>
<td>10 (38)</td>
<td>65 ± 13</td>
<td>73.7 ± 18.7</td>
</tr>
</tbody>
</table>

**Table 2: Outcomes**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Number of occurrences (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary infection</td>
<td>17 (25)</td>
</tr>
<tr>
<td>Secondary infection</td>
<td>46 (88)</td>
</tr>
</tbody>
</table>

**Discussion Points**
This study serves to characterize what was being done at our center during the study period:
- The infection cure rate across all patients in this study was 68%. In order to best achieve clinical cure and to prevent the development of resistant organisms, the literature suggests maintaining trough serum vancomycin concentrations above 10mg/L. (2) In some studies the target for hemodialysis, trough serum vancomycin concentrations of 15-20 mg/L are recommended. When only cases of infection caused by MRSA were considered, the mean pre-dialysis trough serum vancomycin level in the group that experienced clinical cure was not significantly different from the group that experienced treatment failure. It is acknowledged that the sample size of this group was quite small with only 19 cases. However, the result was similar when all cases of infection were considered.
- The proportion of cases in which the measured pre-dialysis vancomycin levels were within the range of 15-20 mg/L was relatively low, at 25%. Moreover, only 53% of the pre-hemodialysis vancomycin levels were within the range of 10-20 mg/L, and a significant proportion (22%) of pre-dialysis levels were under 10 mg/L. This suggests that the current dosing guidelines need further study to determine the considerable failure rate of 25% seen in this study.
- It is noted that uptake of the 2007 Fraser Health Renal Program Vancomycin Dosing Guidelines was relatively low, given that only 49% of all cases were in concurrence with these guidelines. Reasons include the lack of a formal education plan when these dosing guidelines were developed and a lack of a standardized pre-printed order outlining these suggested regimens.

**Limitations**
Although our study provides valuable information about our hospital’s vancomycin dosing practices during the time period studied, some limitations are acknowledged with our data:
- Only patients who had a pre-dialysis trough vancomycin level drawn while they were on this drug were included. We did not consider patients who received vancomycin therapy but did not get a pre-hemodialysis vancomycin level drawn. This study does not provide information about the outcomes of this latter group of patients.
- Patients may have been on other antibiotics in addition to vancomycin during the study period. This may have influenced the clinical outcome seen in this study.
- Our sample sizes were relatively small for some of the analyses. It is possible that type II errors may have occurred due to the limited number of patients.
- Lastly, patients’ dialysis schedules and the amount of time from hemodialysis runs were not considered in the interpretation of the collected data.

**Conclusions**
- Based on this data, there was not a clear vancomycin dosage strategy practiced at our hospital for initial dosing in hemodialysis patients.
- The uptake of the 2007 Fraser Health Renal Program Vancomycin Dosing Guidelines has been low and the mean vancomycin loading dose of 17.3 mg/L used at our centre is lower than the literature described increase of 20-30 mg/L. (1,3)
- Only 25% of pre-dialysis vancomycin levels measured were within the range of 15-20 mg/L. When the range was expanded to 10-20 mg/L, the percentage increased to 36%.
- Based on the results of this study, it is reasonable to consider increasing our loading dose of vancomycin beyond 17.3 mg/L.

Follow-up studies are warranted to determine the impacts of any changes in our dosing practices on vancomycin levels and patient outcomes, such as infection cure rates or vancomycin-related toxicity.

**References**

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