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

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**Background**

Vancomycin is a bacteriocidal 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 2009, 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. (2) It is agreed that trough serum concentrations are the most accurate and practical method to monitor the effectiveness of this drug.

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

In hemodialysis patients, infection is the second leading cause of death, accounting for 12-36% of the mortality that occurs in this population. (4,5) Staphylococcal 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 Pharmacotherapy Specialists of the Fraser Health Renal Program devised a set of weight based vancomycin dosing guidelines for patients undergoing hemodialysis with a weight of less than 50 kg. For a patient weighing 50-75 kg, a single loading dose of 1.0 g mg/L was followed by a maintenance dose of 0.5 g every other day. (1,2) For patients weighing over 75 kg, a single loading dose of 1.5 g mg/L was followed by a maintenance dose of 0.75 g mg/L every other day. (1,2)

This was a retrospective chart review conducted at Surrey Memorial Hospital.

**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 (P-RAMS). Fraser Health Renal Program, Meditech, our hospital’s medication dispensing software. All episodes of care where a patient on haemodialysis 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 vancomycin trough level drawn during their course of therapy. It was required that the pre-dialysis vancomycin level was drawn, at earliest, immediately prior to the secondary 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 vancomycin serum level 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-dialysis level, or if the patient was admitted to the intensive care unit.

**Methods: Outcomes & Statistics**

**Primary Outcome**: Percentage of serum trough pre-dialysis vancomycin levels that fall within the range of 10-20 mg/L inclusive.

**Secondary Outcomes**, with data to be expressed using descriptive statistics:

- Infection cure rate, based on chart documentation of resolution of infection
- Proportion of serum trough pre-dialysis vancomycin levels within the range of 10-20 mg/L (inclusive)
- Proportion of serum trough pre-dialysis vancomycin levels within the range of greater than 20 mg/L
- Number of vancomycin doses prescribed in accordance with the 2007 Fraser Health Renal Program weight-based dosing guidelines

Further analysis will be performed to assess whether an association exists between mean vancomycin levels and infection cure rates for MRSA infections. For this analysis, a two-sample t-test for independent means will be used, with a p-value less than 0.05 being considered statistically significant.

**Table 1: Patient Demographics**

| Number of courses of vancomycin in patients meeting inclusion criteria | 68 |
| Number of patients | 58 |
| Vancomycin initiated as outpatient, n (%) | 33 (49) |
| Vancomycin initiated as inpatient, n (%) | 35 (52) |
| Mean age, years ± SD | 63 ± 17 |
| Male, n (%) | 37 (64) |
| Mean dry weight, kg ± SD | 73.5 ± 18.7 |

**Table 2: Outcomes**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Number of occurrences (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infection cure rate</td>
<td>48 (68)</td>
</tr>
<tr>
<td>Proportion of serum trough pre-dialysis vancomycin levels within the range of 10-20 mg/L (inclusive)</td>
<td>36 (53)</td>
</tr>
<tr>
<td>Proportion of serum trough pre-dialysis vancomycin levels in excess of 20 mg/L</td>
<td>11 (16)</td>
</tr>
<tr>
<td>Mean initial loading and maintenance doses of vancomycin ordered, and mean pre-hemodialysis vancomycin level</td>
<td>17 (25)</td>
</tr>
<tr>
<td>Proportion of initial vancomycin doses prescribed in accordance with the 2007 Fraser Health Renal Program weight-based dosing guidelines</td>
<td>15 (22)</td>
</tr>
</tbody>
</table>

**Table 3: Additional Outcomes**

| Mean pre-hemodialysis vancomycin level in patients cured of MRSA infection, mg/L ± SD | 16.5 ± 4.1 * |
| Mean pre-hemodialysis vancomycin level in patients not cured of MRSA infection, mg/L ± SD | 12.0 ± 4.7 * |
| Courses of vancomycin therapy where initial dose was in concordance with the 2007 Fraser Health Renal Program Vancomycin Dosing Guidelines, n (%) | 14 (2) |
| Mean initial vancomycin loading dose, mg/kg ± SD | 17.3 ± 5.8 |
| Mean QHD initial vancomycin maintenance dose, mg/kg ± SD | 9.7 ± 3.1 |
| Mean pre-hemodialysis vancomycin achieved with initial dose, mg/L ± SD | 15.9 ± 6.9 |

* No statistically significant difference

**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 10 mg/L, and in some types of infections, 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 vancomycin level in the group that experienced clinical cure was not statistically 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, which may have limited our ability to demonstrate statistical significance; however, the difference in levels may have been clinically significant.

- 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-dialysis vancomycin levels were within the range of 10-20 mg/L, and a significant proportion of the pre-dialysis levels were under 10 mg/L, which may have contributed to the considerable failure rate of 29% seen in this study. It is noted that up to the 2007 Fraser Health Renal Program Vancomycin Dosing Guidelines were relatively low, given that only 21% of studied cases were dosed in concordance with these guidelines. Potential reasons aside the lack of a formal education plan when these dosing guidelines were developed and the 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, a number of 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-dialysis vancomycin level drawn. This study does not provide information about the outcomes of this latter group of patients.
- Potential for use of other antibiotics in addition to vancomycin during the study period. This may have had an effect on the rate of clinical cure.
- Case 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.
- Lack of patients’ dialysis schedules and the amount of time between hemodialysis runs were not considered in the interpretation of the collected data.

**Conclusions**

- Based on these data, the initial vancomycin dosing strategy in hemodialysis patients at Surrey Memorial Hospital led to highly variable pre-dialysis trough concentrations of the drug. There was a low uptake of the internal 2007 Fraser Health Renal Program Vancomycin Dosing Guidelines.
- The mean vancomycin loading dose was 17.3 mg/L. Likely as a result, only 25% of measured pre-dialysis vancomycin levels fell within the range of 15-20 mg/L. This increased to 32% when the range was expanded to 10-20 mg/L.
- There is a need to determine the necessity of vancomycin loading doses of at least 20 mg/L, especially for treating infections requiring trough levels of 15 to 20 mg/L (1,3)

Further 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**

4. Vancomycin loading dose was 17.3 mg/L. Likely as a result, only 25% of measured pre-dialysis vancomycin levels fell within the range of 15-20 mg/L. This increased to 32% when the range was expanded to 10-20 mg/L.
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