Characterization of Vancomycin Dosing in Outpatient Hemodialysis Patients at Surrey Memorial Hospital

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Background

Vancomycin is a bacteriocidal glycopeptide commonly used in the treatment of infections caused by gram-positive organisms, especially MRSA[1]. The American Society of Health-System Pharmacists (ASHP), Infectious Disease Society of America (IDSA), and Society of Infectious Diseases Pharmacists (SIDP) recommend targeting serum trough levels of 10-20 mg/L in order to reduce the risk of treatment failure and the development of resistant organisms[1]. Target trough levels of 15-20 mg/L are recommended for complicated infections such as bacteremia, endocarditis, osteomyelitis, hospital acquired pneumonia, meningitis and severe soft-tissue infections[1]. In order to achieve the higher target trough levels of 15-20 mg/L, several studies in the literature have suggested using loading doses ranging from 15-20 mg/kg or 20-25 mg/kg [2,3,4,5,6]. The maintenance doses used in these studies generally ranged from 500 mg to 750 mg IV at the end of each hemodialysis session based on the weight of the patient, which equated to approximately 7-10 mg/kg [2,3,4,5,6].

In 2013, the Clinical Pharmacotherapy Specialists of the Fraser Health Renal Program conducted a study to examine vancomycin dosing practices in hemodialysis patients at Surrey Memorial Hospital, in an effort to characterize current practices and identify opportunities for improvement. It was found that the mean loading and maintenance doses prescribed at the time were 17.3 mg/kg and 9.7 mg/kg IV after each hemodialysis session, respectively. This resulted in 53% of pre-hemodialysis vancomycin trough levels falling within the range of 10-20 mg/L, and 25% falling within the range of 15-20 mg/L. Based on the results of the evaluation in 2013, the vancomycin dosing recommendations at Fraser Health were revised and education was provided to prescribers and renal pharmacists, encouraging the use of a more aggressive loading dose to the magnitude of 25 mg/kg, and a maintenance dose of 10 mg/kg IV at the end of each hemodialysis (QHD) session. This is a follow-up study to assess vancomycin dosing practices and performance after these interventions were made.

Purpose

To characterize vancomycin dosing practices in hemodialysis outpatients at Surrey Memorial Hospital (SMH) between 2014 and 2016 (inclusive), and to determine the proportion of serum trough pre-hemodialysis vancomycin levels that meet specific targets recommended by the ASHP, IDSA, and SIDP. Uptake of the vancomycin dosing recommendations from the previous Fraser Health study and patient outcomes will also be assessed.

Methods: Project Design

Patients were identified through the BC Provincial Agency's Patient Records and Outcome Management Information System (PROMIS). All episodes where a patient on hemodialysis received vancomycin at our Surrey Memorial Hospital during the period of January 1, 2014 through December 31, 2016, inclusive, were identified.

Design: Single-centre, retrospective chart review

Inclusion criteria:

- Stage 5 chronic kidney disease (eGFR < 15 mL/min)
- Received outpatient hemodialysis at SMH
- Prescribed intravenous (IV) vancomycin during the time of hemodialysis

Exclusion criteria:

- <18 years old
- Pregnant or breastfeeding at the time of vancomycin therapy
- No vancomycin trough levels drawn
- Inpatient status at the time of initiating vancomycin

Statistics: Descriptive statistics, unpaired t-test and chi-square test. P-values less than 0.05 were considered statistically significant.

Outcomes

Primary Outcomes

Proportion of trough serum vancomycin levels within the range of 10-20 mg/L (inclusive)

Proportion of vancomycin orders prescribed with a loading dose approximating 25 mg/kg (allowable range 22-28 mg/kg) and maintenance dose approximating 10 mg/kg (allowable range 9-11 mg/kg) IV QHD session, as per recommendations from our previous study

Secondary Outcomes

Proportion of trough serum vancomycin levels within the range of 5-9.9 mg/L (inclusive)

Proportion of trough serum vancomycin levels within the range of 10-14.9 mg/L (inclusive)

Proportion of trough serum vancomycin levels within the range of 15-20 mg/L (inclusive)

Proportion of trough serum vancomycin levels within the range of 20.1-25 mg/L (inclusive)

Proportion of trough serum vancomycin levels greater than 20 mg/L

Proportion of trough serum vancomycin levels less than 10 mg/L

Compliance of medication administration to the ordered vancomycin regimen

Infection cure rate, defined as complete clinical resolution of the infection that vancomycin was intended to treat and where *treatment failure* or *death due to any cause* was not documented

- *Treatment failure* was defined as any of the following: *(i)* admission due to the primary infection; *(ii)* recurrence of the primary infection within 30 days after the cessation of vancomycin therapy; or *(iii)* a change in antibiotic therapy from vancomycin to other antibiotic(s).

Rate of all-cause mortality

Rate of hospitalization secondary to the primary infection

Rate of hospitalization secondary to causes unrelated to the primary infection

Patient outcomes (infection cure rate, failure rate, all-cause mortality rate, and hospitalization rates) were assessed from the initiation of vancomycin therapy until 30 days after vancomycin therapy was discontinued.

Results

Figure 1 – Patient Selection

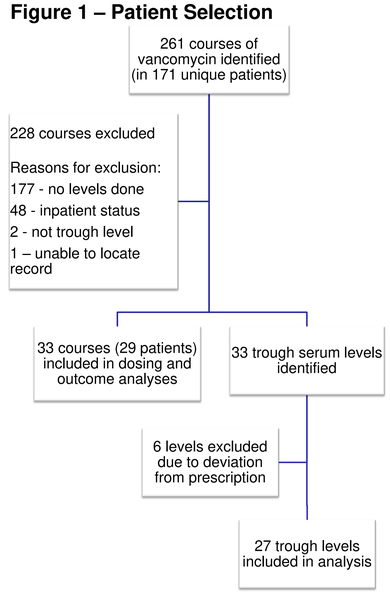


Table 1: Patient Demographics; N=29	
Age (years ± SD)	65.6 ± 11.1
Gender (male)	20 (69%)
Weight (kg ± SD)	84.0 ± 20.6
Mean eGFR (mL/min ± SD)	8.3 ± 2.9
Mean HD frequency (sessions/week ± SD)	3.2 ± 0.5
Comorbidities	
Hypertension	28 (97%)
Diabetes	25 (86%)
Coronary artery disease (incl. history of MI)	19 (66%)
Dyslipidemia	17 (59%)
Peripheral vascular disease	9 (31%)

Table 2: Infection Type; n=33	
Wound infection without osteomyelitis	12 (36%)
Osteomyelitis	7 (21%)
Catheter-related sepsis/bacteremia	5 (15%)
Catheter-related infection (not including sepsis)	4 (12%)
Cellulitis	4 (12%)
UTI	1 (3%)
Common Causative Organisms on Microbiology (32 cultures done)	
Methicillin-resistant *Staphylococcus aureus* (MRSA)	11 (34%)
Methicillin-sensitive *Staphylococcus aureus* (MSSA)	6 (19%)
Coagulase-Negative Staphylococci	3 (9%)
Skin Flora	3 (9%)

Primary Outcomes

Table 3: Primary Outcomes	Occurrence (%)
Proportion of trough serum vancomycin levels within the range of 10-20 mg/L	18/27* (67%)
Proportion of vancomycin orders prescribed with a loading dose approximating 25 mg/kg (range 22-28 mg/kg)	11/33 (33%)
Proportion of vancomycin orders prescribed with a loading dose approximating 10 mg/kg (range 9-11 mg/kg)	13/33 (39%)

*6 levels excluded from this analysis due to deviation from order prior to 1st level, resulting in 27 levels being analysed

Secondary Outcomes

Figure 2 – Distribution of Vancomycin Trough Levels

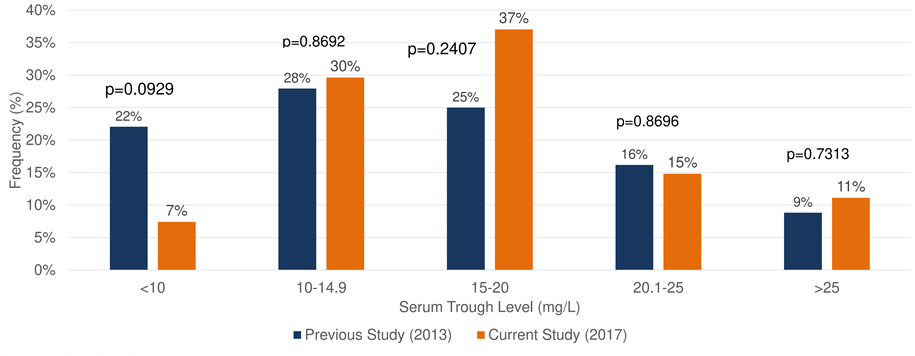
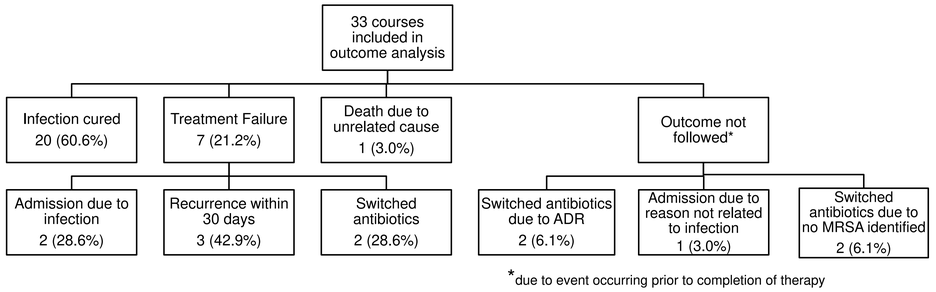


Figure 3 – Patient Outcomes



*due to event occurring prior to completion of therapy

Discussion

Table 4: Prescriber Initiating Therapy; n=33	
Nephrologist	32 (97.0%)
Pharmacist Involvement	*13 (40.6%)*
Emergency Room Physician	1 (3.0%)

Table 5: Current Study Comparison with *Cho et al. 2013*

	Cho et al. 2013 (n=68)	Current Study (n=33)	P-value
Mean loading dose (mg/kg ± SD)	17.3 ± 5.8	19.3 ± 5.3	0.0952
Mean maintenance dose (mg/kg ± SD)	9.7 ± 3.1	10.1 ± 2.2	0.5247
Mean serum trough Level (mg/L ± SD)	15.9 ± 6.9	17.0 ± 5.4*	0.4376
Infection cure rate	46/68 (68%)	20/33 (61%)	0.4864
MRSA cure rate	7/19 (37%)	5/10 (50%)	0.4676
Treatment failure rate	20/68 (29%)	7/33 (21%)	0.7627

* n=27

Discussion Points

- Only 33% of vancomycin loading doses and 39% of maintenance doses were prescribed in concordance to the recommendations from the previous study. In consideration of the possibility that the maintenance dose range of 9-11 mg/kg may have been too narrow to accommodate rounding, we found that 64% of the initially prescribed maintenance doses would have complied with the recommendations if the accepted range was expanded to 8-12 mg/kg.
- A trend toward higher mean loading doses being prescribed compared to previous practice was found. This may have contributed to the greater proportion of serum trough vancomycin levels achieving the target ranges of 10-20 mg/L (67% vs. 53%) and 15-20 mg/L (37% vs. 25%). However, these differences were not found to be statistically significant.
- The first serum trough levels were, on average, drawn 8.4 days (±4.4 days) after the loading dose, before the hemodialysis session for the fourth dose of vancomycin.
- Vancomycin courses that resulted in cure of infection had a trend towards higher serum trough levels when compared to courses where the infection was not cured (16.5 mg/L vs. 14.7 mg/L), although this difference was not statistically significant (p=0.3749).

Limitations

- Small sample size
- Only patients with trough levels were included
  - Reason for having a vancomycin level drawn may be a confounding variable that influenced our patient selection. Therefore, our results may not reflect dosing practices and patient outcomes for those that did not have a trough level drawn.
- Comparator group had a slightly different patient population
  - Inpatients were included in *Cho et al. 2013*
  - *Cho et al. 2013* had a greater variety of infection types, potentially selecting for more severely ill patients, which may have affected prescribing patterns and patient outcomes

Conclusions

- Trends toward a greater proportion of serum trough vancomycin levels falling within the target range of 10-20 mg/L and a higher mean serum trough level (17.0 mg/L vs. 15.9 mg/L) compared to previous practice.
- Levels captured in the current study are reflective of trend towards higher loading doses being used (mean of 19.3 mg/kg vs. 17.3 mg/kg), while maintenance doses being used remained relatively similar to previous practice (10.1 mg/kg vs. 9.7 mg/kg).
- It is reasonable to continue with the current practice of prescribing vancomycin using loading doses of 20 mg/kg IV and maintenance doses of 10 mg/kg IV QHD session, which is consistent with recommendations found in literature.

References

1. Rybak M, Lomaestro B, Rotschafer JC, Moellering Jr R, Craig W, Billeter M, et al. Therapeutic monitoring of vancomycin in adult patients: a consensus review of the American Society of Health-System Pharmacists, the Infectious Diseases Society of America, and the Society of Infectious Diseases Pharmacists. Am J Health-Syst Pharm 2009;66:82-98.
2. Nekidy WS, El0Masri MM, Umstead GS, Dehoorne-Smith M. Factors Influencing Vancomycin Loading Dose for Hospitalized Hemodialysis Patients: Prospective Observational Cohort Study. Can J Hosp Pharm. 2012;65(6):436-442
3. Vandecasteele SJ, De Vriese AS. Vancomycin Dosing in Patients on Intermittent Hemodialysis. Seminars in Dialysis. 2011 Jan;24(1):50–5.
4. Vandecasteele SJ, Vriese AS. Recent changes in vancomycin use in renal failure. Kidney Int 2010;77:760-4.
5. Crew P, Heintz SJ, Heintz BH. Vancomycin dosing and monitoring for patients with end-stage renal disease receiving intermittent hemodialysis. Am J Health-Syst Phar. 2015;72:1856-1864
6. Maxson R, Pate J, Starr J. Evaluation of weight-based vancomycin dosing for hospitalized hemodialysis patients. Renal Failture. 2016;38(10):1677-1682