Vancomycin Dosing in Obesity

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Background

- Vancomycin is used to treat infections caused by gram positive bacteria, especially methicillin resistant *S. aureus* (MRSA) infections
- 2009 Infectious Disease Society of America (IDSA) guidelines recommending dosing vancomycin based on total body weight (TBW) for all patients, acknowledging that limited data is available for dosing in obese patients
- This vancomycin Drug Utilization Review was undertaken to help the clinical pharmacists at St. Luke's Boise and Meridian facilities better manage obese patients in order to improve patient outcomes

Objectives

Primary

- To determine whether dosing by total body weight (TBW) or adjusted body weight (AdjBW) in obese patients more reliably achieves therapeutic vancomycin trough levels

Secondary

- To describe goal trough level achievement based on initial dosing in terms of total daily dose received in mg/kg/day by TBW and by AdjBW
- To assess appropriateness of St. Luke's Boise and Meridian vancomycin dosing guidelines for obese patients.

Methods

Retrospective chart review of 80 patients who received vancomycin therapy between Jan 1, 2012 and Jun 30, 2012

Inclusion criteria:

- Inpatients at St. Luke's Boise or Meridian facilities
- ≥ 18 years of age
- ≥ 100 kg with a BMI ≥ 30
- Receiving vancomycin ≥ 3 days
- Appropriately drawn trough levels

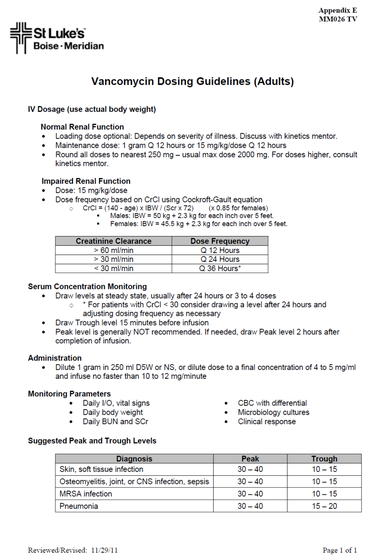
Exclusion criteria:

- Patients who did not meet the above criteria

- Chi-square analysis was performed to evaluate the number of patients who reached a therapeutic vancomycin trough within 15% of expected total daily dose (TDD) by TBW or by AdjBW
  - Expected TDDs were determined based on St. Luke's Boise and Meridian Vancomycin Dosing Guidelines
- IRB approved

Results

Figure 1: St. Luke's Vancomycin Dosing Recommendations



Appendix E
MM026 TV

St Luke's Boise · Meridian

Vancomycin Dosing Guidelines (Adults)

IV Dosage (use actual body weight)

Normal Renal Function
- Loading dose optional: Depends on severity of illness. Discuss with kinetics mentor.
- Maintenance dose: 1 gram Q 12 hours or 15 mg/kg/dose Q 12 hours
- Round all doses to nearest 250 mg – usual max dose 2000 mg. For doses higher, consult kinetics mentor.

Impaired Renal Function
- Dose: 15 mg/kg/dose
- Dose frequency based on CrCl using Cockroft-Gault equation
  - CrCl = (140 - age) x IBW / (Scr x 72) (x 0.85 for females)
    - Males: IBW = 50 kg + 2.3 kg for each inch over 5 feet.
    - Females: IBW = 45.5 kg + 2.3 kg for each inch over 5 feet.

Creatinine Clearance	Dose Frequency
> 60 ml/min	Q 12 Hours
> 30 ml/min	Q 24 Hours
< 30 ml/min	Q 36 Hours*

Serum Concentration Monitoring
- Draw levels at steady state, usually after 24 hours or 3 to 4 doses
  - * For patients with CrCl < 30 consider drawing a level after 24 hours and adjusting dosing frequency as necessary
- Draw Trough level 15 minutes before infusion
- Peak level is generally NOT recommended. If needed, draw Peak level 2 hours after completion of infusion.

Administration
- Dilute 1 gram in 250 ml D5W or NS, or dilute dose to a final concentration of 4 to 5 mg/ml and infuse no faster than 10 to 12 mg/minute

Monitoring Parameters
- Daily I/O, vital signs
- Daily body weight
- Daily BUN and SCr
- CBC with differential
- Microbiology cultures
- Clinical response

Suggested Peak and Trough Levels

Diagnosis	Peak	Trough
Skin, soft tissue infection	30 – 40	10 – 15
Osteomyelitis, joint, or CNS infection, sepsis	30 – 40	10 – 15
MRSA infection	30 – 40	10 – 15
Pneumonia	30 – 40	15 – 20

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Table 1: Baseline Population Characteristics

Characteristic	n (%) patients*
Number of patients	80 (100%)
Sex (male)	48 (60%)
Boise/Meridian inpatients	40 (50%)/ 40 (50%)
Mean weight (kg)	124.9 ± 22.5
Mean height (cm)	175.7 ± 10.9
Mean age (years)	59 ± 14.6
Mean BMI	40.6 ± 7.2
Mean estimated CrCl (ml/min)	72 ± 33.5
Indication	
Sepsis	40 (50%)
Pneumonia	19 (23.8%)
Cellulitis	17 (21.3%)
Osteomyelitis	1 (1.3%)
Meningitis	1 (1.3%)
Other	8 (10%)

*Continuous variables represented as mean ± standard deviation

Table 2. St. Luke's recommended vancomycin dosing

CrCl (mL/min)	Recommended Dose	Recommended Total Daily Dose
≥ 60	15 mg/kg Q 12 hours	30 mg/kg/day
≥ 30 and < 60	15 mg/kg Q 24 hours	15 mg/kg/day
< 30	15 mg/kg Q 36 hours	10 mg/kg/day

Table 3. Average doses received when therapeutic

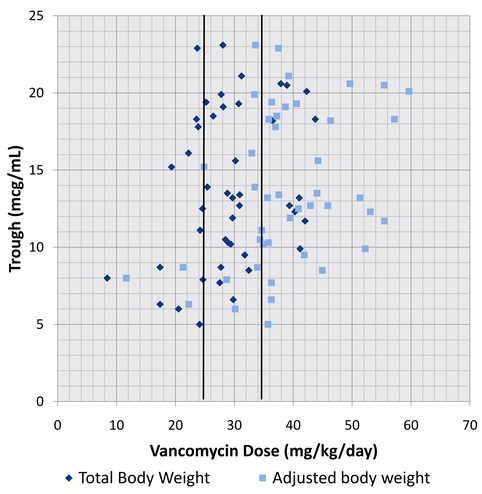
Estimated CrCl (mL/min)	Total Body Weight	Adjusted Body Weight
≥ 60	30.8 mg/kg/day	41.2 mg/kg/day
≥ 30 and < 60	22.3 mg/kg/day	32.2 mg/kg/day
< 30	14.6 mg/kg/day	19.8 mg/kg/day

Table 4: Population characteristics between patients who met therapeutic trough when dosed by TBW versus AdjBW

Characteristic	TBW n (%) patients*	AdjBW n (%) patients*
Number of patients⁺	23	6
Sex (male)	18 (78.3%)	6 (100%)
Boise/Meridian inpatients	10 (43.5%)/ 13 (56.5%)	4 (66.7%)/ 2 (33.3%)
Mean weight (kg)	130 ± 26.1	135.1 ± 30.9
Mean height (cm)	181.2 ± 9.7	183.7 ± 2.6
Mean age (years)	57.1 ± 14.7	62.8 ± 13.4
Mean BMI	39.6 ± 7.4	39.8 ± 8.4
Mean estimated CrCl (ml/min)	85.8 ± 36.4	70.3 ± 25.2
Indication		
Sepsis	9 (39.1%)	0
Cellulitis	6 (26.1%)	4 (66.7%)
Pneumonia	4 (17.4%)	1 (16.7%)
Osteomyelitis	1 (4.3%)	0
Meningitis	1 (4.3%)	0
Other	3 (13%)	1 (16.7%)

*Continuous variables represented as mean ± standard deviation
⁺p <0.001

Figure 1: Initial Total Daily Dose (TDD) received and trough levels in patients with CrCl ≥ 60 mL/min



Discussion

- Significantly more patients reached a therapeutic vancomycin trough with doses within 15% of expected total daily dose in mg/kg/day by TBW than by AdjBW (p <0.001)
  - A dose within 15% of expected was allowed to account for dose rounding
- In patients with an estimated CrCl between 50 and 60 mL/min, 6/11 (54.5%) patients achieved therapeutic trough when receiving doses within 15% of 30 mg/kg/day TBW vs 1/11 (9.1%) of patients within 15% of 15 mg/kg/day TBW
  - Our data suggests that obese patients with CrCl between 50 and 60 ml/min may benefit from vancomycin doses based on TBW administered every 12 hours

Limitations

- Retrospective design - patients may have preferentially received TBW dosing, when dosing by AdjBW may have also have achieved a therapeutic trough
- Not every patient in this study received initial dosing consistent with available guidelines.
- Assessing by total daily dose may not fully reflect pharmacokinetic considerations
- Most patients' trough goal was 10-15, which may not reflect optimal dosing in certain infections

Conclusion

- The most appropriate vancomycin dosing strategy in obese patients to reach therapeutic troughs appears to be dosing via total body weight versus adjusted body weight
- St. Luke's Boise and Meridian Vancomycin Dosing Guidelines appropriately suggest to dose patients by total body weight
- Further research is necessary to determine whether patients with estimated CrCl between 50 and 60 mL/min are appropriate candidates for total body weight dosing every 12 hours

References

- Rybak MJ, et al. Vancomycin therapeutic guidelines: a summary of consensus recommendations from the infectious diseases Society of America, the American Society of Health-System Pharmacists, and the Society of Infectious Diseases Pharmacists. Clin Infect Dis. 2009 Aug 1;49(3):325-7.

- Authors have the following relationship(s) to disclose related to this presentation: No relationships to disclose