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Vancomycin dosing in Obese and Morbidly Obese Patients with methicillin-resistant *Staphylococcus aureus* (MRSA) Pneumonia

Haley Morrill, PharmD[1,2], Aisling Caffrey, PhD, MS[1,2], Eunsun Noh, PhD[1,2], and Kerry LaPlante, PharmD[1,2,3]

[1]Infectious Diseases Research Program, VA Medical Center, Providence, RI;

[2]College of Pharmacy, University of Rhode Island, Kingston, RI; [3]Alpert Medical School of Brown University, Providence, RI

University of Rhode Island
7 Greenhouse Road
Kingston, RI 02881
(401) 874-5560

ABSTRACT

•**Background:** Despite the increasing burden of obesity, the optimal dose of vancomycin in obese and morbidly obsese (MO) patients with MRSA pneumonia is largely unknown.

•**Methods:** This national retrospective cohort study included obese patients (pts; BMI ≥ 30) admitted to VA hospitals with MRSA-positive cultures from respiratory sites between 2002 - 2012. Pts initiating vancomycin (VAN) in the hospital were selected for inclusion. Exclusion criteria included death or discharge within 2 days of treatment initiation and exposure > 2 consecutive days of MRSA antibiotic therapy in the 3 days prior to treatment initiation or during treatment with VAN. Pts were included if they had appropriately collected VAN troughs and no evidence of acute kidney injury prior to VAN initiation per VAN guidelines. Logistic regression models were used to measure the effect of various VAN dosing regimens on trough levels in obese and MO (BMI ≥ 40) pts.

•**Results:** We identified 263 obese and 73 MO pts treated with VAN with appropriately collected VAN trough levels. Total body weight ranged from 69 to 244 kg. The mean total daily dose of VAN was lower in obese vs. MO pts (2005 ± 736 vs. 2298 ± 923 mg, p <0.05) however the mean mg/kg/day dose was higher in obese vs. MO pts (20 ± 7 vs. 17 ± 7 mg/kg/day, p<0.05). About 20% of pts in each group had a vancomycin trough level of ≥15-20 mg/L. The mean mg/kg/day VAN dose was also higher in obese vs. MO pts with a trough of ≥15-20 mg/L (20 ± 7 vs. 15 ± 7 mg/kg/day, p<0.05). In obese pts, the standard dose of ~30mg/kg/day was appropriate for reaching a VAN trough of ≥15-20 mg/L (odds ratio [OR] 3.348, 95% confidence interval [CI] 1.2 - 9.2). In MO pts, as the mg/kg/day VAN dose increased, the odds of achieving a VAN trough of 15-20 mg/L decreased (OR 0.870, 95% CI 0.78 - 0.98).

•**Conclusions:** We offer additional consideration on the dosing of VAN in obese and MO pts. MO patients may require a lower mg/kg/day VAN dose than obese patients to reach a trough of ≥15-20 mg/L. However, further research is warranted to determine which VAN trough levels are associated with the best outcomes in obese and MO patients.

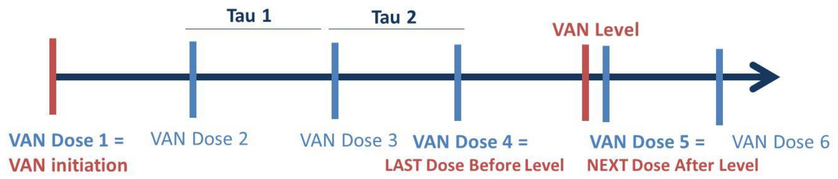
BACKGROUND

- MRSA is one of the most prevalent, pathogenic antimicrobial-resistant organisms, causing invasive infections worldwide.[1]
- MRSA has become a leading cause of pneumonia in both healthcare and community settings.[2,3]
- Approximately 69% of adults in the United States (US) are either overweight or obese.[4]
- The optimal dose of vancomycin, the gold-standard treatment for MRSA pneumonia, in obese and morbidly obese patients is largely unknown.

METHODS

- National VA retrospective cohort study of obese (BMI ≥ 30 kg/m^2) inpatients treated with vancomycin (VAN).
- Inclusion criteria
  - Appropriately collected VAN troughs (see Figure 1)[5]
  - No evidence of acute kidney injury prior to VAN initiation[5]
- Logistic regression models used to measure the effect of various VAN dosing regimens on trough levels in obese and morbidly obese (BMI ≥ 40 kg/m^2) patients

Figure 1. Vancomycin Trough Cohort Identification



1436 • At least 3 VAN doses before VAN level

961 • Tau1 and Tau2 lengths no more than 4 hours different

537 • Trough ≤2 h before NEXT dose OR time from LAST dose to LEVEL w/in 2 h of anvtau

352 • Baseline SCr (1 week prior) and Scr at VAN initiation (day of VAN)

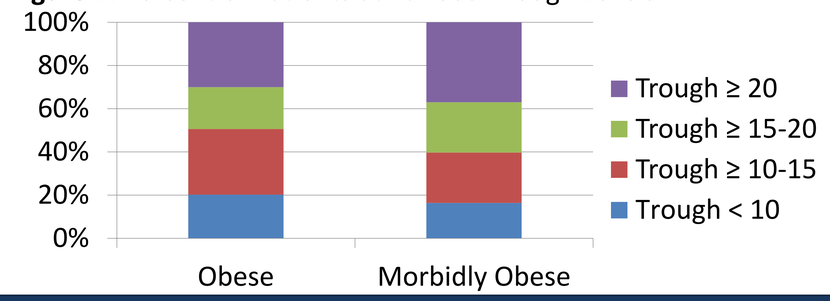
336 • Baseline and VAN initiation SCrs change of < 0.5 mg/dL and < 50%

RESULTS

Table 1. Weight, Trough Levels, and VAN Dosing by Obese Category

Characteristic	Obese (N=263)	Morbidly Obese (N= 73)	P-value
Total body weight(kg)	103 (13.1); 72-149	138 (32.2); 69 -244	<0.05
VAN trough concentration (mg/L)	17 (8.3); 1 - 46	20 (10.8); 6- 55	NS
Total Daily Dose (mg)	2005 (736.3); 500 - 4500	2298 (922.7); 750-6000	<0.05
Mg/kg/day	20 (7.4); 4 - 44	17 (6.9); 6 - 46	<0.05

Figure 2: Percent of Patients at Various Trough Levels



RESULTS

Table 2. VAN Dosing by Trough Level and Obese Category

Characteristic	Obese (N=263)	Morbidly Obese (N= 73)	P-value
Mg/kg/day if VAN trough < 10 mg/L:	17.0 (6.2)	16.8 (5.8)	NS
Mg/kg/day if VAN trough ≥ 10 - 15 mg/L:	19.0 (7.5)	13.5 (4.1)	<0.05
Mg/kg/day if VAN trough ≥ 15 - 20 mg/L:	20.5 (7.2)	15.3 (6.7)	<0.05
Mg/kg/day if VAN trough ≥ 20 mg/L:	21.7 (7.5)	21.0 (7.3)	NS

Table 3. VAN dosing on Trough Levels in Obese Patients

Outcome	Odds Ratio (95% CI)	P value
Trough ≥ 15 – 20 versus trough < 15 mg/L -Dose category 25-30 mg/kg/day	3.348 (1.214 - 9.234)	<0.05

- In obese patients, the standard dose of ~25-30mg/kg/day is appropriate for reaching the goal VAN trough of 15-20 mg/L

Table 4. VAN dosing on Trough Levels in Morbidly Obese Patients

Outcome	Odds Ratio (95% CI)	P value
Trough ≥ 15 – 20 versus trough > 20 mg/L - Mg/kg/day	0.870 (0.775 - 0.978)	<0.05

- In morbidly obese patients, as the mg/kg/day increased, the odds of achieving the goal VAN trough of 15-20 mg/L decreased

CONCLUSIONS

- We offer additional consideration on the dosing of VAN in obese and MO pts.
- MO patients may require a lower mg/kg/day VAN dose than obese patients to reach a trough of ≥15-20 mg/L.
- Further research is warranted to determine which VAN trough levels are associated with the best outcomes in obese and MO patients.

References 1. Diekema DJ, et al. JAMA 2008; 299(10): 1190-2. 2. Kollef MH, et al. Chest 2005; 128(6): 3854-62. 3. Mandell LA, et al. Clin Infect Dis 2007; 44(Suppl 2): S27-72. 4. Flegal KM, et al. JAMA 2012; 307(5): 491-7. 5. Rybak MJ, et al. Clinical Infectious Diseases 2009; 49(3): 325-7.

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