Impact of Weight-Based Dosing Guidelines on Vancomycin Dosing and Trough Levels, Including in Obese Patients

Erlaine F. Bello, MD, MS[1] Koh Okamoto, MD[2], James Davis, PhD[1], Teppei Shimasaki, MD[1]

[1] *University of Hawaii, Honolulu, Hawaii* [2] *Rush University, Chicago, Illinois, United States.*

ABSTRACT

Background: In 2009, the American Society of Health System Pharmacists (ASHSP), Infectious Diseases Society of America (IDSA) and Society of the Infectious Diseases Pharmacists (SIDP) released guidelines on vancomycin. The appropriateness of these guidelines for a local population, particularly the subset of obese patients, has not been well-studied.

Methods: A retrospective chart review was done on patients at an acute care, university-affiliated, community hospital who received intravenous vancomycin for suspected/documented infections before and after implementing the 2009 guidelines. Before 2009, patients received vancomycin 1 gm every 12 hours. After the guidelines, patients were dosed on actual body weight (ABW), 15 -20 mg/kg or 25-30 mg/kg in seriously ill patients, every 8-12 hours. We compared the frequency of therapeutic troughs, nephrotoxicity and trough group levels stratified by Body Mass Index (BMI) .

Results: There were no significant differences in therapeutic troughs and nephrotoxicity. Adjusted for BMI, there was a significant difference in trough levels between the two groups, P=0.0109. However, a large number of patients in the conventionally-dosed group were excluded due to inconsistent doses in the ABW-dosed group there was a high number of supra-therapeutic trough levels

Conclusion: Obese patients may require an alternate dosing strategy as the ABW-dosing based on the 2009 national guidelines resulted in supra-therapeutic levels in patients with high BMIs. Implementing guidelines –based monitoring resulted in more consistently and appropriately drawn levels.

INTRODUCTION

National guidelines for vancomycin dosing recommend actual body weight (ABW) –dosing over conventional dosing regardless of BMI. The guidelines acknowledge limited data in obese patients. This study tested the applicability of the guidelines to our hospitalized patients with suspected or proven infections who represented a wide range of BMIs. The achievement of therapeutic trough levels using conventional dosing was compared to ABW -dosing in obese and non-obese patients. The rate of nephrotoxicity in patients receiving conventional and ABW-dosing was also examined.

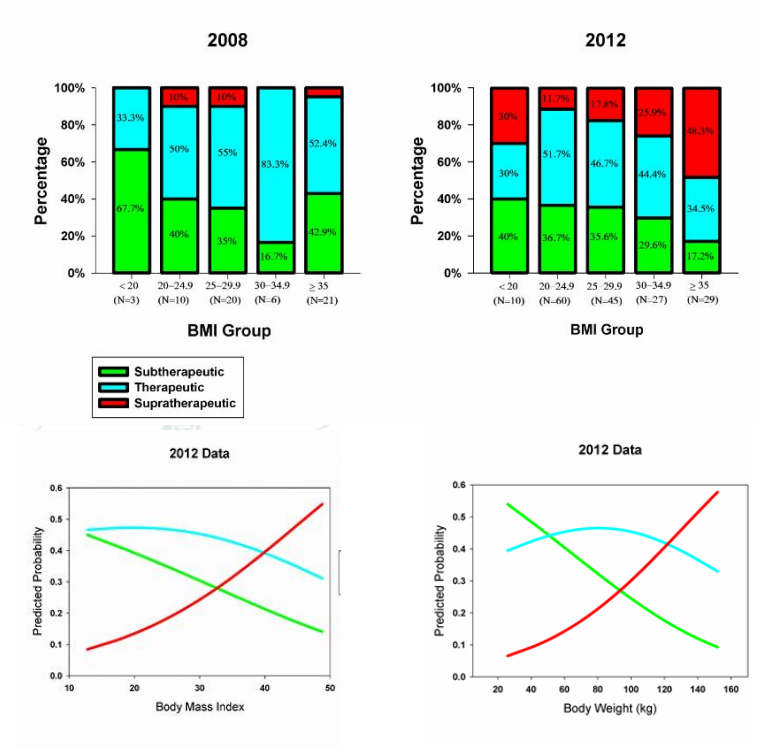
METHODS

- The study was conducted at The Queen's Medical Center (QMC) a 530 bed, university-affiliated, community teaching hospital in Honolulu, Hawaii between 2012-14 according to protocols approved by the QMC Institutional Research and Review Committee and the University of Hawaii Human Subjects Program.
- Retrospective review of the electronic charts of hospitalized patients who received intravenous vancomycin for documented or suspected infection between March-June 2008 (conventional) and March-June 2012 (ABW-dosing).
- Pre- guidelines in 2008, patients received vancomycin 1 gm every 12 hours. By 2012 patients were dosed based on ABW, 15-20mg/kg or 25-30mg/kg in seriously ill patients every 8 to 12 hours.
- Inclusion criteria: 1. adults>18 yoa; 2. received at least 3 doses of vancomycin 3. initial trough dose obtained within 96 hours of treatment initiation. Exclusion criteria: 1. calculated creatinine clearance <60ml/min/1.73m2; 2. hemodialysis; 3. given vancomycin with inconsistent dosing schedule; 4. trough level checked before third consecutive dose; 5. prescribed vancomycin for prophylaxis.
- Definitions: vancomycin levels: sub-therapeutic <10mg/L, therapeutic 10-20mg/L, supra-therapeutic >20mg/L. Nephrotoxicity was defined as an increase in serum creatinine level of 0.5mg/dL or an increase of 50% from baseline on at least two consecutive days during the period from start of vancomycin to 72 hrs after treatment completion. Obesity was defined as having a BMI of ≥ 30.
- Chi –square test (p<0.05) was used to show the difference between the 2008 and 2012 groups in achieving therapeutic trough levels , rates of nephrotoxicity and patient demographics . The Jonckheere-Terpstra test was used to compare differences in percentages of different trough groups (SAS, Cary, NC).

RESULTS

- 207 patients received vancomycin from March-June 2008 but only 60 patients met study criteria. 236 patients received vancomycin from March-June 2012 but only 171 of them met study criteria
- No significant differences in mean age , sex, ethnicity, site of infection.
- Large numbers of Asians and Pacific Islanders: 2008: 20% and 47% 2012: 36% and 30%.
- Only significant difference in underlying disease: high rate of CVD in 2012, P<0.0001.
- Significant difference in calculated creatinine clearance : 2008: 82.66 ±22.76 SD 2012: 103.3±42.01 SD, p<0.0001.
- No difference in nephrotoxicity, p=0.06
- No difference in achieving therapeutic trough levels, p=0.18
- When the two groups were stratified by BMI group, there was a significant difference between the 2008 and 2012 groups, p=0.0109.

RESULTS



DISCUSSION

- ABW-dosing did not confer any benefit over conventional dosing when groups were compared overall.
- Having a guideline in place which specified dose, dosing interval and timing of trough resulted in far fewer patients being excluded for inconsistent dosing and inappropriately drawn troughs but compliance still not 100%
- ABW-dosing was most effective in achieving therapeutic troughs in patients with BMIs between 20-24.9 but even in this group only 50% of the time
- ABW-dosing was least effective at low and high BMI subgroups.
- ABW-dosing in pts with BMI ≥ 35 had 48% supra-therapeutic trough levels.
- In ABW-dosed patients with BMI ≥ 30, the mean supra-therapeutic trough was 29.3. This was nearly identical to the values obtained by Reynods et al in their obese patients who received ABW-dosing. They developed their own protocol specifically for obese patients which deserves further testing in other populations.
- Our study was limited by the small size of the 2008 cohort relative to 2012.

CONCLUSION

- The 2009 guidelines based on actual body weight dosing did not confer any advantage in achieving therapeutic trough levels over conventional 1 gm every 12 hour dosing when applied to our patient population.
- There was no difference in the rate of nephrotoxicity between these dosing regimens.
- Patients with low and high BMIs may not be well-served by compliance with the current guidelines. In our obese patients there was a significantly high rate of supra-therapeutic troughs.
- Our findings are very consistent with Reynolds et al. who found similarly high rates of supra-therapeutic troughs and almost identical mean trough levels in their obese patients.
- Optimal vancomycin dosing is more complex for patients at extremes of weight and deserves further study.
- Implementation of the other aspects of the guidelines in addition to the actual dose of drug did result in more consistent vancomycin dosing and appropriately timed troughs levels compared to pre-guideline practices.

References

Reynolds DC, Waite LH, Alexander DP, DeRyke CA. Performance of a vancomycin dosage regimen developed for obeste patients. AJHP. 2012: 69(11):944-50. Epub 2013/06/27.

Acknowledgements: : Thanks to Lois Dement ,PharmD and Kurt Schanzenbach , PharmD for providing access to pharmacy records. Thanks to Todd Seto, MD for his general advice on data analysis.

Supported by Grant U54 MD007584 (NIMHD/NIH) "RCMI Multidisciplinary And Translational Research Infrastructure EXpansion, (RMATRIX)"

RMATRIX
RCMI Multidisciplinary And Translational Research Infrastructure eXpansion

UNIVERSITY of HAWAI'I MĀNOA

JOHN A. BURNS SCHOOL OF MEDICINE · UNIVERSITY OF HAWAII MANOA

NIMHD

NATIONAL INSTITUTES OF HEALTH