A Retrospective Clinical Informatics Study: Improving and valiDating the use of a VANCOmycin nomogram (ID-VANCO)

Christopher Yearwood, BSc(Pharm); Ajay Bains, BSc(Pharm), ACPR, BCPS; Faeka Husain, PharmD, BCPS; Richard Bachand, PharmD; Teg Bains, BSc(Pharm), BScSEng

island health

Introduction

- Vancomycin is an antibiotic that has been utilized clinically for nearly 60 years against serious, life-threatening, gram-positive infections.
- **Studies have linked low vancomycin levels (<10 mg/L) to therapeutic failure and the emergence of resistance.**
- A 2009 IDSA consensus guideline paper proposed *that serum vancomycin trough concentrations of 15-20 mg/L be targeted for serious infections* and that loading doses be administered in order to rapidly attain these serum vancomycin trough levels.
- Empiric vancomycin dosing nomograms have been developed to aid clinicians and they are 52-70% predictive for the 15-20 mg/L target trough range.
- These nomograms take into account patient age, gender, weight, and serum creatinine levels to provide an empiric loading dose, maintenance dose, and initial dosing frequency in the period before the first steady-state vancomycin trough level is obtained (usually prior to 3rd dose).
- **Island Health has a published nomogram, however, anecdotal observation suggests that the nomogram is used infrequently.**

Uniqueness of Research

- Analysis of health information databases can aid in refining clinical practice.
- Laboratory and pharmacy informatics resources were combined to create an electronic database to evaluate the effectiveness of a clinical dosing tool.

Study Objectives

1° Objective: to evaluate the adherence to the Island Health empiric vancomycin dosing nomogram

Outcome measure:

- proportion of vancomycin orders that adhere to the nomogram in terms of dose and frequency given patient age, weight, and serum creatinine.

2° Objective: to characterize the performance of adherent orders

Outcome measure:

- determine the proportion of first serum vancomycin troughs that fall within the target range of 15-20 mg/L with empirically dosed vancomycin orders.

Methods

Design

- Retrospective, observational, clinical informatics study spanning Island Health

Study population

Inclusion	Exclusion
• Age ≥ 18 years • Acute, inpatient at Island Health • Received IV vancomycin for at least 48 hours	• Data created before January 1, 2009 • Cases outside nomogram parameters • Incomplete data sets

Data Management

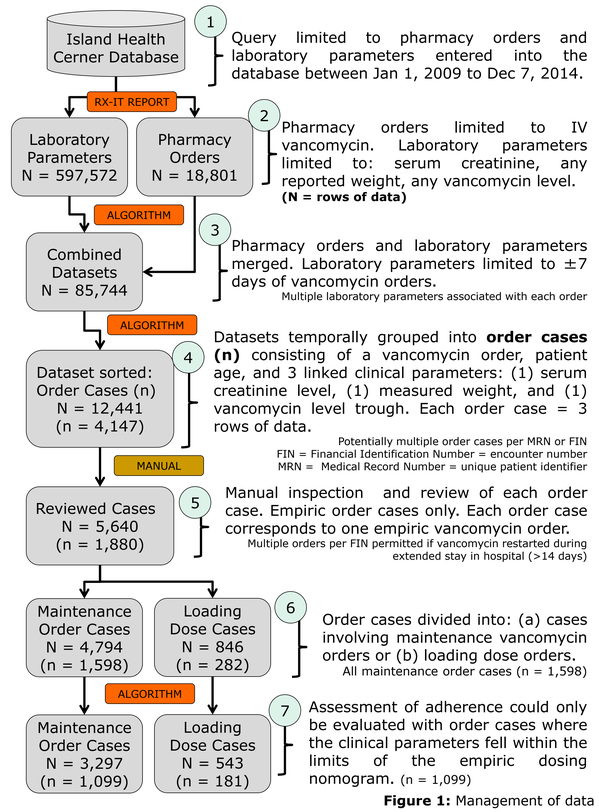


Figure 1: Management of data

Results

Table 3: Characteristics of adherent and non-adherent order cases.

Characteristic	Adherent (n = 319, 29%)	Non-Adherent (n = 780, 71%)
Age (years), median (IQR) [range]	66 (25) [20-89]	65 (24) [20-89]
Sex, no. (%) male	145 (45.5%)	447 (57.3%)
Weight (kg), mean ± SD	69 ± 14	76 ± 14
Initial serum creatinine (µmol/L), median (IQR)	70 (30)	79 (43)
Vancomycin dose (mg/kg), mean ± SD	16.1 ± 1.3	14.3 ± 3.3
Initial vancomycin level (mg/L), median (IQR)†	12.6 (7.4)	11.7 (8.1)

IQR = interquartile range, SD = standard deviation
†Mann-Whitney U test, two tailed, p-value = 0.08

Table 4: Proportion of levels among adherent and non-adherent order cases in ranges of interest.

Initial vancomycin level (mg/L)	Adherent (n = 319, 29%)	Non-Adherent (n = 780, 71%)
< 10	74 (23%)	235 (30%)
10 - 15	121 (38%)	258 (33%)
15 - 20†	64 (20%)	150 (19%)
20 - 25	38 (12%)	71 (9%)
> 25	22 (7%)	66 (8%)
10-20‡	185 (58%)	408 (52%)

†Pearson's χ^2, two tailed, p-value = 0.75
‡Pearson's χ^2, two tailed, p-value = 0.09

Table 5: Proportion of loaded order cases.

No. (%)	Adherent	Non-Adherent
Loaded	68 (6%)	113 (10%)
Not Loaded	251 (23%)	667 (61%)

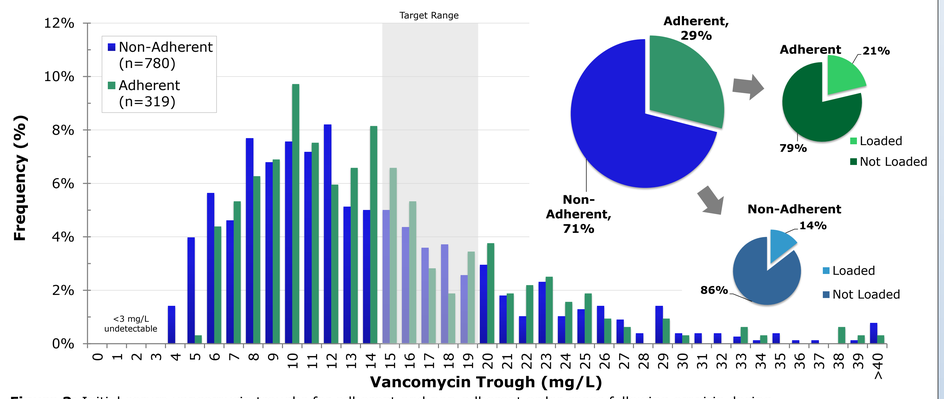
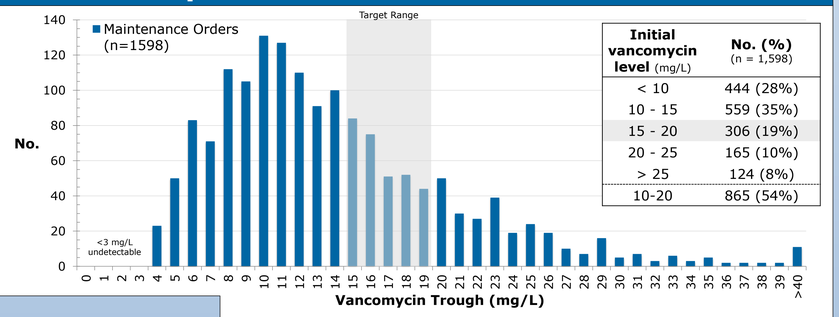


Figure 3: Initial serum vancomycin troughs for adherent and non-adherent order cases following empiric dosing.

Baseline Population Characteristics



Initial vancomycin level (mg/L)	No. (%) (n = 1,598)
< 10	444 (28%)
10 - 15	559 (35%)
15 - 20	306 (19%)
20 - 25	165 (10%)
> 25	124 (8%)
10-20	865 (54%)

Figure 2: Initial serum vancomycin troughs for all order cases following empiric dosing.

Table 2: Baseline population characteristics

Characteristic	Maintenance Cases (n = 1,598)
Age (years), median (IQR) [range]	65 (24) [18-99]
Sex, no. (%) male	908 (56.8)
Weight (kg), mean ± SD	83 ± 26
Initial serum creatinine (µmol/L), median (IQR)	79 (48)
Vancomycin dose (mg/kg), mean ± SD	14.1 ±3.4
Initial vancomycin level (mg/L), median (IQR)	11.9 (8.1)

IQR = interquartile range, SD = standard deviation

Island Health Empiric Vancomycin Dosing Nomogram

Table 1: Island Health empiric vancomycin dosing nomogram

Actual body weight (kg)	Maintenance dose (15 mg/kg)
40-50	750 mg
51-60	1000 mg
61-70	1000 mg
71-80	1250 mg
81-90	1250 mg
91-100*	1500 mg

*For 100 kg and above obtain Pharmacy Consult.
Max 2500 mg/dose.
Shaded areas = nomogram may not be as predictive

SCr (µmol/L)	Age group (years) 20-29	30-39	40-49	50-59	60-69	70-79	80-89
40-60	8	8	8	8	8-12*	12	12
61-80	8	8	8-12*	12	12	12	12-18*
81-100	12	12	12	12	12-18*	18	18
101-120	12	12	12-18*	18	18	18	18
121-140	12	18	18	18	18	18-24*	
141-160	18	18	18	18-24*	24		
161-180	18-24*	24	24	24			

*If more aggressive therapy is desired, select more frequent dosing interval.

Discussion

Findings

- Overall, 19% of all maintenance orders analyzed were in the target range of 15-20 mg/L; median (IQR) trough concentration of 11.9 (8.1) mg/L.

1° Outcome Measure

- 29% of assessed orders adhered to the suggested nomogram dose and frequency
- 16% of assessed cases received a loading dose and 6% were loaded and adherent to the dosing nomogram.

2° Outcome Measure

- Adherence led to a non-statistically significant (NSS) proportion of vancomycin trough levels in the range of 15-20 mg/L: 20% vs 19%.
- Similarly, adherence to the nomogram led to higher NSS median initial vancomycin trough levels (IQR): 12.6 (7.4) mg/L vs 11.7 (8.1) mg/L.

Limitations

- The sample of orders studied is reflective of only orders with complete electronic footprints (only a small fraction of vancomycin orders).
- Limits of clinical informatics data: e.g. order entry is not perpetually updated on a 24hr basis potentially leading to timing discrepancies.

Conclusion

- Adherence to the empiric vancomycin dosing nomogram is limited.
- Target troughs of 15-20 mg/L are not attained >80% of the time when vancomycin is empirically dosed at Island Health.
- Adherence to the nomogram does not appear to improve the proportion of trough levels in the 15-20 mg/L range – a discrepancy seeing as previous studies have demonstrated the nomogram to be 52-70% predictive.

Acknowledgements: Jeffrey Hocking, BSc(Pharm), RPEBC. References available on request.