Pharmacokinetics of Vancomycin in Pregnant and Postpartum Women

Sydney Huebner, B.S.P., Pharmacy Resident; Vanessa Paquette, B.Sc.(Pharm), ACPR, Pharm.D; Roxane Carr, B.Sc.(Pharm), ACPR, Pharm.D, BCPS, FCSHP

Background

- Indications for vancomycin in pregnant and postpartum women include:
  - Treatment of methicillin-resistant *Staphylococcus aureus* (MRSA) infections
  - Alternative for patients with anaphylaxis to beta-lactam antibiotics
- Empiric dosage regimen is 15 mg/kg Q8H, however, other empiric dosages are often used
- Target troughs adopted from non-pregnant patient guidelines:
  - 15 – 20 mg/L: MRSA and other serious infections
  - 10 – 15 mg/L: nonserious infections
- Recommended target for treatment of MRSA infections is an AUC/MIC of ≥ 400 mg·h/L, and a trough of 15 – 20 mg/L is used as a surrogate
- Physiologic changes in pregnancy can alter pharmacokinetics (PK):
  - ↑ in extracellular fluid by 30-50%
  - ↑ in glomerular filtration rate by 50%
- Despite these known physiological changes vancomycin PK has not been studied in pregnant women

Objectives

Primary:
- Describe PK parameters of vancomycin in pregnant and postpartum women

Secondary:
- Describe proportion of patients reaching their target trough with initial dosage regimen
- Correlate vancomycin troughs to AUC_{24}
- Describe the dosage administered to achieve target trough concentration
- Describe adverse effects associated with vancomycin

Methods

Design: Retrospective cohort study

Inclusion:
- Pregnant or postpartum (< 6 weeks)
- Admitted to BC Women's Hospital (BCWH)
- ≥ 1 trough serum concentration drawn prior to 3rd dose or later

Exclusion:
- Trough concentrations drawn > 60 minutes prior to next dose
- Patients with pre-existing chronic kidney disease (≥ stage 3)

Formula Used to Calculate Patient PK: Sawchuk - Zaske

Adverse Effects:
- Ototoxicity: failed hearing testing
- Acute kidney injury (AKI): serum creatinine (SCr) > 88 µmol/L, or ↑ by 50% or ≥ 26.4 µmol/L from baseline
- Nephrotoxic/Ototoxic medications: aminoglycosides, ACE inhibitors, ARBs, furosemide, NSAIDs, and piperacillin-tazobactam
- Naranjo Score used to assess association of adverse effect to vancomycin

Statistics: Descriptive

Sample Size: 35
- Precision of 1.0 and confidence level of 0.95
- Calculated with a standard deviation (SD) of 3 hours based on vancomycin half-life

Results

Table 1: Patient Characteristics

	All (N = 34)	Pregnant (N = 7)	Postpartum (N = 27)
Gestational Age/ Post Partum, weeks [mean (SD)]		32.4 weeks (6.0)	1.8 weeks (1.8)
Age, yr [mean (SD)]	33.2 years (4.8)	33.7 years (6.6)	33.0 years (4.2)
Weight, kg [median (range)]	71.3 (55.6 – 154)	71.4 (57.8 – 97.3)	71.2 (55.6 – 154)
Nephrotoxic / Ototoxic Medications [n (%)]	31 (91)	5 (71)	26 (96)
Baseline SCr, µmol/L [median (range)]	56 (37 – 89)	56 (50 – 84)	56 (37 – 89)
Beta-lactam Allergy [n]	0	0	0

Table 2: Empiric Dosing

	All (N = 34)	Pregnant (N = 7)	Postpartum (N = 27)
Received Loading Dose [n (%)]	10 (29)	3 (43)	7 (26)
Loading Dose, mg/kg [mean (SD)]	23.2 (4.8)	24.5 (2.9)	22.6 (5.3)
Empiric Dose, mg/kg [mean (SD)]	15.4 (3.1)	15.5 (2.6)	15.4 (3.2)
Empiric Dosing Interval Q8H [n (%)] Q12H [n (%)]	19 (56) 15 (44)	4 (57) 3 (43)	15 (56) 12 (44)

Table 3: Pharmacokinetic Parameters

	All (n = 14)	Pregnant (n = 5)	Postpartum (n = 9)
K, h^{-1} [median (range)]	0.17 (0.1 – 0.27)	0.20 (0.01 – 0.27)	0.17 (0.12 – 0.21)
Half-life, h [median (range)]	4.2 (2.6 – 7.1)	3.4 (2.6 – 7.1)	4.2 (3.3 – 6.0)
V_d, L/kg [median (range)]	0.5 (0.3 – 0.9)	0.56 (0.37 – 0.8)	0.47 (0.3 – 0.9)
AUC_{24}, mg•h/L [median (range)]	432 (204 – 746)	365 (204 – 675)	439 (399 – 746)

Figure 1: Patients Achieving Target Serum Concentrations After Empiric Dosing Regimen

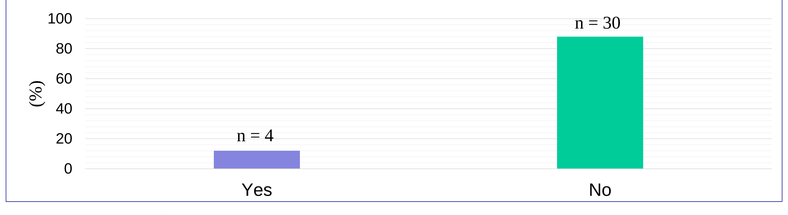

Figure 2: Serum Concentration vs AUC

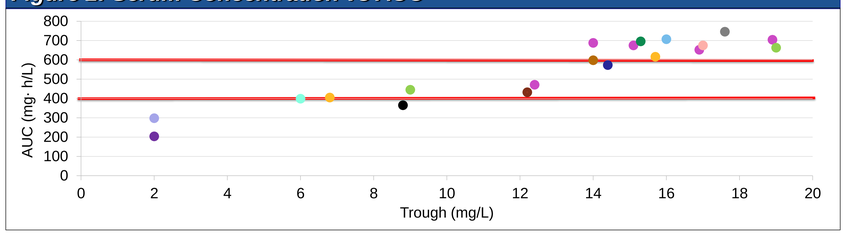

Figure 3: Dosage Regimen vs Serum Concentration

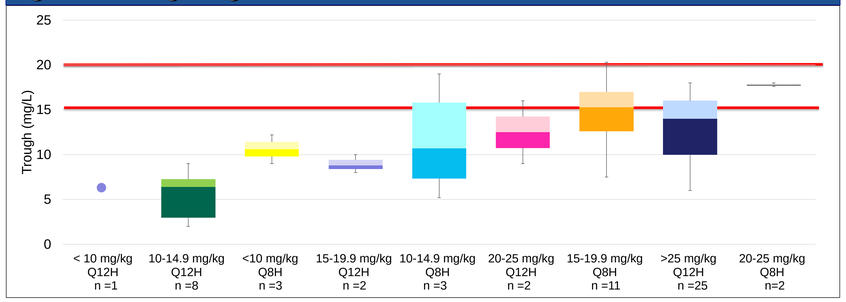

Figure 4: Dosage Regimen vs AUC

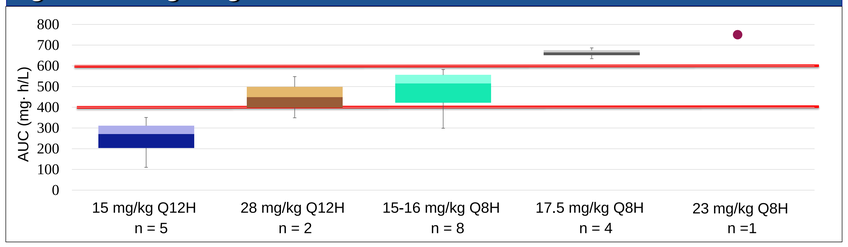

Table 4: Adverse Effects

	Pregnant (n = 7)	Postpartum (n = 27)
AKI – n (%)	1 (3)	0
Patient Characteristics: Trough, mg/L – median (range) AUC_{24}, (mg • h/L) – median (range) Naranjo Score	16.0 (15.1 – 16.9) 664 (651 – 675) 7	
Ototoxicity – n (%)	0	0

Conclusions

- PK of pregnant and postpartum women fell within reported "non-pregnant" adult parameters
- Target trough concentrations (15 – 20 mg/L) resulted in AUC greater than the target range
- Dosage regimens of 15 – 16 mg/kg IV Q8H achieved target AUC and trough concentrations of 10 – 15 mg/L
- If trough concentration is to be used as surrogate for AUC, target trough concentration ranges should be re-evaluated