1.13. Vancomycin

Pharmacokinetic Parameters

Table 1.13-1. Volume of Distribution by Age Group

Age	Volume L/kg (Mean ± SD)[a]
Premature neonates	
27–30 weeks PCA	0.55 ± 0.02
31–36 weeks PCA	0.56 ± 0.02
> 37 weeks PCA	0.57 ± 0.02
Infants and full-term neonates	0.69–0.79[b]
Infants (≥ 1 month – < 1 year)	0.69 ± 0.17
Children (2.5–11 years)	0.63 ± 0.16
Adults (≥ 16 – < 65 years)	0.62 ± 0.15
Obese adults (> 30% over IBW)	0.56 ± 0.18
Geriatrics (≥ 65 years)	0.76 ± 0.06

[a]Actual body weight.
[b]Range rather than ± SD.
PCA, postconception age: the sum of the gestational age at birth and chronological age;
IBW, ideal body weight.

Table 1.13-2. Average Clearance Values

Age	Clearance L/hr/kg (Mean ± SD)
Premature neonates	
27–30 weeks PCA	0.06 ± 0.004
31–36 weeks PCA	0.07 ± 0.004
>37 weeks PCA	0.08 ± 0.004
Infants and full-term neonates	0.07 ± 0.021
Children (2.5–11 years)	0.11 ± 0.02
Adults (≥16–<65 years)	0.07 ± 0.025
Geriatrics (≥65 years)	0.05 ± 0.003

PCA, postconception age: the sum of the gestational age at birth and chronological age.

Dosing Strategies

Infants

A population pharmacokinetic analysis of vancomycin concentration-time data obtained from 374 infants with a median postnatal age of 70 days and a median gestational age of 33.5 weeks yielded the following equation:

$$CL_{vanc} \text{ (L/hr)} = [W \times ((0.028/S_{Cr}) + (0.000127 \times age) + (0.0123 \times GA28))] + 0.006$$

where

W = weight (kg);

S_{Cr} = serum creatinine (mg/dL);

age = postnatal age (days) if S_{Cr} <0.7 mg/dL (62 μmol/L in SI units) or
   age = 0 if $S_{Cr} \geq 0.7$ mg/dL (62 μmol/L);

GA28 is 1 if gestational age >28 weeks and 0 if gestational age ≤28 weeks.

Adults

$$CL_{vanc} \text{ (mL/min)} = 0.689(CrCl) + 3.66$$

where CrCl is in mL/min.

Self Assessment Problems

1. A 23-year-old female with serum creatinine on admission of 0.9 mg/dL weighs 60 kg and is 5′ 6″ tall. Her estimated creatinine clearance is 92 mL/min and her admission diagnosis is osteomyelitis secondary to compound fracture. The organism is *Staphylococcus aureus* with an MIC to vancomycin of <2 mg/L and the patient is allergic to penicillin.

   A. Design an every 12 hour vancomycin dosing regimen to have a steady state trough of 10 mg/L (*assume the correct time for troughs is 30 minutes before the next dose*). First determine the exact dose and then a reasonable one that might be used clinically. Doses will be given as 2-hour infusions.

   B. If gentamicin is added to the course of therapy, what additional concerns might you have?

   C. What would the patient's estimated volume of distribution have been if she had weighed 80 kg?

2. Use the following predictor of vancomycin clearance[1] to estimate the half-lives for a 50-year-old patient who weighs 80 kg at creatinine clearance values of 0, 40, 80, and 120 mL/min. Use V from Table 1.13-1.

   $$CL_{vanc} \text{ (L/hr)} = [0.711 \times (CrCl) + 18.9] \times 0.06$$

3. Estimate the clearance of vancomycin in an infant who currently weighs 6.1 kg, is 5 weeks old, and who was 36 weeks gestation at birth. S_{Cr} = 0.8 mg/dL. Use the population predictor for infants from the dosing strategies.

4. A 55-year-old male weighing 70 kg who is 5′ 9″ tall has *Staphylococcus epidermidis* septicemia. The MIC to vancomycin is 1 mg/L. The patient's serum creatinine is 2.3 mg/dL (estimated CrCl of 36 mL/min). He is started on 500 mg of vancomycin every 8 hours (given as 1-hour infusions on a schedule of 12 noon, 8 p.m., and 4 a.m.).

   A. Calculate the predicted trough (0.5 hours before next dose) on this regimen. Use the CL_{vanc} predictor in the dosing strategies and volume of distribution from Table 1.13-1 to estimate k for estimating the patient's trough concentration.

   B. What suggestions would you have for altering the regimen if the new dosing interval will be 24 hours and desired trough concentrations are 10–15 mg/L? Do the initial calculations assuming a desired trough of 12.5 mg/L and then suggest a reasonable dose.

   C. Determine the trough on the dose chosen to be given every 24 hours.

   D. Vancomycin area under the curve (AUC_{24})/MIC ratio > 400 has been shown to predict efficacy in adults. Troughs between 15–20 mg/L are considered to produce a ratio > 400. Determine the AUC_{24}/MIC on the chosen dose to determine if the dosing is adequate from this perspective.

5. A patient is receiving vancomycin 1.5 g every 96 hours. Doses are given at 10 a.m. and infused over 2 hours. The following steady state concentrations were measured on the same day around a dose:

C (mg/L)	4	26
time	9 a.m.	1 p.m.

   A. Calculate the patient's half-life (in hours).

   B. Determine the patient's volume of distribution (in L).

6. A patient is receiving 750 mg of vancomycin every 12 hours by 1-hour infusion. A steady state trough concentration is measured 0.5 hours before a dose and reported as 11 mg/L.

   A. You wish to raise the trough to 17.5 mg/L. What dose (exact, don't round off) would you suggest if the interval would remain at 12 hours?

   B. If you rounded the dose to the nearest 250 mg rather than giving the exact dose, what would you estimate the new trough concentration to be?

Reference

1. Ducharme MP, et al. Vancomycin pharmacokinetics in a patient population: Effect of age, gender, and body weight. *Ther Drug Monit.* 1994;16:513–8.

Answers

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1. A. Dose = 836.6 mg

   Since this dose is not one actually used, round off to either 750 mg or 1000 mg every 12 hours.

   Trough on 1000 mg

   $$10.0 \text{ mg/L} \times \frac{1000 \text{ mg}}{836.6 \text{ mg}} = 12.0 \text{ mg/L}$$

   B. Gentamicin is also a potential nephrotoxin and may increase the risk of nephrotoxicity with vancomycin. Creatinine might be monitored more frequently and perhaps lower vancomycin concentrations could be targeted. Also, monitor gentamicin concentrations.

   C. V = 44.8 L

2.

CrCl	Half-Life
0	28.9
40	12.2
80	7.5
120	5.5

3. CL (L/hr) = 0.295 L/hr

4. A. trough = 32.7 mg/L

   B. Exact dose = 699 mg/L. A dose of 750 mg every 24 hours would be reasonable.

   C. 13.4 mg/L

   D. AUC_{0-24} = 439.1

5. A. t½ = 34.1 hr

   B. V = 64.9 L

6. A. 1193 mg

   B. 1250 mg is the nearest 250 mg.

   C_{trough} = 18.3 mg/L