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:[1]

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

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

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

where CrCl is in mL/min.

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

where CrCl is in L/hr.

*AUC**

$$AUC_{0-24} = \frac{\text{Vancomycin Daily Dose}}{\text{Vancomycin Clearance}}$$

References

1. Capparelli EV, Lane JR, Romanowski GL, et al. The influences of renal function and maturation on vancomycin elimination in newborns and infants. *J Clin Pharmacol.* 2001;41(9):927–34.
2. Ducharme MP, Slaughter HI, Edwards, DJ. Vancomycin pharmacokinetics in a patient population: Effect of age, gender, and body weight. *Ther Drug Monit.* 1994;16:513–18.

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 predictor of vancomycin clearance by Ducharme et al.[2] 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**.

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.).

*AUC: the area under plasma concentration versus time curve