1.10. Phenobarbital

Pharmacokinetic Parameters

Table 1.10-1. Volume of Distribution by Age Group

Age	Volume (Mean ± SD)[1,2]
Neonates (<2 weeks)	0.96 ± 0.02 L/kg
Infants and children (2 weeks–19 years)	0.63 ± 0.09 L/kg
Adults and geriatrics (>19 years)	0.61 ± 0.05 L/kg

Table 1.10-2. Clearance by Age Group

Age	Clearance (Mean ± SD)
Neonates and infants (<1 year)	0.0047 ± 0.0002 L/hr/kg
Children (1–<19 years)	0.0082 ± 0.0031 L/hr/kg
Adults (19–65 years)	0.0056 ± 0.0026 L/hr/kg
Geriatrics (>65 years)	0.0024 L/hr/kg

[1]Anderson GD. Phenobarbital and other barbiturates: Chemistry, biotransformation, and pharmacokinetics. In: Levy RH, Mattson RH, Meldrum BS, et al., eds. *Antiepileptic Drugs*. 5th ed. New York: Raven Press; 2002:496–503.

[2]Landrum-Michalets E. Update: Clinically significant cytochrome P-450 drug interactions. *Pharmacotherapy*.1998;18(1):84–112.

Bioavailability is 100% for IV and IM dosing and approximately 90% (F = **0.9**) for oral and rectal dosing. S = 0.9 for IV phenobarbital sodium and S = 1 for oral products.

Self-Assessment Problems

1. Determine an oral loading dose for an initial concentration of 25 mg/L, and an oral maintenance dose and interval to produce average steady state phenobarbital concentrations (Css_{avg}) of 25 mg/L for a 5-year-old, 25-kg child.

   Note: Use of the IV bolus formula is acceptable since half-life (t½) is very long compared to absorption rate.

2. A 2-day-old, 2.4-kg neonate presents with seizure activity secondary to asphyxia at birth. The neonatal neurologist would like to start this baby on phenobarbital sodium IV and would like a concentration of 35 mg/L.

   A. Design an IV bolus loading dose for an initial concentration of 35 mg/L.

   B. What IV maintenance dose (given every 12 hours) would be used for a Css_{avg} of 35 mg/L.

3. The infant in Problem 2 has a 2-hour post-load phenobarbital concentration of 30 mg/L. Because he still has seizure activity, the neurologist requests that the concentration be increased to 40 mg/L.

   A. What would the loading dose be to achieve the new desired concentration (assume no loss of concentration from the initial load since half-life is very long)?

   B. What new maintenance dose should be used for a Css_{avg} of 40 mg/L?

4. After 3 weeks of the maintenance dose above, the baby has a mid-point phenobarbital concentration (Css_{avg}) measured and reported as 31 mg/L. The baby now weighs 2.9 kg.

   A. What is the baby's phenobarbital clearance (in L/hr/kg)? Compare this to the population clearance.

   B. What maintenance dose should now be suggested (in mg every 12 hours) to raise the concentration to 40 mg/L?

5. A 4.5-kg, 6-week-old infant is to receive phenobarbital sodium IV every 12 hours, and the desired steady state phenobarbital concentration is 20 mg/L.

   A. Determine the loading dose (given as IV bolus) based on population values to produce a post-load concentration of 20 mg/L.

   B. Determine the maintenance dose (given as IV bolus every 12 hours) based on population values to produce a steady state (Css_{avg}) concentration of 20 mg/L.

6. A 14-year-old, 60-kg female who has not done well on other anticonvulsants has been receiving phenobarbital tablets at 90 mg twice daily. She is admitted to the ER in a very sedated condition, and her phenobarbital concentration is reported as 65 mg/L.

   Discuss the management of this patient with the assumption she requires the continuation of phenobarbital long term for her seizure activity. Predict her concentration using population averages to help in the assessment.