1.7. Digoxin

Pharmacokinetic Parameters

Table 1.7-1. Volume of Distribution (V)[1,2]

Age	Volume[a] (Mean ± SD)
Neonates	10.0 ± 1.0 L/kg
Infants	16.3 ± 2.1 L/kg
Children (1–12 years)	16.1 ± 0.8 L/kg
Adults	6.7 ± 1.4 L/kg[b]

[a]When patient weight is used in *V* calculations, IBW is used for patients whose actual weight > IBW.

[b]The volume of distribution is decreased in patients with renal impairment, so a reduced total loading dose should be used.

Table 1.7-2. Clearance (CL)[1]

Age	Clearance
Neonates[a]	1.8 L/hr/m^2
Infants[a]	11.2 L/hr/m^2
Children[a] (1–12 years)	8 L/hr/m^2
Adults	See dosing strategies

[a]In patients with normal renal function for age.

Table 1.7-3. Digoxin Bioavailability (F) of Dosage Forms[3]

Dosage Form	Bioavailability
Intravenous	100% (1.0)
Intramuscular	Intramuscular injection is not recommended
Oral capsules[a,b]	95 ± 13% (0.95)
Oral tablets[a]	75 ± 14% (0.75)
Oral elixir[a]	80 ± 16% (0.80)

[a]Several agents may decrease absorption and erythromycin and tetracycline can increase it. Food may reduce the peak concentration achieved without affecting total absorption.

[b]The dose of oral capsules is 80% of that of tablets, allowing for almost equivalent bioavailable dose between the capsules and tablets.

Dosing Strategies

Estimating Digoxin Clearance (for Adults and Children >12 Years of Age)

Method 1[4,a,b]

Heart failure (HF) absent

$$CL_{dig} = (1.303 \times CrCl) + 41 \text{ mL/min}$$

HF present

$$CL_{dig} = (1.303 \times CrCl) + 20 \text{ mL/min}$$

[a]F was assumed to be 0.6 by study authors when calculating clearance.

[b]CL_{dig} and CrCl are expressed in units of mL/min.

Method 2[5,6,a,b]

$$CL_{dig} = 3 \text{ L/hr} + (0.0546 \times CrCl)$$

(If concomitant quinidine, multiply by 0.56.)

[a]F was assumed to be 0.82 by study authors when calculating clearance.

[b]CL_{dig} is expressed in units of L/hr while CrCl is in units of mL/min. No conversion of CrCl units is necessary.

Estimating Digoxin Dose for a Desired Css_{avg} (for Adults)

Method 3[7,a,b,c]

(a predictive performance model based on creatinine clearance values for patients with HF):

$$D = Css_{avg} \times [2.22 \times (CrCl + 25.7)]$$

[a]D = dose in mcg/day.

[b]Css in mcg/L.

[c]CrCl in mL/min.

Estimating V in Patients with Reduced Renal Function

The following equations adjust volume of distribution estimates based on renal function.

Method 1[8]

$$V(L/1.73\ m^2) = V_{min} + \frac{V_n(CrCl)}{(K_d + CrCl)}$$

where

V_{min} = 226 L/1.73 m^2

V_n = 298 L/1.73 m^2

K_d = 29.1 mL/min/1.73 m^2

CrCl in mL/min/1.73 m^2

Method 2[5]

$$V_{(L)} = [5.05 + (0.0882 \times CrCl)] \times IBW$$

where CrCl is in units of mL/min and IBW is ideal body weight in kg. No unit cancellation is required.

References

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