Spring 2003

PHA 5128

Homework II (Answers)

1. Estimate the half-life of gentamicin in two male patients with normal renal function (CL=0.12 L/min) if their weight is 55 kg vs. 90 kg. Assume a height of 6'.

- Since clearance is given, only V_d remains to be found in order to calculate $t_{1/2}$ for the two patients. (remember CL=ke*V_D)
- Both patients are <20% IBW so use normal weight

(To use these expressions, we must first calculate IBW for each patient:

IBW = 50 + 2.3(height in inches > 60 in) [kg]

= 50 + 2.3 · (12)

= 77.6 kg

this is the IBW for both since both are 6'.)

- Volume of distribution for each patient is then:

$$V_d(55kg) = (0.25L/kg)(55kg) = 13.8L$$

$$V_d(90kg) = (0.25L/kg)(90kg) = 22.5L$$

- Half-lives may be calculated using the common expression relating Cl and V_d to k_e:

$$Cl = k_e \cdot V_d$$

Or $k_e = Cl/V_d$

And then applying $t_{1/2} = \frac{\ln 2}{k_e}$

For the 55 kg patient,

$$k_e = \frac{Cl}{V_d} = \frac{0.12L/min}{13.8L} \cdot \frac{60min}{1hr} = 0.522hr^{-1}$$

$$t_{1/2} = \frac{\ln 2}{k_e} = \frac{0.693}{0.418hr^{-1}} = \underline{1.3hr}$$

For the 90 kg patient,

$$k_e = \frac{0.12L/min}{22.5L} \cdot \frac{60min}{1hr} = 0.32hr^{-1}$$

$$t_{1/2} = \frac{0.693}{0.3478hr^{-1}} = \underline{2.2hr}$$

2. How long after the end of an intravenous infusion do you draw a peak serum concentration of gentamicin? Discuss the reason for not drawing the peak concentration immediately following the end of the infusion.

Wait at least 30 minutes to allow for tissue distribution. You can sample at later points and correct by extrapolation. By convention, the 30 min. sample after the end of the infusion represents the "clinical" peak.

3. Based on the Cockcroft-Gault-Equation, calculate the amount of creatinine that is produced every hour from muscle in a normal 20 year old and 90 year old male subject (body weight 70 kg) with a serum creatinine of 0.9 mg/dl.

- The Cockroft-Gault equation allows us to predict the creatinine clearance (and therefore renal function/GFR) for patients differing in age and weight. For male patients,

$$Cl_{creat}(male) = \frac{(140 - age) \cdot weight}{72 \cdot Cp_{creat}}$$

where age is in years, weight is in kg, and Cp_{creat} is in mg/dL. The Cl_{creat} is then in ml/min. This is an empirical equation which works only if the age, weight, and Cp_{creat} (or Scr) are entered in the units specified.

- <u>For the 20 y.o.</u>

$$Cl_{creat} = \frac{(140 - 20)(70)}{(72)(0.9)} = 129.6 ml/min$$

Although clearance is expressed in volume-per-time, the amount of creatinine eliminated-per-time may be found using the creatinine concentration given:

Creatinine cleared per hour =

$$(129.6 ml/min)(0.9 mg/dL) \cdot \frac{60 min}{1 hr} \cdot \frac{10 dL}{1 L} \cdot \frac{1 L}{1000 ml}$$

= 69.98 ~ <u>70mg/hr</u>

(so in 1 day, almost 2 g of creatinine is lost which is balanced by eating and producing 2 g of creatinine per day))

- <u>For the 90 y.o.</u>

$$Cl_{creat} = \frac{(140 - 90)(70)}{(72)(0.9)} = 54.0 ml/min$$

Creatinine cleared per hour =

$$(54.0 ml/min)(0.9 mg/dL) \cdot \frac{60 min}{1 hr} \cdot \frac{10 dL}{1 L} \cdot \frac{1 L}{1000 ml}$$

= <u>29.2 mg/hr</u>

(Remember, elderly have less muscle mass which means less creatinine production)

4. A 3 month old infant, born at full- term gestational age, is admitted to Shands Hospital for possible pneumonia. The infant weighs 3.5 kg. Ampicillin 175 mg iv q6h and Gentamicin 5 mg iv q8h (30 min infusion) is started. On day 3 of therapy, gentamicin serum concentrations are drawn as listed below:
Gentamicin dosing schedule 06-14-22 h.
Gentamicin peak serum conc. 6.6 μg/ml drawn at 0700 on 4/23.
Gentamicin trough serum conc. 1.1 μg/ml drawn at 1330 on 4/23.

a. Determine the estimated k_e and $t_{1/2}$ of gentamicin in this patient.

$$k = \frac{\ln \frac{6.6}{1.1}}{6.5} = 0.276h^{-1}$$

$$t_{1/2} = \frac{0.693}{k} = 2.5h$$

b. Calculate the dose and dosage schedule necessary to achieve a peak serum gentamicin concentration of at least 10 μg/ml.

$$C_{\max} = \frac{6.6}{e^{-0.276 \cdot 0.5}} = 7.6\mu g / mL$$

$$C_{\min} = 1.1 \cdot e^{-0.276 \cdot 0.5} = 0.96\ \mu g / mL$$

$$Vd = \frac{5}{0.276 \cdot 0.5} \cdot \frac{\left(1 - e^{-0.276 \cdot 0.5}\right)}{\left(7.6 - 0.96 \cdot e^{-0.276 \cdot 0.5}\right)} = 36.36 \cdot \frac{0.129}{6.76} = 0.69L$$

$$\tau = \frac{\ln\left(\frac{10}{1}\right)}{0.276} + 0.5 = 8.8h\ (8h)$$

$$D = 10 \cdot 0.276 \cdot 0.69 \cdot 0.5 \cdot \frac{\left(1 - e^{-0.276 \cdot 8}\right)}{\left(1 - e^{-0.276 \cdot 0.5}\right)} = 0.952 \cdot \frac{0.89}{0.129} = 6.6mg \Rightarrow 7mg\ q8h$$