

PHA 5127

Fall 2005

Answers Homework #3

1. A 34 year-old male patient needs to take gentamicin (aminoglycosides) for treatment of gram-negative pneumonia infection. The body weight of this patient is 74kg. The volume distribution of gentamicin is 18 L.
 - a. Calculate the Creatinine Clearance (CrCL) for this patient (1pt)
 - b. Calculate the elimination rate constant (k_e) (1pt)
 - c. Calculate the total clearance (CL_T) (1pt)
 - d. Calculate the non-renal clearance (CL_{nonren}) (Hint: using the intercept of k_e) (1pt)
 - e. Calculate the renal clearance (CL_{ren}) (1pt)

Answers:

- a. $CrCL = (140 - \text{age}) * \text{weight} / 70 = (140 - 34) * 74 / 70 = 112 \text{ mL/min}$
- b. $k_e = 0.00293 * CrCL + 0.014 = 0.00293 * 112 + 0.014 = 0.34 \text{ /hr}$
- c. $CL_T = k_e * V_d = 0.34 * 18 = 6.1 \text{ L/hr}$
- d. $k_{e-nonren} = 0.014 \text{ /hr}$, so $CL_{nonren} = k_{e-nonren} * V_d = 0.014 * 18 = 0.3 \text{ L/hr}$
- e. $CL_{ren} = CL_T - CL_{nonren} = 6.1 - 0.3 = 5.8 \text{ L/hr}$

2. Drug X is a weak base with $pK_a=9.0$. Its unionized form is non-polar. It has a volume distribution of 30L, $t_{1/2}$ of 2 hour and fraction unbound (f_u) of 0.2. The renal clearance accounts for 20% of the total clearance.
- Calculate the total and renal clearance. (1pt)
 - Is secretion or reabsorption definitely involved in the renal clearance of drug X? Why? (1pt)
 - If we know that reabsorption is involved, will the renal clearance increase or decrease if pH of urine changes from 7.5 to 4.5? Why? (1pt)

Answers:

a. $K_e=0.693/t_{1/2}=0.35/\text{hr}$

$$CL_{\text{tot}}=K_e \cdot V_d=0.35 \cdot 30=10.5 \text{ L/hr}$$

$$CL_{\text{ren}}=CL_{\text{tot}} \cdot 0.2=10.5 \cdot 0.2=2.1 \text{ L/hr}$$

b. Secretion is definitely involved because

$$CL_{\text{ren}}=2.1 \text{ L/hr}=35 \text{ mL/min} > f_u \cdot GFR=0.2 \cdot 130=26 \text{ mL/min.}$$

c. The renal clearance of drug X will increase if pH of urine changes from 7.5 to 4.5 because at pH 4.5 more drug X will be of ionized form and not be able to be reabsorbed (only the non-polar unionized form can be reabsorbed).

3. Which of the following factors does NOT influence glomerular filtration: (2pt)

- molecular size
- protein binding
- lipid solubility
- renal blood flow

Answer:

- lipid solubility