

Case Study 2 (Fall 2008) Solution

Q1) A 80 kg male patient was given a single i.v. dose of 45 mg cocaine which is known to have a half-life of 0.693 hr and a volume distribution of 2 L/kg.

- (1) What is the clearance of cocaine? Is it solely metabolized by liver? Why?
 (2) Predict $AUC_{0-\infty}$,

(1)

$$k_e = 0.693 / t_{1/2} = 1 \text{ hr}^{-1} \quad V_d = 2 * 80 = 160 \text{ L}$$

$$Cl = k_e \cdot V_d = 1 * 160 = 160 \text{ L/hr} > 90 \text{ L.hr}$$

There exists non-hepatic metabolism .

(2)

$$AUC_{0-\infty} = Dose / Cl = 45 / 160 = 0.28 \text{ mg. hr/ L}$$

Q2) A patient is to be started on two medications (A and B) administered by IV bolus injections. Blood samples were taken at 1 and 4 hours following the first injections of drug A or B alone in order to determine whether concentrations were in an appropriate range for each drug. See table below for these levels and additional information.

Drug	Dose (mg)	Cp at 1h (mg/L)	Cp at 4h (mg/L)	EH	fu
A	400	1.22	0.76	0.8	0.1
B	1200	0.92	0.51	0.1	0.3

Assume liver blood flow of 90 L/h, where EH is the extraction ratio and fu is the fraction unbound. Both drugs are metabolized by CYP 3A4.

Is it possible to calculate the $AUC_{0-\infty}$ for drug B, if yes how much is it ? if no , why not ?

$$k_e = \ln C_2 - \ln C_1 / (t_2 - t_1) = 0.20 \text{ /hr}$$

$$T_{1/2} = 0.693 / 0.2 = 3.45 \text{ hr}$$

$$C_0 = C_t / \exp(-k_e * t)$$

$$C_0 = 1.13 \text{ mg/L}$$

$$V_d = \text{dose} / C_0$$

$$V_d = 1200 / 1.13 = 1062 \text{ L}$$

$$CL = V_d * K_e = 1062 * 0.20 = 212.4 \text{ L/hr}$$

$$AUC_{0-\infty} = \text{dose} / CL = 1200 / 212.4 = 5.65 \text{ mg.hr/L}$$

Q3) Say True or False

T F For a drug with high tissue binding, the volume of distribution will be very low.

T F Volume of distribution is not important to determine what loading dose is required.

T F Drug A has 98% protein binding and has a narrow therapeutic index. Any change in the protein binding is not of significant consequence since already 98% drug is bound and very less is available for receptors

T F If volume of distribution changes, this will affect the drug clearance as well since this means less volume of drug to be cleared.

T F If Drug A and Drug B are being administered at the same time then dose adjustment may be needed if there are drug interactions between A and B

T F Clearance and Volume of distribution are independent parameters.

T F If the drug clearance changes then the volume of distribution changes since $k_e = CL / V_d$

T F If Drug A is cleared only by hepatic metabolism only, then the clearance of drug A cannot be greater than liver blood flow.

T F If Drug A and Drug B are being administered at the same time then dose adjustment may be needed if there are drug interactions between A and B

T F For a low extraction drug, the lower the protein binding the higher will be the clearance