Deacon's Challenge No. 56 Answer

Calculate the loading dose of digoxin (bioavailability 0.75, salt factor = 1) required to achieve an initial plasma concentration of 1.5 µg/L in a 60 kg man (assume volume of distribution = 7 L/kg):

a) If the patient has never taken digoxin
b) If the patient is currently on digoxin with a plasma concentration of 0.5 µg/L

In principle this question is no different than being asked how to make up a chemical solution! The available space in the body (known as the volume of distribution) is the volume of the volumetric flask and the dose to be given is the amount you would weigh out to make up that solution.

$$\text{Concentration (= plasma level)} = \frac{\text{Weight (=dose)}}{\text{Volume (of distribution)}} \quad \text{..... (i)}$$

First calculate the volume of the solution. We are told what the volume is for each kg body weight (the volume of distribution, which is equal to 7 L/kg). The reason why the volume is so great is that a large amount of the drug is taken up by tissues and not freely in solution. This doesn't matter as far as the calculation is concerned, we just work on the assumption that it is all in solution and occupies a certain hypothetical volume. The total volume of distribution (Vd) is calculated from this value and the total body weight:

$$V_d \text{ (L)} = V_d \text{ (L/kg)} \times \text{Body weight (kg)}$$

$$= 7 \times 60 = 420 \text{ L}$$

Equation (i) can be rearranged to give an expression for the loading dose (LD) in terms of target plasma concentration (Cp_{target}) and volume of distribution (V_d):

$$LD = Cp_{target} \times V_d \quad \text{..... (ii)}$$

The dose of drug may need to be modified if it is not completely absorbed (i.e. its bioavailability is low) and if it is administered as a salt rather than the free drug (i.e. its salt factor is not 1). The dose must therefore be divided by the drug's bioavailability (F, in this case 0.75) and salt conversion factor (S, in this case 1):

$$LD = \frac{Cp_{target} \times V_d}{F \times S} \quad \text{…..... (iii)}$$

a) If the patient is not already on digoxin then the target concentration of 1.5 µg/L is substituted:

$$LD = \frac{1.5 \times 420}{0.75 \times 1} = 840 \text{ µg}$$

b) If the patient is already on digoxin and the steady state plasma concentration is 0.5 µg/L, then the LD is the increment required to raise the digoxin concentration by 1.5 - 0.5 = 1.0 µg/L:

$$LD = \frac{1 \times 420}{0.75 \times 1} = 560 \text{ µg}$$

Question 57

A 60 kg patient requires phenobarbitone to be given at 12 hourly intervals.

Calculate the dose required to give an average steady state plasma concentration of 25 mg/L assuming that the clearance of the drug is 5 mL/h/kg and that both the bioavailability and salt conversion factors are 1.