Deacon's Challenge
No 108 - Answer

Calculate the loading dose of intravenous aminophylline required to achieve a plasma theophylline concentration of 15 mg/L in a 55 kg man, given that aminophylline is 80% w/w theophylline and the volume of distribution of theophylline is 0.5 L/kg.

What infusion rate would be required to maintain this concentration if the half life is 8 hours?

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Calculation of the loading dose is identical to calculating the weight of a chemical required to make up a volume of a solution of a required concentration

i.e. weight = concentration x volume, remembering to ensure that all units are compatible.

The weight is the loading dose, the volume is the volume of distribution and the concentration is the plasma concentration of the drug. Allowance must also be made for the purity of the drug (often called its salt factor) and the bioavailability of the drug (the fraction of the drug which is actually absorbed).

$$\textbf{Loading dose } (LD) = \frac{\textbf{Plasma concentration } (Cp_0) \times \textbf{Volume of distribution } (V_d)}{\textbf{Purity } (S) \times \textbf{Bioavailability } (F)}$$

Cp_0 = Initial target plasma concentration = 15 mg/L

V_d = volume of distribution = 0.5 L/Kg. Body wt = 55 Kg. Total Vd = 0.5 x 55 = 27.5 L

S = salt factor or purity = 80% = 0.8

F = bioavailability. Not given so assume value of 1 (probably irrelevant as IV route used)

$$LD = \frac{15 \times 27.5}{0.8 \times 1} = \mathbf{520\ mg} \quad \text{(2 sig figs)}$$

If the drug is infused to maintain a constant plasma concentration (Cp_{ss}) then a steady state exists in which the administration rate is equal to the rate of removal.

Rate of administration = Infusion rate x F x S
Rate of removal = Clearance x Cp_{ss}

Therefore: Infusion rate x F x S = Clearance x Cp_{ss}

$$\text{Infusion rate} = \frac{\text{Clearance} \times Cp_{ss}}{F \times S}$$

Cp_{ss} = plasma steady state concentration = 15 mg/L

F = bioavailability = 1; S = salt factor or purity = 0.8

The clearance is not given. However we are given the half life (8_h) which is related to the elimination rate constant (k_d) by the expression:

$$k_d = \frac{0.693}{t_{1/2}} \qquad \text{Therefore } k_d = \frac{0.693}{8} = 0.0866\ h^{-1}$$

And clearance is, in turn, related to k_d by the expression

$$\textbf{Clearance} = k_d \times Vd \qquad \text{Therefore, clearance} = 0.0866 \times 27.5 = 2.38\ L/h$$

Substituting these values to calculate infusion rate:

$$\text{Infusion rate} = \frac{2.38 \times 15}{1 \times 0.8} = \mathbf{45\ mg/h} \quad \text{(2 sig figs)}$$

Question 109

Fractionated urinary metanephrines are a useful test for diagnosis of phaeochromocytoma. Your assay has a diagnostic sensitivity of 100% and a specificity of 95%. It is known that that prevalence of phaeochromocytoma in patients under investigation for hypertension is 0.8%.

You investigate 1250 patients in a year. Calculate the number of false positive test results you would generate and the probability that a patient with a positive test result really has a phaeochromocytoma.

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