Deacon's Challenge

No 163 - Answer

Calculate the loading dose of intravenous aminophylline required to achieve a plasma theophylline concentration of 15 mg/L in a 65 kg man, given that the volume of distribution of theophylline is 0.5 L/kg and that aminophylline is 80% w/w theophylline. What infusion rate would be required to maintain this concentration if the half-life is 8 hours?

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

Cp_0 = target plasma concentration = 15 mg/L
V_d = volume of distribution = 0.5 L/Kg. Body wt = 65 Kg.
Total V_d = 0.5 x 65 = 32.5 L
S = salt factor or purity = 80 % = 0.8
F = bioavailability. Not given so assume value of 1 (probably irrelevant as IV route used)

$$LD = \frac{15 \times 32.5}{0.8 \times 1} = \mathbf{609\ mg}$$

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}

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

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 (8h) which is related to the elimination rate constant (k_d) by the expression:

$$k_d = \frac{0.693}{t_{1/2}}$$

Therefore $k_d = \dfrac{0.693}{8} = 0.0866\ h^{-1}$

Clearance is related to k_d by the expression

$$\textbf{Clearance} = k_d \times V_d$$

Therefore, clearance = 0.0866 x 32.5 = 2.81 L/h

Substituting these values to calculate infusion rate:

$$\text{Infusion rate} = \frac{2.81 \times 15}{1 \times 0.8} = \mathbf{53\ mg/h} \quad \text{(2 sig figs)}$$

Question 164

A neonate weighing 850 g is admitted to the Neonatal Intensive Care Unit. Following intubation and artificial ventilation, blood gases reveal an arterial blood hydrogen ion concentration of 120 nmol/L and a pCO_2 of 6.2 kPa. Estimate the dose of sodium bicarbonate (1.25%) required to reduce the hydrogen ion concentration to 80 nmol/L. You should assume that ventilator settings remain unchanged, and ignore any effects due to changes in plasma volume and peripheral circulation. You should assume also that the total body water in neonates is 80% of body mass, due to an expansion of extracellular fluid volume compared to adults, and is evenly distributed between intra- and extracellular compartments.

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