Question #1.

H.H., a 60-year-old, 70 kg woman receiving 25mg/h of aminophylline, has a steady-state theophylline level of 14mg/L. She is starting to take cimetidine. Should her aminophylline dosing regimen be adjusted? If so, how?

Answer:

Cimetidine reduces the theophylline clearance by about 40% \( \rightarrow \) new clearance should be about 60% of the original theophylline clearance;

\( \rightarrow \) Yes, the infusion rate needs to be adjusted

\[
\text{Cl (Theophylline only)} = \frac{S \times F \times R_0}{C_s \times R_0} = \frac{0.8 \times 1 \times 25 \text{ mg} \text{ h}^{-1}}{14 \text{ mg} \text{ L}^{-1}} \approx 1.43 \frac{\text{L}}{\text{h}}
\]

\[
\text{Cl (after cimetidine)} = \text{Cl (Theophylline only)} \times 0.6 \approx 0.86 \frac{\text{L}}{\text{h}}
\]

Maintenance Dose = \( \frac{\text{Cl} \times C_s \times \tau}{S \times F} = \frac{0.86 \frac{\text{L}}{\text{h}} \times 14 \frac{\text{mg}}{\text{L}} \times 1 \text{h}}{0.8 \times 1} \approx 15 \frac{\text{mg}}{\text{h}} \) of Aminophylline
**Question #2.**

During a phase I clinical trial, a single 500mg tablet of drug X was given orally. It was found that drug X has a total clearance of 80L/h and was only eliminated by CYP2D6 metabolism in the liver.

As the new member in the research team you are now asked to interpret these results.

T  F  This drug is a low extraction drug.

T  F  Drug X should not be administered together with CYP2D6 inducers since they will significantly affect the metabolism of drug X.

T  F  A change in plasma protein binding will affect the clearance of drug X.

T  F  A change in plasma protein binding will affect the bioavailability of drug X.

**Question #3.**

J.D. is a 80-year-old, 65kg female with liver cirrhosis. She was put lidocaine to treat her arrhythmia.

Please calculate the loading necessary to achieve an initial plasma concentration of 3mg/L. What would be the maintenance dose necessary to achieve plasma steady-state concentrations of 3mg/L?

Answer:

\[
LD = \frac{V_c \times C(\text{desired})}{S} = \frac{0.6 \frac{L}{kg} \times 65kg \times 3 \frac{mg}{L}}{0.87} \approx 134mg
\]

\[
MD = \frac{CL \times C_{ss}}{S} = \frac{0.36 \frac{L}{h \times kg} \times 65kg \times 3 \frac{mg}{L}}{0.87} = 80.7 \frac{mg}{h} \approx 80 \frac{mg}{h}
\]

**Question #4.**

I.N., a 35-year-old female (Cp_{\text{creat}} = 1.3mg/dL), was diagnosed with congestive heart failure (CHF). She is 5’8” tall and weighs 65kg. At 9:30AM on the day of admission (day 1), I.N. was given a 0.75mg digoxin capsule for her CHF. From day 2 on, she was given 0.5mg digoxin orally (tablets) at 9:30AM.

Please predict the plasma concentration on day 4 at 9:30PM.
Answer:

\[ \text{IBW(female)} = 45.5 \text{kg} + 2.3 \times (\text{height} - 5') = 45.5 \text{kg} \times 2.3 \times 8'' = 63.9 \text{kg} \]

\[ \text{Cl}_{\text{creat}} \text{(female)} = \frac{(140 - \text{age}) \times \text{weight}}{85 \times C_{p_{\text{crea}}}^{\text{mg/dL}}} = \frac{(140 - 35) \times 65\text{kg}}{85 \times 1.3 \text{mg/dL}} = 61.76 \text{mL/min} \]

\[ \text{Cl(CHF)} = 0.33 \times \text{IBW} + 0.9 \times \text{Cl}_{\text{creat}} = 0.33 \times 63.9 \text{kg} + 0.9 \times 61.76 \text{mL/min} = 76.67 \text{mL/min} = 4.6 \frac{\text{L}}{\text{h}} \]

\[ V_d = 3.8 \times \text{IBW} + 3.1 \times \text{Cl}_{\text{creat}} = 3.8 \times 63.9 \text{kg} + 3.1 \times 61.76 \text{mL/min} = 434.28L \]

\[ k_e = \frac{\text{Cl}}{V_d} = \frac{4.6 \frac{\text{L}}{\text{h}}}{434.28 \text{L}} = 0.011 \text{h}^{-1} \]

\[ C = \frac{F \times LD}{V_d} \times e^{(-k_e \times t_1)} + \frac{F \times D_1}{V_d} \times e^{(-k_e \times t_2)} + \frac{F \times D_2}{V_d} \times e^{(-k_e \times t_3)} + \frac{F \times D_3}{V_d} \times e^{(-k_e \times t_4)} = \]

\[ C = \frac{1 \times 750 \mu\text{g}}{434.28 \text{L}} \times e^{(-0.011 \text{h}^{-1} \times 3.5 \times 24 \text{h})} + \frac{0.7 \times 500 \mu\text{g}}{434.28 \text{L}} \times e^{(-0.011 \text{h}^{-1} \times 2.5 \times 24 \text{h})} + \frac{0.7 \times 500 \mu\text{g}}{434.28 \text{L}} \times e^{(-0.011 \text{h}^{-1} \times 1.5 \times 24 \text{h})} = \]

\[ = 0.685 \frac{\mu\text{g}}{\text{L}} + 0.417 \frac{\mu\text{g}}{\text{L}} + 0.542 \frac{\mu\text{g}}{\text{L}} + 0.706 \frac{\mu\text{g}}{\text{L}} = 2.35 \frac{\mu\text{g}}{\text{L}} \]