

Situation 1a

A 65-year-old patient (male, weight 70 kg and height 1.75 m) was admitted with a diagnosis of hepatic encephalopathy and cirrhosis. On the fourth hospital day, he developed ventricular arrhythmias, and lidocaine was ordered. Calculate bolus dose and maintenance infusion rate that will achieve a steady-state lidocaine level of 2.0 mg/L.

Information that have to be considered for further calculations:

<i>Parameter</i>		<i>Conclusion</i>
BMI of the patient	[kg/m ²] value:	<input type="checkbox"/> underweight <input type="checkbox"/> normal weight <input type="checkbox"/> overweight <input type="checkbox"/> obesity
Ideal Body Weight (IBW)	[kg] value:	Has to be considered in further calculations? <input type="checkbox"/> yes <input type="checkbox"/> no
Patient's history of CHF and/or liver disease?		
	[yes]	[no]
<i>(choose the answer)</i>		
Chemical form of the drug (S)		
	value:	
<i>Lidocaine is available as hydrochloride salt</i>		
<i>(M_{lidocaine} = 234.4 g/mol; M_{HCl} = 36.5 g/mol)</i>		

Calculate the pharmacokinetic parameters of lidocaine:

<i>Parameter</i>	<i>Value</i>
<p><i>Lidocaine's distribution following an intravenous bolus is described by two-compartment model, therefore the initial volume of distribution (V_i) has to be considered. The initial volume of distribution of lidocaine appears to be ≈ 0.5 L/kg. The final volume following distribution (V) is ≈ 1.3 L/kg.</i></p> <p><i>The volume of distribution increases in proportion to weight – total body weight should be used to calculate it in obese subjects.</i></p> <p><i>In congestive heart failure (CHF) both volumes of distribution of lidocaine are decreased: V_i is 0.3 L/kg and V is 0.88 L/kg.</i></p> <p><i>In contrast, both volumes of distribution are increased in chronic liver disease: V_i is 0.61 L/kg and V is 2.3 L/kg.</i></p>	
initial volume of distribution (V_i)	[L]
final volume of distribution (V)	[L]
<p><i>Lidocaine has a high hepatic extraction ratio. Clearance of lidocaine is ≈ 10 mL/kg/min. CHF (decreased cardiac output) and hepatic cirrhosis decrease the clearance of lidocaine by $\approx 40\%$. In obese subjects, the clearance of lidocaine appears to correlate more closely with ideal body weight (IBW) rather than total body weight.</i></p>	
clearance (CI)	[mL/min] [L/h]
elimination rate constant (k_e)	[h ⁻¹]
k_e [h ⁻¹] = CI [L/h] / V [L]	
half-life ($t_{0.5}$)	[h]
$t_{0.5}$ [h] = ln2 / k_e [h ⁻¹]	

Calculate the initial bolus dose of lidocaine (therapeutic range of lidocaine is 1.0 to 5.0 mg/L) and the level of lidocaine in plasma after final distribution (C_0).

Lidocaine is available as hydrochloride salt ($M_{\text{lidocaine}} = 234.4 \text{ g/mol}$; $M_{\text{HCl}} = 36.5 \text{ g/mol}$) in an aqueous solution of 1% and 2% concentration.

Bioavailability for parenteral administration of lidocaine is 1.0.

The dose of each bolus injection of lidocaine should be based on V_i and not V . Plasma concentration resulting from each bolus injection will fall as the drug distributes into the larger final volume of distribution.

initial bolus dose [mg]

$$D_{\text{load}} = \frac{V_i \cdot C}{S \cdot F}$$

the level of lidocaine in plasma after final distribution [mg/L]

$$C_0 = \frac{S \cdot F \cdot D_{\text{load}}}{V}$$

Estimate the maintenance infusion rate that will achieve the desired steady-state lidocaine concentration of 2.0 mg/L.

maintenance infusion rate [mg/min]

$$D = \frac{Cl \cdot C_{\text{SS,ave}} \cdot \tau}{S \cdot F}$$

**Clearance value has to be in L/min*

Situation 1b

Twelve hours after starting the infusion of lidocaine, the patient appears to be more confused than usual. It is unclear whether his present condition is secondary to hepatic encephalopathy or lidocaine. Is it possible that the lidocaine is still accumulating and is causing the impaired mental state?

Calculate the half-life of lidocaine assuming that the subject is healthy and compare that value with the half-life estimated in the part 1a. Has the steady-state been achieved (the steady state is achieved after $5 \cdot t_{0.5}$)?

** Remember that the patient suffered from hepatic encephalopathy therefore the volume of distribution and clearance were changed in comparison to healthy subject.*

half-life of lidocaine for the patient (part 1a) [h]

half-life of lidocaine for the healthy subject [h]

Conclusion:.....
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