PHA 5127
Case Study #VI
Fall 2004

Case 1.

A 58-year-old male Caucasian patient is admitted to the hospital due to a rupture of his chronic stomach ulcer. Before the surgery, it is usual to start a preventive antibiotic (aminoglycoside) therapy. As a pharmacist, it is your task to develop the patient's antibiotic dosing regimen. The patient Ali Gator is 5 ft. 1 in. height, weighs 55kg and has a serum creatinine of 1.3 mg/dl. (Assume population parameters for Vd: 0.24 L/kg(IBW))

Question 1A.
Calculate the aminoglycoside maintenance dose with the most feasible dosing interval for Ali G. As $C_{peak}$ the assume a value of 6mg/L and as $C_{trough}$ 1 mg/L.

IBW=50 + 2.3 * 1 = 52.3 kg

CrCL = (140-59)52.(72*1.3)=45ml/min

$k_e$ = 0.00293 $h^{-1}$ * creatinine clearance (in ml/min) + 0.014
=0.146 $h^{-1}$
⇨ $t_{1/2}$= 4.3h

Vd=0.24L/kg (IBW)
=0.24*52=12.48 ≈ 12.5L

$$\tau = \frac{\ln\left(\frac{C_{max(desired)}}{C_{min(desired)}}\right)}{k_e} + T$$

τ=13.26h ≈ 12h

Maintanace dose:

$$C_{max} = \frac{D}{CL \cdot T} \cdot \frac{\left(1 - e^{-k_e \cdot T}\right)}{\left(1 - e^{-k_e \cdot \tau}\right)}$$

remembering $k_0 = \frac{D}{T}$ and $CL = V \cdot k_e$

6mg/l= $k_o$*(1-$e^{-.146\ h-1*1h}$) / (0.146$h^{-1}$)(12.5L)*(1-$e^{-.146h-1*12}$)

7mg/l = $k_o$*(0.1358)/((1.825)*(0.8265))
= $k_o$ * 0.0898

$k_o$=66.7 mg ≈ 70 mg  as a 1 hr infusion

Hence Ali Gator receives a 70mg/hr infusion every 12 hours.

Note: since we rounded the actual dose, his measured $C_{trough}$ will be slightly higher.

---- for Immo : write down the calculation for that -----

6*70/66.7=6.30

Question 1B:

Calculate the trough concentration expected for the dose calculated in question 1A (70mg)

$$C = C_0 \cdot e^{-k_e t}$$

I order to use this equation we have to rewrite it to fit our needs.

$C_{trough=}$ $C_{peak}$ * $e^{-ke*t'}$  where t' is τ-time of infusion.

$= 6.3$ mg/l * $e^{-0.146*(12-1)}$
$=$  6.3 mg/l * .0.200
$=$1.26 mg/l ≈ 1.3mg/l

The value is lower than the actual desired value, since we decreased  the desired dosing interval and increased the dose.

Question 1C:
After four days (Steady state) the nurses drew some new samples while Ali Gator was receiving 80mg every 8 h. The following values were obtained (note: his renal function was decreased)

7:55 am  $C_{trough}$ : 3.2 mg/l
8-9 am:   an 1 hour infusion of 80 mg was given
9:00 am  $C_{peak}$ : 9.2 mg/l
Calculate the new $k_e$, τ, $t_{1/2}$ and Vd.

$K_e$= - ln($C_{trough}$ / $C_{peak}$)/ τ-t
   =  -ln(3.2/9.2)/8-1 = .151
$t_{1/2}$=ln2/$_{ke}$$_{4}$.6h

VD:

$$C_{max} = \frac{D}{CL \cdot T} \cdot \frac{\left(1 - e^{-k_e \cdot T}\right)}{\left(1 - e^{-k_e \cdot \tau}\right)}$$

9.2=(80mg/Vd*0.151)*((1-$e^{-0.151*1}$)/(1-$e^{-0.151*8}$)

Vd=11.1 L

$$\tau = \frac{\ln\left(\frac{C_{max(desired)}}{C_{min(desired)}}\right)}{k_e} + T$$

=(ln(6/1)/0.151)+T

= 12.6 => 12h

new maintenance dose:

$$C_{max} = \frac{D}{CL \cdot T} \cdot \frac{\left(1 - e^{-k_e \cdot T}\right)}{\left(1 - e^{-k_e \cdot \tau}\right)}$$

6= $k_0$*(1-$e^{-.151*1}$) / (0.151*11.1)*(1-$e^{-.151*12}$)

$k_0$= 60 mg

Case 2:

A 52 year old white female is admitted to he hospital with diagnosis of a severe pulmonary infection. She is 5 ft. and 3 in. high and weighs 52kg. Her serum creatinine reported from the lab was 0.8 mg/dl.

Question 2A:
Recommend a once daily dose for that patient. Knowing that the average dose for gentamicin is 5-7 mg/kg based on IBW.

IBW: 45.5 + 2.3 * 3 = 50.8

The recommended dose should be:

Dose=6 mg/kg * 50.8 = 304.8
Which is rounded to 300 mg every 24 h.

Question 2B:
Is the once daily dosing interval appropriate for the womans renal status?

To make sure that the once daily dosing is appropriate for the patients renal status, we have to perform the following calculations:

CrCl= 0.85 * ((140-age)*IBW / 72 *SCr)
= 0.85 * ((140-52)*50.8 / 72 * 0.8)
= 66 ml/min

populkation $k_e$= 0.00293 * (66) +0.014
= 0.21

$t_{1/2}$=ln 2 / $k_e$ = 3.3 h

A total dose is almost totally eliminated after 5 half lives. 3.3 * 5 = 16.5 h . That means that the dose is eliminated within the 24 h interval according to the woman’s renal status. The once daily dosing regimen is appropriate.

Question 2C:

With the dosing you just calculated, what peak and trough levels do you expect at steady state. Assume an 1hour infusion. And population Vd = 0.24 L/Kg * IBW.

$C_{max(SS)}$ = $k_0$ $(1-e^{-ket})$ / ( Vd*$k_e$*$(1-e^{-ke*\tau})$
= 300 $(1-e^{-.21*1})$ / (12.2 * 0.21 * (1 – $e^{-0.21*24}$))=22.37 mg/l

$C_{min(SS)}$= $C_{max(SS)\,*}{}^{e-ke\,*\,t'}$ = 22.37 * $e^{-0.21*23}$ = 0.178 mg/l