Deacon's Challenge

No 154 – Answer

An adult male (body weight 60 kg) volunteered to donate one of his kidneys to his brother. The pre-op investigations included a carefully conducted creatinine clearance with the following results: plasma creatinine 80 µmol/L, 24h volume 1.45 L and urine creatinine 8.0 mmol/L. The donor operation proceeded without any problems but a routine blood 24h showed a plasma creatinine concentration of 162 µmol/L. A worried on-call SHO reviewing his result that evening queried whether a creatinine concentration this high would be expected so soon after the operation. In order to answer this question calculate:

a) The expected new steady state plasma creatinine concentration.

b) The time taken to achieve 95% of the new steady-state value.

A number of assumptions are necessary:

- Creatinine is cleared predominantly by glomerular filtration, following first order kinetics.
- Both kidneys function equally.
- Creatinine production by the body remains constant.
- Creatinine is confined to the ECF.
- Total body water is 60% of body weight and a third of this is located in the ECF.

a) Creatinine clearance $= \frac{UV}{P}$

Since UV is constant it follows that if the clearance is halved then the plasma concentration must double. Therefore the new steady state plasma creatinine concentration is 2 x 80 = **160 µmol/L.**

b) Applying the above assumptions, the plasma creatinine concentration will behave exactly as a drug infused at a constant rate and whose clearance follows first order kinetics. The only difference is that creatinine arises endogenously within the body rather than being added by infusion. Therefore we can use the same integrated form of the rate equation as in question 153.

$$Cp = \frac{V_i (1 - e^{-kd.t})}{k_d}$$

It is important to use the correct units for each term.

Calculation of the elimination rate constant, k_d (h^{-1}):

$$k_d = \frac{Cl}{V_d}$$

Where Cl = clearance (L/h) and V_d = volume of distribution (L).

The pre-op clearance can be calculated from the data given:

$$Cl \text{ (L/h)} = \frac{U\text{(mmol/L)} \times 1000 \times V\text{(L)}}{P\text{(µmol/L)} \times 24} = \frac{8.0 \times 1000 \times 1.45}{80 \times 24} = 6.04 \text{ L/h}$$

Assuming removal of one kidney halves the clearance the post-op clearance is 6.04/2 = 3.02 L/h

$$V_d = \text{Body wt (kg)} \times \frac{60}{100} \times \frac{1}{3} = 60 \times \frac{60}{100} \times \frac{1}{3} = 12 \text{ L}$$

Substituting for Cl and V_d to calculate k_d:

$$k_d = \frac{Cl}{V_d} = \frac{3.02}{12} = 0.252 \text{ h}^{-1}$$

Calculation of V_i:

Rate of creatinine formation = rate of excretion = U(mmol/L) x V(L/24 h)

= 8.0 x 1.45 = 11.6 mmol/24h

Since plasma concentration is in µmol/L multiply by 1,000.

To express as amount formed per h divide by 24.

To convert to rate of plasma concentration change divide by the ECF vol (assuming creatinine is confined to the ECF).

Rate of addition of creatinine to plasma (V_i) $= \frac{11.6 \times 1000}{12 \times 24} = 40.28$ µmol/h/L

Calculation of C_p:

This is 95% of the expected new steady state creatinine concentration = 160 x 95/100 = 152 µmol/L

Substitute these values for C_p, k_d and V_i into the integrated rate equation and solve for t:

$$152 = \frac{40.28 (1 - e^{-0.252t})}{0.252}$$

Rearranging:

$$\frac{152 \times 0.252}{40.28} = (1 - e^{-0.252t})$$

$$0.9509 = (1 - e^{-0.252t})$$

$$e^{-0.252t} = 1 - 0.9509 = 0.0491$$

Taking natural logarithms: $-0.252t = -3.014$

$$t = \frac{-3.014}{-0.252} = 12.0 \text{ h}$$

This is the time taken to reach 95% the new steady state concentration of 160 µmol/L *starting from an initial concentration of zero.* To find the time taken to reach this value starting from 80 µmol/L subtract the time it would take for the concentration to increase from zero to 80 µmol/L.

Repeat the calculation of t using C_p = 80 µmol/L:

$$80 = \frac{40.28 (1 - e^{-0.252t})}{0.252}$$

Solving for t gives t = 2.8 h

Time taken to rise from 80 to 152 µmol/L = 12.0 - 2.8 = **9.2 h**

Therefore for practical purposes by the time the second blood was collected at 24h the new steady state value is virtually achieved so the measured value of 162 µmol/L is unremarkable.

Note that it is not possible to calculate the time taken to reach 100% steady state since this value is approached asymptotically and is never achieved. If a C_p value of 160 is used in the integrated rate equation then we end up trying to take the logarithm of a negative number – which has no meaning! Similarly it is impossible to calculate the time taken to reach a concentration greater than the steady state value! ■

Question 155

A screening programme for Down's Syndrome has a screen positive rate of 2.3% and a detection rate of 85%. Calculate the probability that a pregnancy judged to be at low risk will result in an affected child, given that the incidence of Down's Syndrome at term is 1.84/1000 live births in the absence of selective abortion. State any assumptions made.

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