Deacon's Challenge No. 12 Answer

A 15 year old boy presents to casualty following a convulsion. It turns out that he had swallowed 30 of his mother's lithium tablets about 10 hours previously. On admission his lithium concentration is 4.1 mmol/L. A decision needs to be made whether to haemodialyse him to reduce the lithium concentration. As this is not going to be available quickly, the physicians want to know how long he will have toxic levels just with endogenous clearance. Estimate the following, indicating clearly any assumptions you have made:

a) The likely volume of distribution of the lithium at this stage in the situation, given a body weight of 65 Kg.
b) How long it will be before his lithium concentration drops to the relatively safe level of 1.5 mmol/L below which toxicity is unlikely, given a clearance of 0.03 L/h/Kg.

(MRCPath, May 2001)

a) The volume of distribution of a drug is usually calculated by dividing the total dose administered by the plasma concentration. In this question we do not have a reliable estimate of the amount taken. Since lithium is readily water soluble its volume of distribution approximates to body water volume.

$$\text{Volume of distribution } (V_d) = \text{Total body water Vol} = \text{Body wt(Kg)} \times \frac{\%\text{body water}}{100}$$

Assuming an average body water content of 60%:

$$V_d = 65 \times \frac{60}{100} = 39\text{ L}$$

b) Lithium is excreted by the body by glomerular filtration (with some reabsorption by the proximal tubule) and so its elimination follows 1st order kinetics:

$$\text{Log}_e\ C_t = \text{Log}_e\ C_o - kd_t \quad \text{.............................(i)}$$

Where C_o = initial concentration = 4.1 mmol/L

C_t = concentration at time 't hours' = 1.5 mmol/L (the 'safe' level)

t = time taken (in hours) to reach the 'safe' level of 1.5 mmol/L

k_d = elimination rate constant

The clearance (Cl) of the drug is given as 0.03L/h/Kg.

Multiply by the patient's weight to obtain the total clearance:

Clearance = 0.03 (L/h/kg) x 65 (kg) = 1.95 L/h

The elimination rate constant can be calculated from the clearance and volume of distribution:

$$K_d = \frac{Cl}{V_d} = \frac{1.95}{39} = 0.050\ h^{-1}$$

Substitute for C_o, C_t and k_d in equation (i) and solve for t:

$$\text{Log}_e\ 1.5 = \text{Log}_e\ 4.1 - 0.050 \times t$$

$$0.405 = 1.411 - 0.050 \times t$$

$$0.050 \times t = 1.411 - 0.405 = 1.006$$

$$t = \frac{1.006}{0.050} = 20.12\text{h} \quad \text{(20h to 2 significant figures)}$$

Exam tip: Commit to memory the 1st order rate equation, relationship between K_d and C_t, and k_d and $t_{1/2}$. They can be derived from first principles but there won't be time in the exam! ■

Question No. 13

Your on-call laboratory service uses 30 different methods, each of which has a 1% probability of failing QC criteria during the course of a night. Assuming that QC of any method is independent of that of the other methods, what is the probability that on any one night all methods will pass the QC criteria?

MRCPath May 2001