Deacon's Challenge

No 171 - Answer

The following data were obtained for a 26 year-old Caucasian male of average build at his routine six-month psychiatric clinic appointment:

Serum lithium = 4.65 mmol/L
Serum creatinine = 275 µmol/L

He was clinically well and told to stop taking his lithium. His psychiatrist has asked you to use the above information to estimate the time it will take for his serum lithium to return to the relatively safe value of 1.5 mmol/L by endogenous clearance alone.

Lithium is distributed throughout body water and is cleared by glomerular filtration. The raised creatinine suggests that the toxic lithium concentration has most likely arisen due to a decreased GFR extending the half life of the drug.

First calculate the patients eGFR from his serum creatinine concentration. The 4v – MDRD formula is usually quoted as:

$$\text{GFR (mL/min/1.73m}^2\text{)} = 175 \times [\text{creatinine (µmol/L)} \times 0.011312]^{-1.154} \times \text{age (y)}^{-0.203} \times 1.21 \text{ (if black)} \times 0.742 \text{ (if female)}$$

However, the imprecision of eGFR is approximately 15% due both to biological variation and the imprecision of serum creatinine measurement. Therefore it makes no sense to include constants expressed to 5 significant figures! A much simpler version is adequate for our purposes – and is easier to remember:

$$\text{GFR (mL/min/1.73m}^2\text{)} = 175 \times [\text{creatinine (µmol/L)} \times 0.011]^{-1.2} \times \text{age (y)}^{-0.2} \times 1.2 \text{ (if black)} \times 0.74 \text{ (if female)}$$

Since the patient is a 26 year-old male Caucasian this simplifies to:

$$\begin{aligned}\text{GFR (mL/min/1.73m}^2\text{)} &= 175 \times (275 \times 0.011)^{-1.2} \times 26^{-0.2} \\ &= 175 \times 3.03^{-1.2} \times 26^{-0.2} \\ &= 175 \times \text{antilog}_{10}(-1.2 \times \log_{10} 3.03) \times \text{antilog}_{10}(-0.2 \times \log_{10} 26) \\ &= 175 \times \text{antilog}_{10}(-1.2 \times 0.481) \times \text{antilog}_{10}(-0.2 \times 1.41) \\ &= 175 \times \text{antilog}_{10}(-0.577) \times \text{antilog}_{10}(-0.282) \\ &= 175 \times 0.265 \times 0.522 \\ &= 24 \text{ mL/min/1.73m}^2 \text{ (to 2 significant figures)}\end{aligned}$$

Alternatively some calculators can work out negative powers directly.

Making the following assumptions:

- That this GFR value is appropriate (the patient's height and weight are unknown so it is not possible to correct this value for his true surface area).
- That any recently ingested lithium is fully absorbed and distributed throughout body water.
- That his total body water is typical of a 70 kg adult male at 42 L and can be used as an approximate value for his volume of distribution (V_d) of lithium.
- That his GFR remains constant.

The time taken to reach a safe value can be calculated from the first-order rate equation. Using the logarithmic form of the integrated rate equation:

$$\ln Cp_t = \ln Cp_0 - k_d.t$$

where Cp_t = target lithium concentration = 1.5 mmol/L
Cp_0 = initial lithium concentration = 4.65 mmol/L
k_d = elimination rate constant for lithium
t = time taken to reach target concentration = ?

k_d is not given but can be estimated from the clearance (eGFR) and volume of distribution (V_d):

$$k_d = \frac{\text{Clearance}}{V_d}$$

The clearance is in mL/min whereas V_d is in litres and it would be useful if t were in hours not minutes:

Therefore converting clearance to L/h:

$$\text{Clearance} = \frac{24 \times 60}{1000} = 1.44 \text{ L/h}$$

Therefore $k_d = \frac{\text{Clearance}}{V_d} = \frac{1.44}{42} = 0.0343 \text{ h}^{-1}$

Substituting Cp_t, Cp_0 and k_d into the first order equation:

$$\begin{aligned}\ln 1.5 &= \ln 4.65 - 0.0343t \\ 0.405 &= 1.537 - 0.0343t \\ 0.0343^t &= 1.537 - 0.405 = 1.132\end{aligned}$$

$$t = \frac{1.132}{0.0343} = \textbf{33 h} \text{ (to 2 significant figures)}$$

Question 172

A patient has the following results:

Serum copper	12.5 µmol/L	(13-26)
Serum caeruloplasmin	155 mg/L	(200-450)

Assuming that caeruloplasmin is the only protein in serum to bind a significant amount of copper, calculate the serum concentration of free (unbound) copper.

Copper content of caeruloplasmin	0.3%
Atomic mass of copper	63.6

FRCPath, Autumn 2014