Deacon's Challenge

No 195 - Answer

A male anuric patient with a body weight of 84 Kg undergoes haemodialysis for 3 h. His plasma urea concentration was initially 20.5 mmol/L and after dialysis 5.4 mmol/L. Estimate the dialyser urea clearance in mL/min stating any assumptions that you make.

Detailed analysis of dialysis adequacy is quite complex. With the limited data provided it is necessary to make the following assumptions:

- That urea is removed from a single compartment i.e. there is rapid equilibrium of urea between the various fluid compartments. This is the largest source of error.
- That no urea is generated by the body during the dialysis period. This contribution is probably relatively minor. E.g. for an individual generating 400 mmol/24 h the expected average hourly rise in plasma urea is approximately 0.3 mmol/L/h.
- That the volume of distribution remains constant throughout the dialysis period. It is not unusual for patients to accumulate extra fluid between dialysis sessions which is subsequently removed during dialysis. This can be assessed from the weight loss during dialysis.

Let: C_0 = pre-dialysis plasma urea concentration (20.5 mmol/L)
C_t = post-dialysis plasma urea concentration (5.4 mmol/L)
k_d = elimination rate constant (unknown)
t = duration of dialysis (3 h = 3 x 60 min = 180 min)

Assuming a first order process the rate of elimination (dC/dt) is directly proportional to concentration (C). Inserting k_d as a proportionality constant gives:

$$\frac{dC}{d_t} = k_d.C$$

Re-arranging, integrating (between C_0 and Ct) and taking natural logarithms gives the familiar first order equation used in pharmacokinetics:

$$\ln C_t = \ln C_0 - k_d.t$$

which can be further re-arranged to give:

$$k_d.t = \ln (C_0/C_t)$$

Substituting values for t, C_t and C_0 enables calculation of k_d:

$$180k_d = \ln (20.5/5.4) = \ln 3.80 = 1.34$$

$$k_d = 1.34/180 = 0.00744 \text{ min}^{-1} \quad \text{(to 3 sig figs)}$$

The relationship between clearance (K mL/min), k_d and the volume of distribution (V mL) is:

$$K = k_d \times V$$

Urea is distributed throughout all body fluid compartments so its volume of distribution approximates to total body water i.e. 60% of body weight.

$$V = 84 \times 60/100 = 50.4 \text{ L} = 50.4 \times 1{,}000 \text{ mL} = 50{,}400 \text{ mL}$$

Therefore $K = 0.00744 \times 50{,}400 =$ **375 mL/min** (to 3 sig figs)

To assess dialysis adequacy K/V is usually substituted for k_d in the integrated first order rate equation to give:

$$\frac{K.t}{V} = \ln (C_0/C_t)$$

The parameter $K.t/V$ is routinely used as a measure of dialysis adequacy and a minimum target of 1.2 is frequently used. It is often said that $K.t/V$ is the proportion of the body's urea space that is completely cleared of urea during dialysis. If that were the case then a value greater than one could never be achieved! The plasma urea only has to fall to less than 37% of the original value for a $K.t/V$ of 1 to be exceeded. Although in the above model the clearance remains constant during dialysis, the amount of urea removed in any given time period is not. In the above example urea would be cleared from 375 mL of plasma during the first minute. At the end of this time the remaining urea would be redistributed throughout the urea space so that the plasma urea concentration actually falls. During the next minute of dialysis although the same volume of plasma is cleared, since its urea concentration is already reduced, the actual amount of urea cleared will be less than during the first minute etc. It would require an infinite dialysis time to completely remove all urea!

Question 196

You need to prepare an isotonic (osmolality = 290 mmol/L) phosphate buffer with a pH of 7.4. Calculate the amounts of anhydrous sodium dihydrogen phosphate and anhydrous disodium hydrogen phosphate that need to be weighed into 1 litre of water. The p*K*s of phosphoric acid are pKa_1 = 1.96, pKa_2 = 6.82 and pKa_3 = 12.32. Atomic weights: Na 23, P 31.

EFLM
EUROPEAN FEDERATION OF CLINICAL CHEMISTRY AND LABORATORY MEDICINE

European Federation of Clinical Chemistry and Laboratory Medicine

Our colleague Nudar Jassam has brought the European Federation of Clinical Chemistry and Laboratory Medicine (EFLM) News Sheet to our attention as a valuable source of information. She has particularly highlighted the EFLM project "Exchange of practical knowledge and skills in Laboratory Medicine" – EFLMLabX within the January/February edition. Further information can be found here: **https://eflmlabx.eflm.eu/en** https://eflmlabx.eflm.eu/enor visit the EFLM website: **www.eflm.eu**