Deacon's Challenge

No 133 - Answer

A 14-year old boy was admitted in an intoxicated state having been suspected to have consumed an unknown quantity of methylated spirit (a mixture of ethanol and methanol). He weighed 55 Kg. The following laboratory results were obtained on a blood sample taken within 15 minutes of admission:

Urea	*3.7*	*mmol/L*
Sodium	*136*	*mmol/L*
Potassium	*4.2*	*mmol/L*
Glucose	*3.2*	*mmol/L*
Osmolality	*342*	*mmol/Kg*
Ethanol	*190*	*mg/dL*

Estimate his serum methanol concentration in mg/dL and the volume of methanol he consumed (volume of distribution 0.6 L/Kg, density 0.791 g/mL), stating any assumptions you make or limitations of this approach.

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First convert the ethanol (EtOH) concentration from mg/dL to mmol/L to give the same concentration units as the other osmotically active species:

$$\text{EtOH (mmol/L)} = \frac{\text{EtOH (mg/dL)} \times 10}{\text{MW}}$$

$$\text{EtOH} = C_2H_5OH = C_2H_6O \quad \text{therefore MW} = (2 \times 12) + (6 \times 1) + 16 = 46$$

$$\text{EtOH (mmol/L)} = \frac{190 \times 10}{46} = 41.3 \text{ mmol/L}$$

Next calculate the expected osmolality (Osmo_{Calc}) from the concentrations of all osmotically active species *normally* present:

$$\text{Osmo}_{Calc} = 2[Na^+] + 2[K^+] + [\text{Urea}] + [\text{Glucose}]$$
$$= (2 \times 136) + (2 \times 4.2) + 3.7 + 3.2$$
$$= 272 + 8.4 + 3.7 + 3.2$$
$$= 287 \text{ mmol/L (3 sig figs)}$$

The osmolal gap is the difference between the measured (Osmo_{Meas}) and calculated osmotic gap and represents the concentrations of *all* non-measured osmotically active species present:

$$\text{Osmolal gap (mmol/L)} = \text{Osmo}_{Meas} \text{ (mmol/L)} - \text{OsmoCalc (mmol/L)}$$
$$= 342 - 287 = 55 \text{ mmol/L}$$

Assuming that methanol and ethanol are the *only* unmeasured species present then the methanol concentration can be calculated from the osmolal gap and the measured ethanol concentration:

$$\text{Osmolal gap} = [\text{EtOH}] + [\text{MeOH}]$$

$$55 = 41.3 + [\text{MeOH}]$$
$$[\text{MeOH}] = 55 - 41.3 = 14 \text{ mmol/L (2 sig figs)}$$

This is likely to be an over estimate since there is always a small osmolal gap due to other unmeasured species.

To convert this result to mg/dL:

$$\text{MeOH (mg/dL)} = \frac{\text{MeOH (mmol/L)} \times \text{MW}}{10}$$

$$\text{MeOH} = CH_3OH = CH_4O \quad \text{therefore MW} = 12 + (4 \times 1) + 16 = 32$$

$$\text{MeOH (mg/dL)} = \frac{14 \times 32}{10} = \mathbf{45 \text{ mg/dL}} \text{ (2 sig figs)}$$

Next calculate the weight of methanol consumed (i.e. total methanol in the body):

$$\text{Plasma concentration (mg/dL)} = \frac{\text{Weight consumed (mg)}}{\text{Total } V_d \text{ (dL)}}$$

$$\text{Weight consumed (mg)} = \text{Plasma concentration (mg/dL)} \times \text{Total } V_d \text{ (dL)}$$

$$\text{Total } V_d \text{ (dL)} = V_d \text{ (dL/Kg)} \times \text{Body weight (Kg)}$$
$$= V_d \text{ (L/Kg)} \times 10 \times \text{Body weight (Kg)}$$

Therefore weight consumed (mg) = Plasma concentration (mg/dL) x V_d (L/Kg) x 10 x Body weight (Kg)

$$= 45 \times 0.6 \times 10 \times 55$$
$$= 14{,}850 \text{ mg}$$

Finally convert this weight to volume:

$$\text{Density (g/mL)} = \frac{\text{Weight (mg)}}{1000 \times \text{Volume (mL)}}$$

$$\text{Volume (mL)} = \frac{\text{Weight (mg)}}{1{,}000 \times \text{Density (g/mL)}}$$
$$= \frac{14{,}850}{1{,}000 \times 0.791}$$
$$= \mathbf{19 \text{ mL}} \text{ (2 sig figs)}$$

The main limitation is the calculation of osmolality since it is based on the following assumptions:

- That all important osmotically active species are accounted for.
- That all potential dissociations are complete.
- That the anions associated with Na^+ and K^+ are free to contribute to osmolality and are not part of a macromolecule (e.g. protein).
- That the activity of each species is the same as concentration i.e. the ions exhibit ideal behaviour.

- That the millimo*lal* concentration of each ion (mmol/Kg *water*) is the same as its millimo*lar* concentration (mmol/L *plasma or serum*). This is not true since plasma or serum is approximately 95% water. Hyperlipidaemia will compound this effect.

Furthermore the imprecision will be considerable since it will consist of the combined imprecisions of **five** individual measurements.

Attempts have been made to improve the agreement between measured and calculated osmolality by modifying the above formula. Employing these will give rise to different answers which are summarised below:

Formula	Calc **Osmo**	**Osmo Gap**	**Plasma MeOH**	**Vol MeOH**
	mmol/L	mmol/L	mg/dL	mL
$2[Na^+] + 2[K^+] + [Gluc] + [Urea]$	287	55	45	19
$1.86[Na^+] + [Gluc] + [Urea] + 9$	253	73	102	43
$2[Na^+] + [Gluc] + [Urea]$	279	63	69	29

Question 134

Replicate analyses are often employed in an attempt to overcome poor assay imprecision.

a) What is the imprecision (expressed as a percentage of the imprecision for a single measurement) for a mean calculated from duplicate measurements?

b) Calculate the minimum number of replicate measurements required to produce a mean value with an imprecision of one half of the value which would be obtained for single measurements.