Determinants of plasma water sodium concentration

Sir,

I read with interest the hypothesis regarding the determinants of the plasma water sodium concentration by Nguyen and Kurtz [1]. The authors have highlighted the importance of parameters other than total exchangeable sodium, total exchangeable potassium and total body water (TBW) as determinants of plasma water sodium concentration. However, there seems to be an error in the calculation of the intercept.

The authors have derived the equation:

\[
[Na^+]_{pw} = \frac{(Na_e+K_e)/TBW - (Na_{osm inactive}+K_{osm inactive})/TBW}{0.11(Nae+Ke)/TBW}
\]

According to Edelman’s equation [2]:

\[
[Na^+]_{pw} = 1.11(Na_e+K_e)/TBW - 25.6
\]

Solving the two equations, we get:

\[
-25.6 = \frac{-Na_{osm inactive}+K_{osm inactive} \right)+K^+_{pw} \left)-osmol_{pw}/V_{pw} - 0.11(Na_e+K_e)/TBW}{(osmol_{ECF} + osmol_{ICF})/TBW}\]

From this it appears that even the sum of (Na_e + K_e) contributes to the \( y \)-intercept of Edelman’s equation.

The authors have used two examples to highlight the clinical application of their hypothesis. In both of the examples, the authors have not considered insensible water losses while calculating TBW. If they had done so, then the predicted [Na^+] would have been higher than the actual value.

While the authors have highlighted some important concepts, these might require modifications to accurately predict the changes in plasma water sodium concentrations with therapeutic interventions.

Conflict of interest statement. None declared.

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1. Nguyen MK, Kurtz I. Are the total exchangeable sodium, total exchangeable potassium and total body water the only determinants of the plasma water sodium concentration? Nephrol Dial Transplant 2003; 18: 1266–1271

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Reply

Sir,

In his accompanying letter to NDT, Lodha raises the issue that the term 0.11(Na_e + K_e)/TBW should be included as a component of the \( y \)-intercept in the Edelman equation. The relationship between the [Na^+]_{pw} and Na_e, K_e and TBW was originally demonstrated empirically by Edelman et al. [1]:

\[
[Na^+]_{pw} = 1.11(Na_e + K_e)/TBW - 25.6
\]

We recently demonstrated quantitatively that there are several physiological parameters in the \( y \)-intercept (~25.6) of the Edelman equation, which independently alter the [Na^+]_{pw} [2]:

\[
[Na^+]_{pw} = \frac{(Na_e+K_e)/TBW - (Na_{osm inactive}+K_{osm inactive})/TBW + (osmol_{ECF} + osmol_{ICF})/TBW - [K^+_{pw} - osmol_{pw}/V_{pw}]}{0.11(Na_e+K_e)/TBW}
\]

where the \( y \)-intercept in Edelman’s equation is represented by four parameters:

\[
[Na_{osm inactive} + K_{osm inactive}]/TBW + (osmol_{ECF} + osmol_{ICF})/TBW - [K^+_{pw} - osmol_{pw}/V_{pw}]
\]

Lodha suggests that the term 0.11(Na_e + K_e)/TBW should be included as a component of the \( y \)-intercept as well. This notion cannot be true. First, equation 2 is mathematically derived based on the assumption that the body fluid compartments are in osmotic equilibrium. Based on this analysis, there is no physiological justification for the inclusion of the additional term 0.11(Na_e + K_e)/TBW in the \( y \)-intercept. Secondly, according to equation 2, the slope in the Edelman equation is 1. Based on the regression equation which best fit their empirical data, Edelman et al. reported a slope of 1.11 [1]. The suggestion by Lodha to include the additional term 0.11(Na_e + K_e)/TBW in the \( y \)-intercept is based on the assumption that there is a 0.11 difference in our mathematically derived slope and Edelman’s empirically determined slope. Given that the slope of 1.11 was empirically determined, additional theoretical and/or empirical justification is required prior to assuming that there exists a 0.11 difference in the two slopes. Indeed, we have recently shown that the slope in equation 2 should be 1.11 rather than 1 [6]. However, the 0.11 difference is not attributed to the term 0.11(Na_e + K_e)/TBW as suggested by Lodha. Instead, our recent analysis indicates that the slope of 1.11 in the Edelman equation is quantitatively determined by the combined effect of Gibbs–Donnan equilibrium and the osmotic coefficient of Na^+ salts under physiological conditions [6]. Finally, it is well known that the Na_e and K_e include osmotically active as well as osmotically inactive Na^+ and K^+ [1,3–5]. The osmotically inactive Na_e and K_e are ‘ineffective osmoles’ and they do not contribute to the distribution of water between the extracellular and intracellular spaces. Importantly, only the osmotically active Na_e

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