ELECTROLYTE TRANSPORT ACROSS THE DIALYZER'S MEMBRANE
A PRELIMINARY STUDY OF THE DONNAN EQUILIBRIUM

KAZUHITO TOTSUNE

Totsune K. Electrolyte transport across the dialyzer's membrane: A preliminary study of the Donnan equilibrium. In order to obtain the formula to calculate the Donnan ratio (R) from protein concentration in plasma (C_{tp}) and sodium concentration in dialysate ([D[Na]]), the experimental equilibrium dialyses were performed in vitro. The formula was represented as follows:

\[ R = 1.0 - \rho_R \times \frac{C_{tp}}{[D[Na]]} \]

where \( \rho_R \) is a constant.

The values of \( \rho \) varied with the measurement methods for Na and Cl. The results indicated that when the Donnan equilibrium phenomenon was discussed, Na concentrations measured by flamephotometry and Cl by potentiometric titration should be used after the correction as to the complex-binding to albumin, and also suggested that Na and Cl concentrations by Ion-Selective Electrode should be carefully dealt with. Keywords: Donnan ratio, Flamephotometry, Ion-Selective Electrode.


Introduction

We have studied the electrolyte transport in a dialyzer and found that a formula to calculate the Donnan ratio\(^1\) from protein concentration in plasma and sodium concentration in dialysate is required for evaluating the sodium transport across a dialyzer's membrane with a mathematical model. When uremic patients are dialyzed, ultrafiltration method is usually used at the same time. Then, blood loses plasma water and the concentration of total protein in plasma (C_{tp}) increases with distance from a blood inlet, and sodium concentration in dialysate ([D[Na]]) changes along the dialyzer, resulting in changing of the Donnan ratio (R).

The purpose of this study was to clarify the relationship among C_{tp}, [D[Na]] and the Donnan ratio, and to determine what kind of measurement methods for electrolyte concentrations should be used when we discuss the Donnan equilibrium phenomenon.

Theory

Donnan equilibrium phenomenon occurs between plasma and dialysate across a semipermeable membrane\(^1\) (Figure 1). On the assumption that only Na and Cl exist in the dialysate compartment and Na, Cl and protein exist in the plasma compartment, the following equation is obtained at equilibrium:

\[ R = \frac{[D[Na]]}{P[Na]} = \frac{P[Cl]}{D[Cl]} \]

where \( P[Na] \), \( P[Cl] \) and \( D[Cl] \) are Na and Cl concentrations in plasma and Cl concentration in dialysate, respectively.

When the concentration of electric colloidal anion ([X^-]) is very low, the following equation could be obtained under the conditions for electroneutrality:

\[ R = 1.0 - 0.5 \times \frac{[X^-]}{[D[Na]]} \]

As it is expected that \([X^-]\) is proportional to \( C_{tp} \), Equation (2) may be modified as follows:

\[ R = 1.0 - \rho_R \times \frac{C_{tp}}{[D[Na]]} \]

where \( \rho_R \) is a constant.

Materials and Methods

Test plasma

Fresh frozen plasma (FFP) and human serum albumin (Albumin 25%-%, Green Cross Corp.) were used as test plasma. FFP was used after thawing at room temperature, packed in cello-
Figure 2. Experimental set-up.

Figure 3 shows the correlation between protein concentration in plasma and Donnan ratio ($R_{1Na}$ and $R_{1Cl}$) calculated from the raw values of Na concentrations in plasma and dialysate measured by flame photometry and those of Cl measured by potentiometric titration:

\[
R_{1Na} = \frac{D[Na]_f}{P[Na]_f} \quad (4)
\]
\[
R_{1Cl} = \frac{P[Cl]_t}{D[Cl]_t} \quad (5)
\]

where the subscripts $f$ and $t$ are flame-photometry and potentiometric titration, respectively.

The Donnan ratio linearly decreased as protein concentration increased. The slopes of the regression lines of $R_{1Na}$ were very gentle, whereas the slopes of the regression lines of $R_{1Cl}$ were steeper than those of $R_{1Na}$. $R_{1Na}$ was higher than $R_{1Cl}$ both with plasma and with albumin, and $R_{1Cl}$ with albumin was lower than $R_{1Cl}$ with plasma.

Figure 4 shows the correlation between the total protein concentration in the test plasma divided by Na concentration in dialysate, $C_{tp}/D[Na]_f$, and the Donnan ratios ($R_{2Na}$ and $R_{2Cl}$). The data measured by flamephotometry for Na and by potentiometric titration for Cl were corrected on the assumption that 1% of Na is complex-bound by protein and 1 mEq of Cl is bound per 10 g of albumin in a complex-type manner, and plasma water concentrations of Na ($P[Na]_{pw}$) and Cl ($P[Cl]_{pw}$) were calculated by the following formulas:

\[
P[Na]_{pw} = 0.99 \times E_p \times P[Na]_f \quad (6)
\]
\[
P[Cl]_{pw} = E_p \times (P[Cl]_t - 1.0 \times C_{alb}) \quad (7)
\]
\[
E_p = 100/(100.6 - 0.8 \times C_{tp}) \quad (8)
\]

where $C_{alb}$ means albumin concentration in the test plasma and $E_p$ is the coefficient to convert concentrations per volume of plasma to concentrations per volume of aqueous phase. There were no significant differences between the regression lines of $R_{2Na}$ and $R_{2Cl}$, and a common regression line was obtained:

Figure 3. The effect of total protein concentration in plasma ($C_{tp}$) on the Donnan ratio where Na concentration in dialysate was kept 150 mEq/L.
Figure 4. The correlation between Ctp divided by Na concentration in dialysate and the Donnan ratio $R_2$ calculated from the corrected values of Na and Cl concentrations.

$$R_2 = 1.011 - 1.28 \times \frac{C_{tp}}{D[Na]_f}$$  \hspace{1cm} (9)

$$= R_{2Na} = R_{3Cl} \hspace{1cm} r = 0.924$$

Figures 5 and 6 show the correlations between Ctp divided by Na concentration in dialysate measured by ISE (D[Na]$_f$) and the Donnan ratios $R_{3Na}$ and $R_{3Cl}$, which were directly calculated from the values measured by ISE. The regression line of $R_{3Na}$ with plasma was not significantly different from $R_{3Na}$ with albumin, and a common regression line was obtained as follows:

$$R_{3Na} = 0.989 - 0.94 \times \frac{C_{tp}}{D[Na]_i}$$  \hspace{1cm} (10)

$$r = 0.933$$

The slope of this line was gentler than the slope of the line of $R_2$ represented by Equation (9).

The regression line of $R_{3Cl}$ with plasma was significantly different from that with albumin. $R_{3Na}$ was lower than $R_{3Cl}$ with albumin but higher than $R_{3Cl}$ with plasma.

Discussion

This study confirmed that there was a linear relationship between Ctp/D[Na] and the Donnan ratio. The relation is represented by Equation (9). It has already known that there is a negative linear correlation between the protein concentration in plasma and the Donnan ratio, but any investigator has never realized the existence of this relationship among the protein concentration, cation concentration in dialysate and the Donnan ratio.

The slopes ($\alpha_p$) of the regression lines varied with methods for measuring Na and Cl. This suggests that it is very important what kind of methods should be used for discussing the Donnan equilibrium phenomenon. This problem was further examined.

Figure 3 shows that it is inadequate to use the raw values of Na concentrations measured by flamephotometry and Cl by potentiometric titration because $R_{1Na}$ and $R_{1Cl}$ did not fit together. Therefore values obtained need a few correction.

The correction used in this study consists of considering the complex-binding of Na and Cl to proteins and then converting to plasma water concentrations. On the assumption that 1% of Na is complex-bound by protein and 1 mEq of Cl is bound per 10 g of albumin in a complex-type manner, close agreement between $R_{Na}$ and $R_{Cl}$ was obtained (Figure 4). Although our correction is based on that of Leeuwen, we used our own correcting factor for Cl larger than that of Leeuwen, because $R_{2Na}$ and $R_{2Cl}$ corrected by using his original factor did not agree so precisely in this study.

Recently Gotch et al. have reported that Na diffusion gradient is a function of Na activity in the blood and dialysate streams and is directly measured by ISE. However, our results suggested that the values measured by ISE should be carefully dealt with. In this study we found that $R_{3Na}$ and $R_{3Cl}$ did not fit together, showing that there was no guarantee in regarding ISE as the correct method to measure "concentration" per volume of aqueous phase. ISE seems not to be really specific. Figure 6 shows that ISE for Cl was apparently affected by gamma globulin. Moreover, it should be noticed that some ISE equipments recently developed have a built-in formula to correct the measured values to the concentration per volume of plasma and in such a case we have no choice but to read the corrected values on the display.

Conclusion

The formula to calculate the Donnan ratio from protein concentration in plasma and sodium concentration in dialysate has been obtained. Furthermore it was indicated that when the Donnan equilibrium phenomenon was discussed, Na concentrations measured by flamephotometry and Cl by potentiometric titration should be used after the correction as to the complex-binding to protein, and also suggested that Na and Cl concentrations measured by Ion-Selective Electrode should be carefully dealt with.
References


Figure 5. The correlation between the $C_{tp}/D[Na]_i$ and the Donnan ratio $R_{3Na}$ calculated from Na concentrations measured by ISE.

Figure 6. The correlation between the $C_{tp}/D[Na]_i$ and the Donnan ratio $R_{3Cl}$ calculated from Cl concentrations measured by ISE.