The Mathematical Basis, Clinical Application and Limitations of Ionic Dialysance

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Morbidity and mortality in hemodialysis patients are closely related to dialysis adequacy. Unfortunately, in real life, the dialysis dose that is delivered during each hemodialysis session, for various reasons, may not even be close to that prescribed. It would be ideal if one could assess and verify the dialysis dose delivered in every dialysis treatment. Formal urea kinetic modeling (Kt/V) has been used widely to quantify the dialysis dosage. Recently, ionic dialysance is becoming more popular as a method to assess the delivered Kt/V of dialysis treatment. Its mathematical basis is reviewed, and its pitfalls, limitations and clinical relevance are briefly described. [Hong Kong J Nephrol 2004;6(1):56–9]

Key words: ionic dialysance, urea clearance, online clearance, dialysis adequacy

INTRODUCTION

After publication of the mechanistic analysis of the National Cooperative Dialysis Study, Kt/V became widely accepted as a means to quantify the hemodialysis dose [1,2]. In order to calculate the value of Kt/V in formal urea kinetic modeling, at least two blood samples are needed, for predialysis and postdialysis urea. However, the calculations are plagued by problems such as the urea rebound phenomenon, cardiopulmonary recirculation, and access recirculation. It would be much simpler to make use of the spent dialysate to estimate the dialysis dose. Recently, an interesting principle called ionic dialysance, also called online clearance monitoring, has attracted a lot of attention [3,4]. It offers an alternative method to monitor the dialysis dose delivered during a hemodialysis session.

IONIC DIALYSANCE

There are several basic assumptions in the principle of ionic dialysance: the ion is not absorbed by or adsorbed on the dialyzer membrane; the ion concentration in the patient’s blood (i.e. in the blood flowing into the dialyzer) and blood flow rate remain constant during the short time needed to make the serial measurements; and in between measurements, the patient’s clinical condition (e.g. blood pressure, blood ion concentration) remains relatively stable and all other parameters (e.g. blood flow rate, ultrafiltration rate) are constant.

The newer models of hemodialysis machines can now measure ionic dialysance. The result generated correlates well with urea kinetic modeling [5–10]. The advantages of ionic dialysance include the fact that no blood sampling is needed, repeated measurements of ion and dialysance can be made at regular intervals, no extra recurrent costs are involved, and the result is available immediately.

The following is a simplified version of the mathematical basis for ionic dialysance theory [3,4]. The formula itself does not specify any special ion or solute to be used. Currently, sodium ion is used in ionic dialysance as it can be measured readily and can easily be verified. It is also the most abundant cation in the extracellular fluid compartment and the dialysate. So-
Sodium concentration is linearly related to the conductivity of the fluid. When sodium is chosen to calculate ionic dialysance, the conductivity of the fluid is measured to reflect sodium concentration.

The flux (J) of a solute across the dialyzer membrane depends on the concentration difference across the membrane. Thus, J is proportional to the concentration difference:

\[ J \propto C_B - C_D \]

where \( C_B \) is the concentration of solute in the blood and \( C_D \) is the concentration of solute in the dialysate.

The relationship can be expressed as equation (1):

\[ J = D (C_B - C_D) \quad (1) \]

where \( D \) is the dialysance.

To take into account the effect of ultrafiltration, the amount of solute removed by ultrafiltration is \( Q_F C_D \), where \( Q_F \) is the ultrafiltration rate, and \( C_D \) is the concentration of solute in the dialysate. Thus, the flux \( J \) of solute across the dialyzer membrane (equation 1) now becomes:

\[ J = D (C_B - C_D) + Q_F C_D \quad (2) \]

The flux of solute is equal to the amount of solute in the dialysate leaving the dialyzer less the amount of solute in the dialysate going into the dialyzer:

\[ J = (Q_D + Q_F)C_{Do} - Q_D C_D \quad (3) \]

where \( C_{Do} \) is the concentration of solute in the dialysate leaving the dialyzer, \( Q_D \) is the flow rate of the dialysate, and \( Q_F \) is the ultrafiltration rate.

Obviously, equation (2) must be equal to equation (3):

\[ D (C_B - C_D) + Q_F C_D = (Q_D + Q_F)C_{Do} - Q_D C_D \]

Rearranging terms, this becomes:

\[ D (C_B - C_D) = (Q_D + Q_F)(C_{Do} - C_D) \]

or

\[ D (C_B - C_D) = (Q_D + Q_F)(C_{Do} - C_D) \]

and simplified to:

\[ D (C_B - C_D) = (Q_D + Q_F)(C_{Do} - C_D) \]

Thus, dialysance can be determined from ultrafiltration rates and solute concentrations:

\[ D = \frac{(C_{Do} - C_D)}{(C_B - C_D)} \quad (4) \]

In this equation, there are only two unknowns, ionic dialysance \( D \) and concentration of solute in the blood \( C_B \). All other data, dialysate flow rate \( Q_D \), ultrafiltration rate \( Q_F \) and concentration of solute in the dialysate going into the dialyzer \( C_{Do} \), are known. The concentration of solute in the dialysate leaving the dialyzer \( C_{Do} \) can be measured.

When two sets of data are available, there are two equations (4 and 5) so that the two unknowns, ionic dialysance \( D \) and concentration of solute in the blood \( C_B \), can be calculated.

\[ D = \frac{(y_2 - x_2)}{(C_B - x_2)} \]

where \( y_2 \) is the concentration of solute in the dialysate leaving the dialyzer when \( x_2 \) is the concentration of solute in the dialysate going into the dialyzer.

\[ D = \frac{(y_1 - x_1)}{(C_B - x_1)} \quad (5) \]

where \( y_1 \) is the concentration of solute in the dialysate leaving the dialyzer when \( x_1 \) is the concentration of solute in the dialysate going into the dialyzer.

Equation (5) becomes:

\[ D(C_B - x_1) = (Q_D + Q_F)(y_1 - x_1) \]

which can be rewritten as:

\[ C_B - x_1 = \frac{(Q_D + Q_F)(y_1 - x_1)}{D} \]

or as

\[ C_B = \frac{(Q_D + Q_F)(y_1 - x_1)}{D} + x_1 \quad (6) \]

Substituting (6) into equation (4) gives:

\[ D = \frac{(Q_D + Q_F)(y_2 - x_2)}{[D (Q_D + Q_F)(y_1 - x_1)] + x_1 - x_2} \]

This can be rearranged to:

\[ \frac{D}{(Q_D + Q_F)(y_2 - x_1)} + x_1 - x_2 \]

then to:

\[ \frac{(Q_D + Q_F)(y_2 - x_1)}{x_1 - x_2} = (Q_D + Q_F)(y_2 - x_2) \]

which becomes

\[ (x_1 - x_2)D = (Q_D + Q_F)(y_2 - x_2) \]

or

\[ (x_1 - x_2)D = (Q_D + Q_F)[(y_2 - x_2) - (y_1 - x_1)] \]

This can be simplified several times:

\[ (x_1 - x_2)D = (Q_D + Q_F)(y_2 - x_2 - y_1 + x_1) \]

\[ (x_1 - x_2)D = (Q_D + Q_F)(y_2 - y_1 + x_1 - x_2) \]
\[(x_1 - x_2)D = (Q_D + Q_F)[(x_1 - x_2) - (y_1 - y_2)] \]

to give an equation for dialysance:
\[D = \frac{(Q_D + Q_F)[(x_1 - x_2) - (y_1 - y_2)]}{(x_1 - x_2)}\]

that can be simplified through:
\[D = \frac{(Q_D + Q_F)}{(y_1 - y_2)}\]

to
\[D = \frac{(Q_D + Q_F)[1 - \frac{(y_1 - y_2)}{(x_1 - x_2)}]}{(x_1 - x_2)}\]

Thus, when the amount of solute in the dialysate going into the dialyzer is varied from \(x_1\) to \(x_2\), and the solute concentrations in the dialysate leaving the dialyzer (\(y_1\) and \(y_2\)) are measured, ionic dialysance can be calculated.

**DISCUSSION**

The clinical implications of ionic dialysance are considerable. Ionic dialysance makes it possible to assess the dialysis dose delivered during each dialysis session, which is impractical with the current pre- and postdialysis urea determination. Repeated measurement of ionic dialysance allows the quantification of the delivered dialysis dose from the very early stage of dialysis treatment. Ionic dialysance changes with any alteration in the efficiency of dialysis, for example, due to partial clotting of the dialyzer, access dysfunction, error in the dialysate flow rate or direction, inadvertent reversal of the access needle, and inadequate blood flow due to poor blood pump calibration. Medical personnel will immediately notice any deviation in the ionic dialysance from the specified clearance of the dialyzer at the captioned blood flow rate. Remedial action can be taken in a timely manner rather than waiting until the end of the dialysis session to find out that something had gone wrong. Ionic dialysance may help medical staff to identify patients who are at risk of under-dialysis and to rectify the issue in time to ensure that the patient receives the dialysis dose prescribed by the nephrologist.

Currently, machines use sodium concentration in the dialysate to calculate ionic dialysance, which correlates with urea clearance very well [5–10]. Sodium ion is originally present in the dialysate, and extra sodium ion can easily be added. Therefore, urea clearance can be projected using computer monitoring of the dialysate in the hemodialysis machine during every treatment. At the end of treatment, \(Kt/V\) will be shown on the screen.

However, ionic dialysance is not without pitfalls. *In vitro*, the amount of urea movement across the dialyzer membrane is equal to the amount of sodium movement. *In vivo*, the correlation between urea movement and sodium movement is good, but they are never identical and there are always discrepancies [5–10]. The causes of the discrepancies are currently under investigation.

Ionic dialysance measures the sodium concentration in the dialysate at certain time intervals but not continuously. A patient’s clinical condition and dialysis parameters, such as hypotension, decreased blood flow rate, or infusion of colloid or crystalloid solution, may change between measurements. This may affect the accuracy of \(Kt/V\) derived from ionic dialysance.

A major component in the calculation of \(Kt/V\) is the volume of distribution of urea (\(V\)). \(V\) is input directly into the machine or is generated by anthropometric methods such as the Watson formula or the body weight method. The accuracy of the \(Kt/V\) determined from ionic dialysance clearly depends on how accurately \(V\) reflects the true urea distribution volume.

Last but not least, urea was used initially as a surrogate marker of uremic toxin. The National Cooperative Dialysis Study proves beyond doubt that urea is not a good surrogate marker of uremic toxin. It is the hemodialysis dose that affects mortality. Recently, it has been shown that \(V\) also has an impact on mortality [11]. We are now using another surrogate marker, sodium, to assess urea removal during hemodialysis treatment. The end result may not even be close to what we really want – accurate hemodialysis quantification.

Ionic dialysance started from a mathematical model and *in vitro* studies. Only lots of clinical studies and scientifically validated data will help to answer the question, “How valid and relevant is ionic dialysance in our clinical practice and day-to-day patient management?”

**REFERENCES**

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