Ionic conductivity of peritoneal dialysate: a new, easy and fast method of assessing peritoneal membrane function in patients undergoing peritoneal dialysis

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ABSTRACT

Background. Peritoneal membrane function can be assessed using the peritoneal equilibration test (PET) and similar tests, but these are almost always complicated to use, require a considerable amount of working time and their results cannot always be easily interpreted. Ionic conductivity is a measure of the ability of an electrolyte solution to conduct electricity. We tested the hypothesis that the ionic conductivity of peritoneal dialysate can be used to evaluate peritoneal membrane function in peritoneal dialysis patients.

Methods. We measured the ionic conductivity and classic biochemical parameters of peritoneal dialysate in 69 patients during a modified PET and compared their ability to evaluate peritoneal membrane function and to diagnose ultrafiltration failure (UFF).

Results. Ionic conductivity was correlated well with classical parameters of peritoneal transport as glucose reabsorption of glucose (D/Dp: r² = 0.62, P < 0.0001) and creatinine transport (D/Pcre: r² = 0.72, P < 0.0001). Twelve patients (17%) experienced UFF and, in them, the ionic conductivity area under the receiver-operating characteristic curve was 0.91 (95% confidence interval: 0.81–0.96) with sensitivity of 1.00 and specificity of 0.84 at a cut-off value of 12.75 mS/cm.

Conclusions. These findings indicate that the ionic conductivity of peritoneal dialysate can be used as a new screening tool to evaluate peritoneal membrane function.

Keywords: ionic conductivity, peritoneal equilibration test, peritoneal membrane function, ultrafiltration failure

INTRODUCTION

Peritoneal dialysis (PD) is a useful means of replacing renal function in patients with chronic renal failure, and the survival of patients on PD is similar to that of patients on haemodialysis (HD) [1]. However, the prolonged use of a peritoneal membrane can lead to alterations in its anatomical and functional characteristics, thus increasing its permeability to small solutes and causing ultrafiltration failure (UFF); [2] the alterations may also predispose to serious complications [3]. Functional changes in a peritoneal membrane can be evaluated using the peritoneal equilibration test (PET) [4], and the results of PET also provide useful information concerning peritoneal UF: a peritoneal UF of <400 mL after a dwell time of 4 h using a 3.86 or 4.25% glucose solution is diagnostic of UFF [5, 6].

PET, in even its simplest form, requires a considerable amount of nurse and doctor working time and resources (laboratory assays, interpretation of data, etc.). In addition, the tests used to measure the reduction in sodium (Na) concentration in dialysis fluid (ΔDNa), a useful means of quantifying free water transport (FWT) through aquaporin-1 (AQ-1) channels or ultra-small pores [7–12], and other parameters [8, 13] are even more complicated.

The ionic conductivity (Cd) of an electrolyte solution is a measure of its ability to conduct electricity [14]. This method is widely used to prepare the HD fluid, check its electrolyte concentrations and quantify the dialysis dose [15, 16]. As the Cd of a solution depends on its electrolyte concentration, it is possible to evaluate the changes in the Cd of a dialysate during a peritoneal dwell, which are caused by changes in electrolyte concentrations due to electrolyte diffusion (especially the changes in Na concentration, the biggest contributor to Cd) and UF. The peritoneal small solute transport, expressed by the ratio between dialysate and plasma concentrations of creatinine at the end of the test (D/Pcrea), is proportional to the peritoneal diffusive transport of Na, expressed by the ratio between dialysate and plasma concentrations of Na at the end of the test (D/PNa) [17].

The presence of glucose in HD fluids reduces Cd by increasing their viscosity, but this variation is very small because of
the relatively low glucose concentration (100 mg/dL) [15]. However, the very high glucose concentrations in PD fluids can significantly increase viscosity and lead to a much greater reduction in Cd. During a dwell with a hypertonic solution, glucose is absorbed from the peritoneal cavity and causes variations in dialysate viscosity and then in dialysate Cd, which may be different in individual PD patients.

In conclusion, dialysate Cd can be correlated with the peritoneal transport for the variation of the concentration of Na, due to small solute transport, UF and FWT, and for the variation of the dialysate glucose concentration during a dwell with a hypertonic solution.

The aim of this study was to assess whether the Cd of peritoneal fluids can be used to evaluate peritoneal membrane transport in PD patients with a single and immediate measurement.

MATERIALS AND METHODS

All of the PD patients attending Manzoni Hospital in Lecco, Italy, who gave their informed consent, underwent a Uni-PET. The Uni-PET integrates the double mini-PET [13] and the classic 4 h 3.86% PET and has been described in detail elsewhere [18]. Briefly, the first mini-PET was performed using 1.36% glucose and the second using 3.86% glucose: the two solutions differed only in terms of their glucose concentrations; all of the other solutes had the same concentrations. The two 1 h mini-PETs and the classic 4 h 3.86% PET were performed consecutively in the same morning.

In all cases, the overnight dwell preceding the Uni-PET was performed using a 1.36% PD solution with lactate as the buffer, which was instilled at about 11 p.m. in the evening before the test and drained at about 7 a.m., after which 2 L of fresh 1.36% glucose solution was infused over 10 min. The fresh PD fluid samples were taken from the bags at the end of the infusion and, after a dwell time of 1 h, the dialysate was collected by means of gravity for at least 20 min. This was followed by the 10 min infusion of 2 L of fresh 3.86% glucose solution, after which samples of fresh fluid and dialysate were taken as before. Once again, after a dwell time of 1 h, the 3.86% glucose dialysate was collected by means of gravity for at least 20 min, measured by weighing and then re-infused into the peritoneal cavity before further dialysate samples were taken from the bags. After a dwell time of 3 h, the dialysate was drained and collected by means of gravity for at least 20 min. Blood samples were taken at the end of re-infusion of the 3.86% glucose dialysate. The volumes of the fresh infused PD solution and the drained dialysate were measured by weighing the bags and then subtracting the weight of the empty bags; no correction was made for the differences in the specific weight of the solutions.

Plasma and dialysate creatinine, total protein and glucose concentrations were determined using a Hitachi 717 chemistry analyser (Hitachi Ltd, Tokyo, Japan), with dialysate creatinine concentration being assessed using an enzymatic method in order to eliminate the effect of the high dialysate glucose concentration. The total dialysate sodium concentration was analysed twice using an IL 943 flame photometer (Instrumentation Laboratory, Milan, Italy).

During Uni-PET, Cd was measured in dialysate. All of the Cd measurements were made using a 90XL Meter™ (Mesa Laboratories, Inc., Lakewood, CO, USA). We made all of the measurements in the laboratory aspirating the fluid into the meter at 37°C.

In addition, in order to evaluate the in vitro effect of high glucose concentrations on Cd, glucose powder was added to fresh glucose-free PD fluid in compartment C of the Trio Gambro bags until it reached the glucose concentrations used in PD (the concentrations of the other solutes remained unchanged).

Calculations

The osmotic conductance to glucose (OCG) equals local hydraulic conductivity \((L_p)\) multiplied by the membrane surface area \((S)\) of pores and the coefficient of glucose reflection \((\sigma)\) \((L_pS\sigma)\) [7, 8].

It is possible to assess \(L_pS\sigma\) \((\text{mL/min/mmHg})\) on the basis of the principle of ‘osmotic transients’ [19] as follows:

\[
\text{OCG} = L_pS\sigma = \left[ \frac{V_{3.86} - V_{1.36}}{19.3 \cdot (G_{3.86} - G_{1.36}) \cdot t} \right] \cdot 1.7
\]

where \(V_{3.86}\) and \(V_{1.36}\) are, respectively, the volumes \((\text{mL})\) of the drained dialysate with the 3.86 and 1.36% glucose solutions during the double mini-PET; 19.3 \((\text{mmHg/mmL})\) the product of absolute temperature and the gas constant at 37°C; \(G_{3.86}\) and \(G_{1.36}\) the molar glucose concentrations \((\text{mmol/L})\) of the fresh PD solutions calculated as glucose \((\text{mmol/L}) = \text{glucose (mg/dL)} / 18\); \(t\) the time of the dwell (in all of the double mini-PETs, effective dwell time was defined as the sum of the 60 min of dwell time with a full fill volume of 2 L and 50% of the time used for instillation and drainage) and 1.7 a correction factor to correct for the dilution of the glucose concentration due to residual peritoneal volumes and the differences in dialysate volumes between the 1.36 and 3.86% tests assessed after 60 min (or more) and not at the beginning of the dwell [8].

During the double mini-PETs, the results of the 3.86% mini-PET were used to calculate the FWT, as described previously [11]:

\[
\text{FWT (mL)} = \text{total UF (mL)} - \text{UFSP (mL)}
\]

During the 3.86% mini-PETs, UFSP was calculated as:

\[
\text{UFSP (mL)} = \frac{\text{Na}_R \cdot 1000}{\text{Na}_p \cdot \text{mmol/L}}
\]

where \(\text{Na}_R \cdot \text{mmol}\) was calculated as:

\[
\frac{[\text{Volume}_{\text{DialysateOut}} (L) \cdot \text{Na}_{\text{DialysateOut}} \cdot \text{mmol/L}]}{[\text{Volume}_{\text{DialysateIn}} (L) \cdot \text{Na}_{\text{DialysateIn}} \cdot \text{mmol/L}]} - \text{Na}_p \cdot \text{mmol/L}
\]

and \(\text{Na}_p\) was the ionized sodium plasma water concentration as assessed using direct ion selective electrode (Stat Profile M, Nova Biomedical Corp., Waltham, MA, USA).
Statistical analysis

The results are expressed as mean values ± 1 standard deviation (SD), together with their 95% confidence intervals (95% CIs); the asymmetrically distributed data are expressed as median values and interquartile (IQ) ranges.

Pearson’s correlation coefficient (r) was used to analyse the linear correlations between $D/P_{\text{Creat}}$ and $D/P_{\text{Na}}$ and between the dialysate Cd and glucose concentrations, $D/D_0$, $D/P_{\text{Creat}}$ and $\Delta D_{\text{Na}}$.

In order to measure the sensitivity and specificity of $D/D_0$, $D/P_{\text{Creat}}$, $\Delta D_{\text{Na}}$ and Cd after 60 min and 240 min, different cut-off values were used to discriminate the patients with or without UFF, and a conventional receiver-operating characteristic (ROC) curve was generated for all the variables [20]. The area under the curve (AUC) was calculated in order to ascertain the quality of the variables as indicators of UFF (an area of 0.5 is no better than what can be expected by chance, whereas a value of 1.0 signifies a perfect indicator). An AUC greater than 0.7 indicates statistical significance. Youden’s index [21] was used to determine the cut-off points. Probability (P) values of 0.05 or less were considered significant. All statistical analyses were made using JMP for Windows statistical software (release 4.0, SAS Institute Inc., Cary, NC, USA).

RESULTS

Sixty-nine PD patients (38 males and 31 females; median age 62.0 years, range 47.0–71.5; median PD vintage of 37.8 months, range 19.7–62.9) underwent a modified PET (Uni-PET).

Figure 1 shows the correlation between Cd and glucose concentration in vitro, and Figure 2 shows the correlation of $D/P_{\text{Creat}}$ and $D/P_{\text{Na}}$. At multiple regression analysis (data not shown), 83% of the variability of Cd at 240 min of dwell was due to the 240 min glucose and Na dialysate concentrations.

Table 1 shows some of the Uni-PET parameters.

At the end of the Uni-PET, there was a good inverse correlation between the dialysate Cd and peritoneal glucose absorption ($D/D_0$) ($r^2 = 0.62$, $P < 0.0001$), $\Delta D_{\text{Na}}$ ($r^2 = 0.62$, $P < 0.0001$) and FWT ($r^2 = 0.50$, $P < 0.0001$) and even better direct correlation between Cd and $D/P_{\text{Creat}}$ ($r^2 = 0.72$, $P < 0.0001$) (Figure 3).

Twelve of the 69 patients (17%) experienced UFF. The ROC curves of Cd after 60 min and 240 min were better than those of $D/D_0$ and $D/P_{\text{Creat}}$ at the end of the test (Figure 4). The area under the Cd ROC curve was 0.90 (95% CI 0.81–0.96), with sensitivity of 1.00 and specificity of 0.79 for a cut-off value of 11.93 mS/cm after 60 min and 0.91 (95% CI 0.81–0.96), with sensitivity of 1.00 and specificity of 0.84 for a cut-off value of 12.75 mS/cm after 240 min. None of the patients with a Cd of <11.93 mS/cm after a dwell time of 60 min or a Cd of <12.75 mS/cm after a dwell time of 240 min experienced UFF (Figure 5).

DISCUSSION

The aim of this study was to evaluate the potential usefulness of using dialysate Cd measurements to assess the function of the peritoneal membrane. Cd can be measured simply, immediately and without the need for laboratory assays.

It is known that Cd is influenced by the concentration of electrolytes (mainly Na), but the effect of the very high glucose concentrations used in PD fluids has never been assessed. Our findings indicate that the Cd of fresh PD fluid is linearly inversely related to its glucose concentration.

Dialysate Na and glucose concentrations change during the PD dwell: transport of Na is proportional to creatinine transport [17] and tends to increase at a rate that is generally inversely proportional to that of glucose, whereas glucose tends to be absorbed from the peritoneal cavity and then its concentration tends to decrease more or less quickly, depending on the characteristics of the transport class to which a patient belongs. Cd represents both glucose and Na concentrations, and it is therefore possible that a single Cd measurement can be used to assess the peritoneal membrane function.
Our findings show that the Cd correlated well with the parameters of the Uni-PET. Furthermore, they were also predictive insofar as it was possible to define Cd cut-off values capable of distinguishing patients with and without UFF, and the ROC curves of Cd were better than those of the classic Uni-PET parameters for diagnostic purposes.

In our opinion, the measurement of dialysate Cd could be a screening tool to evaluate the function of the peritoneal membrane: for example, if the dialysate Cd is <12.75 mS/cm, after 4 h of dwell, it is very likely that the transport of the peritoneal membrane is not increased, otherwise it may be useful to undertake more sophisticated tests such as PET or similar tests. In addition, the Cd dialysate may also be measured by direct connection.

Table 1. Uni-PET parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>1.36%, 60 min</th>
<th>3.86%, 60 min</th>
<th>3.86%, 240 min</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drainage time (min)</td>
<td>20.1 ± 1.2 (19.9–20.4)</td>
<td>20.4 ± 1.5 (20.0–20.7)</td>
<td>20.4 ± 1.5 (20.0–20.8)</td>
</tr>
<tr>
<td>UF (mL)</td>
<td>96 ± 165 (56–135)</td>
<td>379 (294–548)</td>
<td>696 ± 308 (622–770)</td>
</tr>
<tr>
<td>ΔDNa (mmol/L)</td>
<td>—</td>
<td>6.9 ± 3.8 (6.0–7.8)</td>
<td>5.1 ± 4.5 (4.0–6.2)</td>
</tr>
<tr>
<td>D/D0</td>
<td>—</td>
<td>0.49 ± 0.07 (0.47–0.50)</td>
<td>0.23 ± 0.06 (0.21–0.24)</td>
</tr>
<tr>
<td>D/PCreat</td>
<td>—</td>
<td>0.38 ± 0.09 (0.36–0.40)</td>
<td>0.65 ± 0.10 (0.63–0.68)</td>
</tr>
<tr>
<td>UFSP (mL)</td>
<td>—</td>
<td>247 (166–372)</td>
<td>—</td>
</tr>
<tr>
<td>FWT (mL)</td>
<td>—</td>
<td>146 ± 77 (127–164)</td>
<td>—</td>
</tr>
<tr>
<td>OCG (µL/min/mmHg)</td>
<td>—</td>
<td>3.0 ± 2.8 (2.4–3.7)</td>
<td>—</td>
</tr>
</tbody>
</table>

Mean values ± 1 SD with 95% CIs in parenthesis or median values with IQ ranges in parenthesis.

UF, ultrafiltration; ΔDNa, the difference between Na concentrations in fresh PD solution and the dialysate; D/D0, the ratio between glucose concentrations in the dialysate and in fresh PD solution; D/PCreat, the ratio between creatinine concentrations in the dialysate and in plasma; UFSP, UF through small pores; FWT, free water transport; OCG, osmotic conductance to glucose.

*After a dwell time of 60 min using a 1.36% glucose solution.

*After a dwell time of 60 min using a 3.86% glucose solution.

*After a dwell time of 240 min using a 3.86% glucose solution.

**FIGURE 3**: Relationships between measured Cd at the end of Uni-PET and D/D0, D/PCreat, ΔDNa, and FWT. Cd, ionic conductivity; D/D0, ratio between the glucose concentration in the dialysate at the end of test and in the fresh PD solution; D/PCreat, ratio between the creatinine concentration in the dialysate at the end of the test and in plasma; ΔDNa, difference between the Na concentration in the fresh PD solution and dialysate after a dwell time of 240 min; FWT, free water transport.
**FIGURE 4:** ROC curves of Cd values after dwell times of 60 min and 240 min using a 3.86% glucose solution and ROC curves of $D/D_0$ and $D/P_{Creat}$ at the end of the test. ROC, receiver-operating characteristic; Cd, ionic conductivity; $D/D_0$, ratio between glucose concentrations in the dialysate at the end of the test and in fresh PD solution; $D/P_{Creat}$, ratio between creatinine concentrations in the dialysate at the end of the test and in plasma.

**FIGURE 5:** Sensitivity and specificity of dialysate Cd after 60 min (left) and 240 min (right) of Uni-PET for cut-off values of 11.93 and 12.75 mS/cm, respectively. Cd, ionic conductivity; UFF, ultrafiltration failure.
of the drain line with the Cd meter, and this tool could also be used at home by patients.

In conclusion, measuring the Cd of the dialysate of PD patients makes it possible to evaluate, as a screening tool, the function of the peritoneal membrane without the need for a PET. Furthermore, the assessment can be made several times during the follow-up of PD patients (and, in the future, even by patients themselves in their own homes) and could indicate when changes in the peritoneal membrane function occur.

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CONFLICT OF INTEREST STATEMENT

All the authors declared no competing interests.

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