Changes in the Peritoneal Equilibration Test in Selected Chronic Peritoneal Dialysis Patients


ABSTRACT
Fifty-five patients on chronic peritoneal dialysis with two or more peritoneal equilibration tests (PET) performed between 1983 and 1992 with a mean interval of 21.9 ± 22.7 months were studied retrospectively. Repeated PET were performed when transport changes were suspected rather than routinely. According to the initial PET, there were 16 high (HI), 17 high-average (HA), 15 low-average (LA), and 7 low (LO) transporters. There was a significant decrease in the mean creatinine dialysate to plasma ratio (D/P creatinine) in the HI transporters and an increase in the LA and LO transporters. The mean dialysate to instilled glucose ratio (D/Do) significantly increased in the HI transporters. The change in both the D/P creatinine and the D/Do of an individual strongly and inversely correlated to their respective initial values. The change in D/P creatinine and D/Do were significantly and inversely correlated to each other, indicative of an actual transport change. No correlation was found between the change in transport with peritonitis episodes or frequencies. The centrifugal change of transport toward average described here may explain why low clearances or low ultrafiltration rates due to rapid transport are infrequent causes of peritoneal dialysis technique failure, and why patients who have been dialyzed for a long period are usually HA transporters.

Key Words: Transport, peritoneal membrane, peritoneal equilibration test, membrane durability, membrane stability

Since the peritoneal equilibration test (PET) was introduced by Twardowski et al. in 1987 (1), the abridged (standard) PET has been widely accepted as a useful means with which to identify the peritoneal solute transport rate and thereby tailor an individual’s peritoneal dialysis prescription (2-4). The test consists of measuring the dialysate to plasma ratio (D/P) of creatinine at 0.5, 1, 2, and 4 h and dialysate dextrose to baseline dialysate concentration ratio (D/Do). Dialysate drainage volume (DV) at 4 h is determined by completely draining the dialysate. A simplified fast PET, with only the ratios and drainage volume at 4 h measured, was later developed and accepted as a useful alternative to the original PET (5).

According to the 4-h D/P creatinine result, patients can be categorized into high, high-average, low-average, and low transporters (3, 6). Similarly, the D/Do ratio can be used in such a way. The high transporters usually have good dialysis clearances but poor ultrafiltration. Intermittent dialysis, particularly nocturnal automated, is the preferable therapy. The low transporters usually have good ultrafiltration but low small solute clearances with standard continuous ambulatory peritoneal dialysis (CAPD) (3, 7). The high-average and low-average transporters, particularly the former, usually have adequate dialysis clearances and ultrafiltration, and typical CAPD or continuous cyclic peritoneal dialysis is usually the suitable treatment mode.

The result of PET repeated within a short period was demonstrated to be very consistent (1, 8). The reproducibility of the test is important for its value in predicting the best treatment modality for patients. However, changes in the result of the test on a long-term basis are not well delineated. If the transport rate changes with time, it means that the best mode of therapy for a patient may also change.

Since the PET was first used in our center in 1983, we have accumulated a long observation interval to evaluate change in the peritoneal transport rate as indicated by the PET. In this article, we report our data from the analysis of repeated PET in our patients. It is important to stress that this study was not a prospective routine follow-up of our total pop-
ulation; the repeated PET was done in cases where change was suspected. Thus, the incidence of change could be different from a prospective study of a total population.

PATIENTS AND METHODS

All chronic peritoneal dialysis patients in our dialysis center with two or more standard PET performed with 2 L of 2.5% dextrose dialysis solution more than 1 week apart were included in this retrospective analysis. No PET included in the analysis was done within 1 mo of the completion of the peritonitis antibiotic treatment. No PET was performed fewer than 10 days after catheter insertion. The 4-h D/P glucose corrected creatinine ratio (5), the D/Do ratio, and the DV were used as the parameters for study.

Patients were categorized into the four different groups of transporters (high, high average, low average, and low) according to the D/P creatinine ratio of the initial PET, as described by Twardowski (dividing ratios, >0.81, >0.65 to 0.81, >0.50 to 0.65, and 0.50 or less, respectively (3). A change in D/P creatinine in one individual that was more than 1 SD of the initial D/P creatinine of this study population was regarded as significant.

Statistical differences between groups were analyzed by t test, χ² test, and Fisher’s exact test where appropriate. A paired t test was used to analyze changes within the same group.

RESULTS

In an unpublished prior control study, we assessed the reproducibility of 41 paired PET repeated over short intervals (fewer than 2 days); the mean coefficient of variation was 1.75 ± 1.35% (SD), and the absolute mean difference in D/P creatinine between tests was 0.024 ± 0.017.

From 1983 to November 1992, there were 55 patients who had two or more PET performed more than 1 wk apart. They represented nearly 25% of all chronic peritoneal dialysis patients over the same retrospective period. The number of PET performed on each patient ranged from two to seven (mean, 2.85). According to the initial PET, 16 patients were high transporters, 17 were high-average transporters, 15 were low-average transporters, and 7 were low transporters. The mean initial D/P creatinine was 0.687 ± 0.153. The initial mode of dialysis therapy was CAPD, except for two patients on nocturnal intermittent peritoneal dialysis (Table 1). The initial PET were performed at a mean of 5.46 ± 11.8 (SD) mo (range, 0.1 to 47.1) from the start of peritoneal dialysis, and the final PET were performed at 27.3 ± 28.1 mo (range, 1.3 to 132.7). The interval was 21.9 ± 22.7 mo (range, 0.4 to 102.2). The demographic data, the results of the initial and final PET, and the averaged daily dialysate concentration used at the time of initial and final PET of different transporters are shown in Table 1.

The mean D/P creatinine decreased and the mean D/Do increased in the initial high and high-average transporters, but they moved in opposite directions, respectively, in the low-average and low transporters. Statistically significant changes were seen in the high, low-average, and low transporters for D/P creatinine (P < 0.001) and in the high transporters for D/Do (P < 0.001). The final mean D/P creatinine was still significantly higher in the initial high transporters than the final value in the initial low transporters (P < 0.001); final means for low transporters were also significantly different from final means for high-average transporters (P < 0.02) and low-average transporters (P < 0.01). The final mean D/Do of the high transporters remained the lowest and that of the low transporters the highest, with P < 0.001 between the high and low transporters and P < 0.03 between the high-average and low transporters. There was also an increase in the DV in the high transporters and a decrease in the DV in the low transporters, but the changes were not statistically significant (Table 1). The average dialysate daily concentration used at the time of the initial PET was significantly higher in the high than in the low transporters (P < 0.01). Although there was a decrease in the dialysate concentration used in the high transporters and an increase in that used in the low-average and low transporters, the changes were not statistically significant.

The change in D/P creatinine was found to be strongly and inversely correlated with the initial D/P creatinine value (r = -0.746; P < 0.001; Figure 1). Patients with a high initial D/P creatinine had a negative change, whereas those with a low D/P creatinine had a positive change. A similar relationship was found between the change in D/Do and the initial D/Do (r = -0.844; P < 0.001; Figure 2) and between the change in DV and the initial DV (r = -0.844; P < 0.001; Figure 3). The change in D/Do correlated with the change in D/P creatinine significantly (r = -0.709; P < 0.001; Figure 4). No correlation was found between the change in DV and the change in D/P creatinine or the change in D/Do. The high transporters were found to have a significantly older age than the low transporters (P < 0.001; Table 1). A significant correlation between the D/P creatinine and the age of patient was found with the initial transporter (r = 0.371; P < 0.01; Figure 5a) but not with the final PET (Figure 5b). Similarly, the initial D/Do correlated with age in an inverse manner (r = -0.353; P < 0.01; Figure 6a), but not the final D/Do (Figure 6b).
ALL PATIENTS

Figure 1. The correlation between the change in D/P creatinine in individual patients and their corresponding initial D/P creatinine value \( (r = -0.746; P < 0.001) \).

Figure 2. The correlation between the change in D/Do in individual patients and their corresponding initial D/Do value \( (r = -0.816; P < 0.001) \).
ALL PATIENTS

Figure 3. The correlation between the change in DV in individual patients and their corresponding initial DV ($r = -0.844; P < 0.001$).

ALL PATIENTS

Figure 4. The correlation between the change in D/Do in individual patients and their corresponding change in D/P creatinine ($r = -0.709; P < 0.001$).

ALL INITIAL PETs

Figure 5. (a) The correlation between the initial D/P creatinine and the age of the patients ($r = 0.371; P < 0.01$). (b) No correlation was found between the final D/P creatinine and the age of the patients. NS, not significant.

Figure 7 shows the change in D/P creatinine of different individual patients over time. For those who had a decrease in D/P creatinine, the decrease took place in the first 18 mo; the D/P creatinine would usually rise again after 24 mo of peritoneal dialysis. Thirty-eight patients had their PET repeated within the first 18 mo of peritoneal dialysis. Among these 38 patients, a significant drop of D/P creatinine was found in the high transporters ($P < 0.001$) and a significant rise was found in the low-average ($P < 0.01$) and low transporters ($P < 0.001$; Figure 8). Fourteen patients, none of whom were low transporters, had at least one PET performed after 18 mo of peritoneal dialysis and another PET repeated after 24 mo of dialysis. The D/P creatinine increased in these three groups of transporters (Figure 9). Although the numbers in each group are too small for statistical analysis, the overall change in all 14 patients was significant. The D/P creatinine increased from $0.663 \pm 0.086$ to $0.725 \pm 0.089$ ($P < 0.01$).

Changes in transport were not related to peritonitis episodes or their frequency. All PET studies were performed at least 1 mo after any peritonitis episodes resolved. Changes in transport in each group were in
Figure 6. (a) The correlation between the initial D/Do and the age of the patients ($r = -0.353; P < 0.01$). (b) No correlation was found between the final D/Do and the age of the patients. NS, not significant.

Figure 7. D/P creatinine values of individuals in the four transport groups over time.

The same direction in patients without any peritonitis history. There were 28 patients in the study who never had peritonitis.

The change in D/P creatinine in the first 18 mo was significantly correlated with the initial D/P creatinine ($r = -0.705; P < 0.001$; Figure 10), but the change in D/P creatinine after 24 mo of peritoneal dialysis was not correlated with either the initial D/P or the first D/P creatinine after 18 mo of peritoneal dialysis.

The final transport rate status of the different initial transporters is shown in Table 2. There was a significant increase in the proportion of high-average transporters ($P < 0.03$). Only three initial high transporters, eight high-average transporters, four low-average transporters, and 1 low transporter re-
The change in D/P creatinine in 38 patients with their PET repeated within the first 18 mo of peritoneal dialysis. A statistically significant difference was reached in the high transporters (P < 0.001), the low-average transporters (P < 0.01), and the low transporters (P < 0.001). NS, not significant.

The change in D/P creatinine in 14 patients with at least one PET performed after 18 mo and another performed after 24 mo of peritoneal dialysis. No low transporters was found by this criterion. Overall mean D/P creatinine increased from 0.663 ± 0.086 to 0.725 ± 0.089 (P < 0.01).

remained in their initial categories. Most high transporters became high-average (10 of 16) or low-average (3 of 16) transporters, most low-average transporters became high-average (9 of 15) transporters, and most low transporters became low-average (4 of 7) or high-average (2 of 7) transporters. However, most high-average transporters remained in the same category (8 of 17), whereas some became high transporters and some became low-average transporters. There were 15 patients with a change of D/P creatinine of more than 1 SD (0.153) (Table 2). This significant decrease in D/P creatinine was found in four high transporters and two high-average transporters; a significant increase was found in four low transporters, four low-average transporters, and one high-average transporter. Statistical significance was reached between the high and low transporters for significant increase in D/P creatinine (P < 0.01) and low-average transporters for significant decrease (P < 0.03).
There were no statistical differences in the clinical outcome of the four groups of transporters in terms of death and transfer to other modes of replacement therapy. However, more low transporters were transplanted (P < 0.01 versus high transporters and P < 0.02 versus low-average transporters) and more low-average transporters stayed on peritoneal dialysis (P < 0.04 versus low transporters). There was no death directly related to inadequate dialysis. Ultrafiltration failure was the reason for transfer to hemodialysis in two patients, but high lymphatic absorption was documented to be the reason of ultrafiltration failure in one of them. The other patient with type-I ultrafiltration failure was an initial high-average transporter with a final D/P creatinine of 0.822. Inadequate dialysis was the cause of transfer to hemodialysis in an initial low transporter, even though his final D/P creatinine increased to 0.538.

**DISCUSSION**

Our study describes a selected population of patients who stayed on chronic peritoneal dialysis for at least 2 yr on average and had repeated PET. Transport changes in early dropouts are thus not included. Repeated PET studies, rather than routine studies, were done to assess possible changes in transport. Thus, this retrospective analysis of our clinical practice looks for transport changes in patients more likely to have had suspected changes. Further evaluations involving unselected chronic peritoneal dialysis patients are needed. Nevertheless, the pattern of change observed in different transport groups in our study is of interest.

Our data showed that the peritoneal transport rates

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**TABLE 2. The change in transport status in different initial transporters according to D/P creatinine**

<table>
<thead>
<tr>
<th>Transporters According to Initial PET</th>
<th>Final PET Transport Status</th>
<th>Change &gt; 1 SD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>High</td>
<td>High Avg</td>
</tr>
<tr>
<td>High N = 16</td>
<td>3</td>
<td>10</td>
</tr>
<tr>
<td>High avg N = 17</td>
<td>3</td>
<td>8</td>
</tr>
<tr>
<td>Low avg N = 15</td>
<td>2</td>
<td>9</td>
</tr>
<tr>
<td>Low N = 7</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Total N = 55</td>
<td>8</td>
<td>29</td>
</tr>
</tbody>
</table>

*P < 0.03 for the change in the number of high-average transporters, by χ² test; P < 0.01 for the number of patients with an increase >1 SD between high and low transporters; and P < 0.03 for the number of patients with a decrease >1 SD between high and low-average transporters, by two-sided Fisher’s exact test.

**TABLE 3. Clinical outcome of different groups of transporters**

<table>
<thead>
<tr>
<th></th>
<th>High</th>
<th>High Avg</th>
<th>Low Avg</th>
<th>Low</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total, N</td>
<td>16</td>
<td>17</td>
<td>15</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Death, N</td>
<td>7 (44%)</td>
<td>6 (35%)</td>
<td>5 (33%)</td>
<td>1 (14%)</td>
<td>NS</td>
</tr>
<tr>
<td>Change to HD, N</td>
<td>4 (25%)</td>
<td>5 (29%)</td>
<td>1 (7%)</td>
<td>2 (28%)</td>
<td>NS</td>
</tr>
<tr>
<td>Change to IPD, N</td>
<td>8 (50%)</td>
<td>4 (24%)</td>
<td>4 (27%)</td>
<td>3 (43%)</td>
<td>NS</td>
</tr>
<tr>
<td>Transplanted, N</td>
<td>0 (0%)</td>
<td>2 (12%)</td>
<td>0 (0%)</td>
<td>3 (43%)</td>
<td>—</td>
</tr>
<tr>
<td>Still on PD</td>
<td>5 (31%)</td>
<td>3 (18%)</td>
<td>9 (60%)</td>
<td>1 (14%)</td>
<td>—</td>
</tr>
</tbody>
</table>

*NS, not significant.

* Between low and high transporters, P < 0.01; between low and low-average transporters, P < 0.02.

* Between low and low-average transporters, P < 0.04 by two-tailed Fisher’s exact test.
of chronic peritoneal dialysis patients as indicated by PET are not static. They change in a fashion that has never been described before: the direction and the amplitude of change are dependent on their initial transport rate. The initial high transporters tend to have the transport rate decrease, and the low transporters tend to have the transport rate increase with time. Such migration toward the mean seems unlikely because D/P creatinine and D/Do glucose changes were inversely correlated to a high degree, suggesting that actual transport changes and the mean change of D/P creatinine in the high, low-average, and low transporters were much higher than the coefficient of variation we analyzed previously.

In a previous study, we have already noted that patients with a longer duration of peritoneal dialysis were mostly high-average transporters. Our previous hypothesis was that this was because of a natural selection process: those with high-average transport stay on peritoneal dialysis, whereas those at either extreme drop out (1). In this study, we demonstrate that this phenomenon is also the result of changes toward average transport during the course of long-term peritoneal dialysis in the outlying groups.

Increases in peritoneal transport rates with time have been observed by others (10, 11), but no change was found by some (8, 12). In all of the reported series, the change in D/P creatinine was not analyzed according to the initial value. The high and low transporters were mixed together and studied as a group. The opposite directional changes of the transport rate in the first 18 mo of peritoneal dialysis in the outlying groups discovered in our analysis may explain the absence of overall changes in average values. Changes in different directions in some individuals have been noted, despite the lack of changes in a group (1, 8, 12), but no factors related to the change, such as age or number of peritonitis episodes, could be identified. Unfortunately, the initial D/P creatinine value was not included as one of the factors studied.

Increases in transport rates were mainly reported in those series with a long follow-up (10, 11, 13). We also found that the D/P creatinine increases after the first 18 mo of peritoneal dialysis, regardless of the initial transport rate status or the initial direction of change. There have been some mechanisms proposed for this phenomenon, including an increase in peritoneal surface area and/or peritoneal permeability. Although it is unlikely that the peritoneal surface area will increase with dialysis, increases in peritoneal permeability may be explained by structural changes in the peritoneum and its vasculature (14, 15). The causes of the initial centrifugal changes in transport rate reported herein are also unknown. Could the initial high transport rates in some of the patients represent a transient reaction to catheter insertion and/or dialysate solution enhancing transport? Many initial tests were performed in the early months of peritoneal dialysis, but none fewer than 10 days after catheter insertion. Obviously, many of these patients were genuine high transporters to start with because most of their transport rates still stayed higher than the others after some time on peritoneal dialysis. The use of higher concentrations of glucose in the high transporters may play a part, but it is difficult to prove whether change relates to more hyperosmolar dialysate exposure.

No correlation of the transport rate with age in adult peritoneal dialysis patients has been previously reported. However, it has been generally accepted that the transport rate is higher in children than in adults (16). Young children are often high or high-average transporters (17). An age-related D/P creatinine level was described by Schroeder et al. (18). The D/P creatinine ratio decreased with age but did not reach a significant difference between those younger and older than 3. In this report, we found a correlation of the initial transport rate with age, whether the D/P creatinine or the D/Do is used to indicate the transport rate. However, the correlation with age disappeared with the final PET. This means that the age factor may be only applicable in the original, untouched peritoneum. As the duration of peritoneal dialysis increases, other factors may appear and the age factor no longer predominates. This may explain why our previous reports, and many other reports, did not find any age/transport rate relationship in the cross-sectional analyses with PET done at different durations of peritoneal dialysis.

Similar to findings in other reports (10), the change in transport rate did not correlate with the number of peritonitis episodes or the peritonitis rate. This does not mean that peritonitis would not affect the transport rate. It is well established that peritonitis reduces the ultrafiltration acutely by increasing the permeability of the peritoneum (19, 20). In most cases, recovery occurred within a few weeks (21). The long-term effect is not known, but peritonitis may lead to a reduction in peritoneal surface area, resulting in a reduction in transport rate or sclerosing peritonitis with a marked decrease, or sometimes marked increase, in transport rate (22, 23).
death or transfer to hemodialysis might result from a severe episode of peritonitis, the change in transport rate that might have occurred in these patients would never have a chance to be documented.

In conclusion, the peritoneal transport of peritoneal dialysis patients as indicated by repeated PET is not always static. In our select group of patients with clinically suspected changes in transport, the transport rate tended to decrease in the high transporters and increase in the low transporters. This phenomenon may be beneficial to high and low transporters by increasing ultrafiltration and increasing solute clearances, respectively.

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REFERENCES