Personalization of Automated Peritoneal Dialysis Treatment Using a Computer Modeling System

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The use of almost standardized dialysis programs—and the absence of any adjustment over time in these programs—to match the progressive decline in residual kidney function, in addition to the reduction in peritoneal depuration because of the frequency of peritonitis and the use of solutions containing high glucose concentrations—often leads to technique drop-out and transfer to hemodialysis.

Our study enrolled 15 clinically stable patients (13 white men, 2 white women; average age: 67.3 ± 12.99 years; average dialysis vintage: 32.25 ± 25.10 months) who had been on automated peritoneal dialysis treatment with a standard treatment profile for at least 6 months (dwell time per cycle and solutions fixed at various glucose concentrations in all exchanges). After a peritoneal equilibration test had been performed and clearances (peritoneal and renal) were measured, the dialysis program was modified, individualizing it to the patient’s peritoneal membrane transport by the Twardowski system of classification and taking into account the patient’s residual diuresis and need for ultrafiltration. The change was implemented using the Patient on Line software created by Fresenius Medical Care (Bad Homburg, Germany).

After a month of personalized dialysis treatment, weekly peritoneal Kt/V in the study group increased significantly (to 1.47 ± 0.61 from 1.02 ± 0.37, p = 0.001); no difference in renal Kt/V was observed. Total Kt/V reached levels of optimum dialysis adequacy (to 2.21 ± 0.28 from 1.62 ± 0.33, p = 0.0001). Weekly peritoneal creatinine clearance also increased to 32.86 ± 16.94 L/1.73 m² from 22.27 ± 9.16 L/1.73 m² (p = 0.005), with renal creatinine clearance essentially stable, and total weekly clearance increasing to 67.58 ± 14.52 L/1.73 m² from 53.51 ± 16.86 L/1.73 m² (p < 0.0001).

The dialysis adequacy improvements obtained involved no statistically significant differences in the total infused volume of dialysis solution, ultrafiltration, or the duration of dialysis treatment. It should also be noted that no changes in residual diuresis occurred.

Key words
Automated peritoneal dialysis prescription, dialysis adequacy, mathematical modeling, glucose concentration

Introduction
Dialysis treatment is aimed at normalizing the metabolic imbalances caused by uremia. Ideally, adequate dialysis should lead to regression of all disorders of the uremic state and should allow the patient to gain a life expectancy and quality of life the same as that for a nonuremic subject. Adequate dialysis is currently considered to be around one twentieth of the glomerular filtrate volume [a weekly creatinine clearance (wCCr) of 60 L corresponds to 6 mL/min], which indicates that substitution of kidney function is only partial. Moreover, certain components of kidney function, such as secretion and tubular reabsorption, and degradation and synthesis of hormones (renin, erythropoietin, vitamin D), are not substituted by dialysis.

If, therefore, dialysis and its associated treatments can only partly substitute for kidney function, it is difficult to be able to aim at clinical and social rehabilitation of uremic patients. It is the nephrologist’s aim to determine the dialysis dose that will minimize the difference in survival rate between uremic and nonuremic patients, or better still, to identify the “optimum dose” beyond which no further benefits are anticipated for the patient (1). Moreover, the use of almost standardized dialysis programs—and the absence of any adjustment over time in these program
to match the progressive decline in residual kidney function, in addition to the reduction in peritoneal depuration because of the frequency of peritonitis and the use of solutions containing high glucose concentrations—often leads to technique drop-out and transfer to hemodialysis (2).

The availability of new cyclers and management software for patients on automated peritoneal dialysis (APD) allows cycles to be individually differentiated for dwell time, for load and drainage volumes, and for a reduced glucose load. Considering that peritoneal transport capacity varies, it is possible to personalize the final treatment to improve dialysis adequacy or to maintain it by reducing the duration and volume of the total load per session and by using solutions containing lower glucose concentrations, thereby prolonging survival of the technique itself.

Automated peritoneal dialysis is characterized by its ability to manage a high number of exchanges with dwell times depending on the total duration of the session. However, changes in peritoneal permeability and loss of residual kidney function make adjustments in prescription necessary over time. Such adjustments are now facilitated by the availability of new cyclers and management software, which enable dwell times and load and drainage volumes to be varied by the individual cycle.

Aim of the present study

On the basis of the patient’s peritoneal permeability and energy balance, it is possible to increase dialysis adequacy and also reduce the glucose load. The aim of the present study was to ascertain, according to the various peritoneal transport capacities, whether it is possible to obtain an improvement in dialysis adequacy for patients or to maintain dialysis that is already at an optimum level. A second objective was to obtain the aforesaid improvement without significantly increasing either the APD duration or the dialysate volume, and without the use of solutions with high glucose concentrations.

Methods

The study was performed at the Nephrology and Dialysis Unit of the Treviglio Hospital (peritoneal dialysis unit). The study enrolled 15 clinically stable patients (13 white men, 2 white women), whose average age was 67.3 years (± 12.99 years) and whose average dialysis vintage was 32.25 months (± 25.10 months).

The causes of chronic renal insufficiency with uremia in these patients were diabetic nephropathy \((n = 4)\), membranous nephropathy \((n = 2)\), mesangial deposits in immunoglobulin A nephropathy \((n = 2)\), polycystic kidney disease \((n = 1)\), and nephropathy not diagnosed by biopsy \((n = 6)\).

With regard to comorbidity, 13 patients presented with arterial hypertension; 5, with type 2 diabetes mellitus; 5, with ischemic cardiopathy; 4, with ischemic encephalopathy; 4, with chronic obstructive bronchopneumopathy; 3, with dilated cardiomyopathy; 3, with permanent atrial fibrillation; and 2, with chronic liver disease.

The patients had all been on APD treatment, with a standard treatment profile, for at least 6 months (dwell time per cycle and solutions fixed at various glucose concentrations in all exchanges).

As these patients presented with the need for revision of their dialysis prescription because of indications of non-optimal depuration, sudden loss of ultrafiltration, and loss of residual kidney function or routine control, re-assessment of treatment was suggested as provided for by our center.

After peritoneal equilibration tests were performed, and clearances (peritoneal and renal) were measured, the dialysis program was individually modified according to each patient’s peritoneal membrane transport characteristics, using the Twardowski system of classification (2 patients were high transporters; 12, high-average; and 1, low-average) and taking into account the amount of residual diuresis and the patient’s need for ultrafiltration.

The new prescriptions were implemented using the Patient on Line software created by Fresenius Medical Care (Bad Homburg, Germany). The Patient on Line software, through its modeling system, enables a dialysis prescription to be personalized to the patient’s clinical requirements—that is, the program suggests the duration of dialysis exchanges, the amount of dialysate infused and drained, and the glucose concentrations of the solutions for each individual cycle. A different solution may also be infused in 1 or more daytime exchanges. All prescribed personalized treatments were processed using the Patient on Line software, which assesses changes in peritoneal dialysis (PD) adequacy data, starting from the adequacy data measured by the patient.

After a month of personalized dialysis treatment, each patient was assessed for weekly \(\text{Kt/V (peritoneal,}

\[\text{Kt/V)}\]
renal, total), wCCr (peritoneal, renal, total), normalized protein catabolic rate, total volume of dialysate infused, tidal volume, total treatment duration, type of dialysis solution, residual diuresis, indicators of nutrition (serum albumin, total serum protein), anthropometric indicators [body weight, body mass index (BMI), body surface area (BSA), urea volume of distribution (VSA)], creatinine, urea, calcium, serum phosphorus, blood pressure, heart rate, serum hemoglobin, and treatment.

The dialysis adequacy data were analyzed using the Patient on Line software and Microsoft Excel software (Microsoft Corporation, Redmond, WA, U.S.A.). The statistical analysis used the Student t-test (significance set at \( p < 0.05 \)) with the trend line expressed as an equation of the interpolating curve and the relative value of the coefficient \( (R^2) \).

**Results**

All enrolled patients concluded the study without experiencing any adverse events such as mortality, hospitalization, peritonitis, or complications related to the dialysis technique. After a month of personalized dialysis treatment, no statistically significant differences were observed in terms of blood pressure, heart rate, body weight, BMI, BSA, or VSA; no changes had to be applied to the diuretic antihypertensive treatment for calcium and phosphorous balance; and plasma hemoglobin levels and administration of erythropoietin were also unchanged (Table I).

The most notable data were those regarding Kt/V and weekly peritoneal clearances. The weekly peritoneal Kt/V increased significantly (to 1.47 ± 0.61 from 1.02 ± 0.37, \( p = 0.001 \)); the renal Kt/V was unchanged (Figure 1). The total Kt/V reached levels of optimum dialysis adequacy (to 2.21 ± 0.28 from 1.62 ± 0.33, \( p = 0.0001 \), Figure 2).

The peritoneal wCCr also increased to 32.86 ± 16.94 L/1.73 m\(^2\) from 22.27 ± 9.16 L/1.73 m\(^2\) \( (p = 0.005) \), with renal wCCr essentially stable, and total weekly clearance increasing to 67.58 ± 14.52 L/1.73 m\(^2\) from 53.51 ± 16.86 L/1.73 m\(^2\) \( (p < 0.0001) \), Figures 3 and 4).

The improvements obtained in terms of dialysis adequacy involved no statistically significant differences in total infused volume of dialysis solution, ultrafiltration, or duration of dialysis treatment. Tidal volume showed a mild but significant increase. It should also be noted that no changes in residual diuresis occurred (Table II).

In a supplementary analysis, the increases in Kt/V and peritoneal wCCr were observed to most likely relate to an increase in the dialysate volume (in our case, an increase in tidal volume may be considered) compared with total treatment time (Figure 5).

In terms of prescription, the type of dialysis solution used is important (Figure 6). No 4.25% glucose solution was used in the personalized prescriptions, and the use of 2.5% solution was also reduced from 23% to 2% in favor of isotonic solution (97%).

Among the indicators of adequacy and nutrition, a significant increase was observed in the normalized protein catabolic rate (to 1.21 ± 0.22 g/kg from 0.82 ± 0.17 g/kg daily, \( p < 0.01 \)). Significant declines were also recorded in serum urea (to 145.76 ± 36.66 mg/dL from 164.80 ± 37.90 mg/dL, \( p < 0.01 \)), creatinine (to 10.05 ± 2.24 mg/dL from 11.15 ± 2.53 mg/dL,

**Table I** Biochemical and anthropometric parameters and pharmacologic therapy for the study patients at baseline and after 1 month of personalized automated peritoneal dialysis treatment

<table>
<thead>
<tr>
<th>Parameter</th>
<th>At baseline</th>
<th>At 1 month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (kg)</td>
<td>66.45±10.13</td>
<td>66.20±10.35</td>
</tr>
<tr>
<td>Distribution volume of urea (L)</td>
<td>36.02±4.88</td>
<td>35.95±4.92</td>
</tr>
<tr>
<td>Body surface area (m(^2))</td>
<td>1.76±0.16</td>
<td>1.76±0.15</td>
</tr>
<tr>
<td>Body mass index (kg/m(^2))</td>
<td>23.4±2.90</td>
<td>23.03±2.92</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>142.00±16.12</td>
<td>136.67±15.66</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>77.67±7.99</td>
<td>73.67±10.43</td>
</tr>
<tr>
<td>Heart rate (bpm)</td>
<td>76.00±10.95</td>
<td>75.60±4.55</td>
</tr>
<tr>
<td>Hemoglobin (g/dL)</td>
<td>11.79±1.18</td>
<td>11.7±1.11</td>
</tr>
<tr>
<td>Albumin (g/dL)</td>
<td>3.52±0.51</td>
<td>3.63±0.50</td>
</tr>
<tr>
<td>Treatment</td>
<td>Unchanged</td>
<td>Unchanged</td>
</tr>
</tbody>
</table>
A personalized dialysis program to be created. Personalized treatment replaces empiric and standardized prescription, with the personal prescription programmed using computer simulation; the resulting prescription is based on the characteristics of peritoneal transport, anthropometrics, and residual kidney function, and is also adjusted to meet the patient’s social requirements.

As has been described in the literature (3), maintenance of the same dialysis prescription over

\[ p < 0.01 \], and phosphorus (to 1.65 ± 0.27 mmol/L from 1.89 ± 0.46 mmol/L, \( p < 0.01 \)).

No statistically significant changes were observed for albumin, total protein, or plasma calcium.

**Discussion**

This study was planned with the objective of using software in clinical practice for PD prescription, which not only allows for the processing of laboratory data to evaluate adequacy indicators, but which also allows for a personalized dialysis program to be created. Personalized treatment replaces empiric and standardized prescription, with the personal prescription programmed using computer simulation; the resulting prescription is based on the characteristics of peritoneal transport, anthropometrics, and residual kidney function, and is also adjusted to meet the patient’s social requirements.

As has been described in the literature (3), maintenance of the same dialysis prescription over
TABLE II  Total volumes, tidal volumes, treatment times, ultrafiltration, and residual diuresis for the study patients at baseline and after 1 month of personalized automated peritoneal dialysis treatment

<table>
<thead>
<tr>
<th>Parameter</th>
<th>At baseline</th>
<th>At 1 month</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily infusion volume (mL)</td>
<td>8011.87±2277.88</td>
<td>9963.93±3019.59</td>
<td>NS</td>
</tr>
<tr>
<td>Daily treatment time (minutes)</td>
<td>577±120.54</td>
<td>599.07±234.14</td>
<td>NS</td>
</tr>
<tr>
<td>Daily ultrafiltration (mL)</td>
<td>614±404.75</td>
<td>830.47±367.98</td>
<td>NS</td>
</tr>
<tr>
<td>Daily tidal volume (mL)</td>
<td>1076.66±167.82</td>
<td>1186.67±180.73</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Daily residual diuresis (mL)</td>
<td>986±550.12</td>
<td>999.1±578.03</td>
<td>NS</td>
</tr>
</tbody>
</table>

NS = nonsignificant.

FIGURE 5  Correlation between infused volume, peritoneal clearances, and peritoneal Kt/V in patients on personalized automated peritoneal dialysis treatment.

time is known to correlate with reduced dialysis efficiency, increased technique drop-out, and increased morbidity. Supported by that information, we revised the dialysis programs of the study patients. The revision was also motivated by depuration deficit, sudden reduction in residual diuresis or ultrafiltration, and (not least) by changes in lifestyle habits. Dialysis inadequacy was identified by peritoneal equilibration test results for peritoneal clearance and Kt/V, for the reasons already mentioned. Based on those data, use of the Patient on Line software allowed us to create new prescriptions that personalized the duration and total volume of treatment for each patient, and that also individualized the glucose concentrations, dwell time, volume of infusion, and tidal volume for each individual cycle. For example, a patient classified as a low transporter with an ultrafiltration deficit was able to be maintained on an efficient automated routine that included short dwell-time cycles (for example, 15 minutes) to make use of the maximum gradient of the ultrafiltration curve, together with prolonged dwell-time cycles (for example, 120 minutes) to increase the diffusion of small- and medium-sized molecules.

The new programs formulated using this modeling were used in clinical practice for 1 month, after which dialysis efficiency indicators were verified. After only slight changes in times and infusion volumes, the patients showed statistically significant increases in peritoneal wCCr (to 32.86
we observed that the use of 2.5% and 4.25% solutions dramatically decreased. At the same time, to promote ultrafiltration, short-dwell exchanges of isotonic solution or daytime exchanges of polyglucose were used. Notably, the reduced concentrations of the osmotic agent did not cause a decrease, but rather showed an increase in the average volume of ultrafiltrate (to 830.47 ± 367.98 mL from 614 ± 404.75 mL), although this difference was not statistically significant. At the same time, a trend toward improved Kt/V and peritoneal wCCr in relation to the increase in dialysate volume was observed. Although insignificant, this improvement in dialysis adequacy indicators would appear to be more conclusive in terms of duration of treatment. But because no data relating to this observation are currently available in the literature, further studies are necessary.

In addition—and given that adequacy of the dialysis dose is only one factor in a wider concept of clinical adequacy—it seems only right to state that our patients were stable in terms of hydrosaline homeostasis and of calcium, phosphorus, and blood pressure values. The insignificant changes observed in terms of blood pressure, heart rate, BMI, BSA, and VSA can be attributed to the short duration of the study. Personalization of treatment has allowed patients to reach the dialysis depuration targets that are, in guidelines, considered to be optimal. That objective was reached without substantial changes in infusion volumes or increases in treatment times, but only with adaptation of the prescription to the patient’s peritoneal membrane transport characteristics and with preservation of the patient’s social requirements. Personalization also allowed for a reduction in the use of solutions with high glucose concentrations, thereby reducing the damage caused by glucose degradation products and by solution hyperosmolarity.

Conclusions
Although the sample was relatively small (15 patients), we can conclude from our study that treatment using a personalized prescription should be researched to determine the optimum dialysis adequacy indicators in relation to peritoneal membrane characteristics and with preservation of the patient’s social requirements. Personalization also allowed for a reduction in the use of solutions with high glucose concentrations, thereby reducing the damage caused by glucose degradation products and by solution hyperosmolarity.
residual kidney function and with the reduction in peritoneal depuration because of recurrent peritonitis and the use of solutions containing high glucose concentrations, allows for the dialyzing function of the peritoneal biologic filter to be maintained, decreasing technique drop-out.

Disclosures
The authors have no financial conflicts of interest or relationships with any pharmaceutical companies or other entities to declare.

References

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