

## Influence of pH-Neutral Peritoneal Dialysis Solution

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*We evaluated the influence of a neutral peritoneal dialysis solution (PDS) on the peritoneum.*

*The subjects were 10° stable PD patients using conventional PDS. We substituted pH-neutral PDS (PD Solita°A: Shimizu Medical, Tokyo, Japan) for conventional PDS (Gambrosol°A: Shimizu Medical). Effluent from 4-hour dwells was collected, and the appearance rate of cancer antigen°125 (CA125-AR) was calculated using the method of Pannekeet et al and corrected to body surface area. The dialysate-to-plasma creatinine (D/P°Cr) was obtained, and personal dialysis capacity (PDC) was evaluated at 3-month intervals.*

*Mean daily ultrafiltration volumes did not significantly change when pH-neutral PDS was used. The mean CA125-AR obtained 1° month after substitution was twice as high as that before substitution ( $139.2 \pm 47.3$  U/min/1.73° m<sup>2</sup> before substitution vs.  $286 \pm 126.2$  U/min/1.73° m<sup>2</sup> 1° month later). However, mean values of CA125-AR were maintained at higher levels and did not significantly vary for 7° months after PD fluid substitution. When the change in CA125-AR ( $\Delta$ CA125-AR) was calculated as the ratio of the CA125-AR value before substitution to that after substitution at the respective measurement points,  $\Delta$ CA125-AR negatively correlated with D/P°Cr. However, none of %° area, %° absorption, or %° plasma loss significantly correlated with the  $\Delta$ CA125-AR obtained 6° months later.*

*Although mesothelial cell viability may increase with the use of pH-neutral PDS, the level of the increase may differ depending on the severity of peritoneal damage. In addition, the use of a neutral PD fluid did not improve the endothelial cell system. In the future, development of a novel osmotic pressure-regulating substance substituting for glucose is essential to the development of PD fluids with higher biocompatibility.*

### Key words

Neutral peritoneal dialysis solution, CA125, viability

### Introduction

Conventional peritoneal dialysis solutions (PDSs) have low pH, high glucose concentrations, and high osmolality. Long-term PD using conventional PDS therefore damages the peritoneum, probably resulting in the development of encapsulating peritoneal sclerosis. In particular, glucose degradation products (GDPs) produce advanced glycation end-products (AGEs), and precipitation of AGEs in the peritoneum enhances the development of peritoneal fibrosis and sclerosis. A neutral PDS with fewer GDPs would therefore be expected to do less severe damage to the peritoneum.

In the present study, we evaluated the influence of a neutral PDS on the peritoneum, based on the appearance rate of cancer antigen°125 (CA125-AR) and these peritoneal permeability parameters: personal dialysis capacity (PDC) and dialysate-to-plasma creatinine (D/P°Cr) levels.

### Patients and methods

The subjects were 10° patients (5° men, 5° women) undergoing PD using a conventional PDS (Gambrosol°A: Shimizu Medical, Tokyo, Japan). The mean age of the patients was  $51.6 \pm 14$ ° years (range: 36—72° years), and the duration of PD was  $40.8 \pm 14.8$ ° months (range:  $13.7 \pm 61.4$ ° months).

We substituted pH-neutral PDS (PD Solita°A: Shimizu Medical) for the conventional PDS, and measured the total effluent volume by collecting the PD effluent once each month after a 4-hour dwell. The CA125-AR was then calculated using the method proposed by Pannekeet *et al*, based on CA125 levels in the effluent measured by the radioimmunologic method [(RIA) Centocor Diagnostics, Malvern, PA, U.S.A.], followed by correction by body surface area. In addition, D/P°Cr was obtained based on creatinine levels in the effluent and serum creatinine levels ob-

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tained after completion of drainage. The PDC was evaluated at 3-month intervals.

### Results

Before substitution of pH-neutral PDS for conventional PDS, mean values of PDC parameters and CA125-AR were as follows: % area,  $107.6\% \pm 42.6\%$  (range:  $67.6\% - 209.4\%$ ); % absorption,  $99.3\% \pm 30.8\%$  (range:  $66\% - 216\%$ ); % plasma loss,  $106.9\% \pm 54.6\%$  (range:  $42\% - 170\%$ ); D/P<sup>Cr</sup>  $0.66 \pm 0.16$  (range:  $0.44 - 0.93$ ); and CA125-AR,  $139.2 \pm 47.3$  U/min/1.73 m<sup>2</sup> (range:  $67.6 - 209.4$  U/min/1.73 m<sup>2</sup>).

Mean daily ultrafiltration volumes did not significantly change after substitution of pH-neutral PDS for conventional PDS ( $545 \pm 243$  mL before substitution vs.  $561.1 \pm 96.7$  mL 1 month later,  $540 \pm 198.1$  mL 5 months later, and  $623.3 \pm 295.6$  mL 7 months later). The mean CA125-AR obtained 1 month after substitution was twice as high as that before substitution ( $139.2 \pm 47.3$  U/min/1.73 m<sup>2</sup> before substitution vs.  $286 \pm 126.2$  U/min/1.73 m<sup>2</sup> 1 month later). However, mean values of CA125-AR were maintained at higher levels and did not significantly vary for 7 months after PDS substitution (Figure 1).

In one patient (with increased peritoneal permeability), the mean CA125-AR increased slightly immediately after substitution, but decreased 6 months later. In Patient 10, in whom pH-neutral PDS was substituted for conventional PDS 13 months after the in-

roduction of PD, mean values of CA125-AR did not significantly vary for 7 months after PDS substitution. In two patients, pH-neutral PDS substituted for conventional PDS was again changed to conventional PDS. As a result, mean values of CA125-AR increased to  $430.5$  U/min/1.73 m<sup>2</sup> from  $254.1$  U/min/1.73 m<sup>2</sup> after the initial substitution of pH-neutral PDS for conventional PDS, and decreased again to  $125.1$  U/min/1.73 m<sup>2</sup> when conventional PDS was substituted for pH-neutral PDS.

Changes in peritoneal permeability after substitution of pH-neutral PDS for conventional PDS were evaluated based on D/P<sup>Cr</sup> and PDC parameters (% area, % absorption, and % plasma loss). However, mean values of D/P<sup>Cr</sup> and PDC parameters did not significantly change 3 months and 6 months after substitution of pH-neutral PDS. When the change in CA125-AR ( $\Delta$ CA125-AR) was calculated as the ratio of CA125-AR value before substitution to the value after substitution at the respective measurement points,  $\Delta$ CA125-AR obtained 6 months later negatively correlated with D/P<sup>Cr</sup>. However, none of % area, % absorption, and % plasma loss significantly correlated with the  $\Delta$ CA125-AR obtained 6 months later.

### Discussion and conclusion

Compared to conventional PDS, pH-neutral PDS was reported to improve mesothelial cell viability (1) and macrophage function (2), and to inhibit AGE production owing to decreased GDP levels (3). However, neutral PDS did not show any apparent tendency with regard to improvement in peritoneal permeability and ultrafiltration volume. In the present study, neither peritoneal permeability nor ultrafiltration volume improved even after substitution of pH-neutral PDS for conventional PDS.

In our patients, mean values of CA125-AR increased significantly after substitution of pH-neutral PDS, and that tendency was maintained between 1 month and 7 months. Rippe *et al* (1) and Jones *et al* (2) reported that CA125 levels increased after substitution of pH-neutral PDS for conventional PDS. Furthermore, a crossover study (3) reported that CA125 levels increased after substitution of pH-neutral PDS for conventional PDS, and that CA125 levels decreased again after secondary substitution of conventional PDS for pH-neutral PDS. Those findings were similar to ours (Figure 2).

CA125AR (U/min/1.73 m<sup>2</sup>)

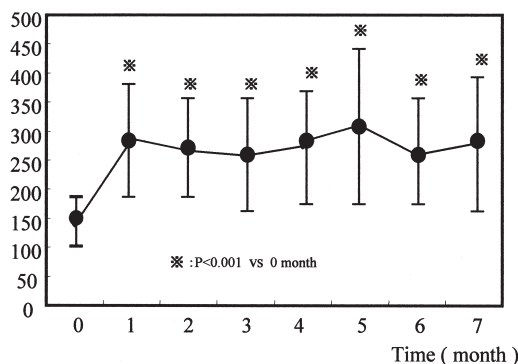


FIGURE 1 Changes in the appearance rate of cancer antigen 125 (CA125-AR) using pH-neutral peritoneal dialysis solution. At all measurement points, CA125-AR increased remarkably ( $p < 0.001$ ).

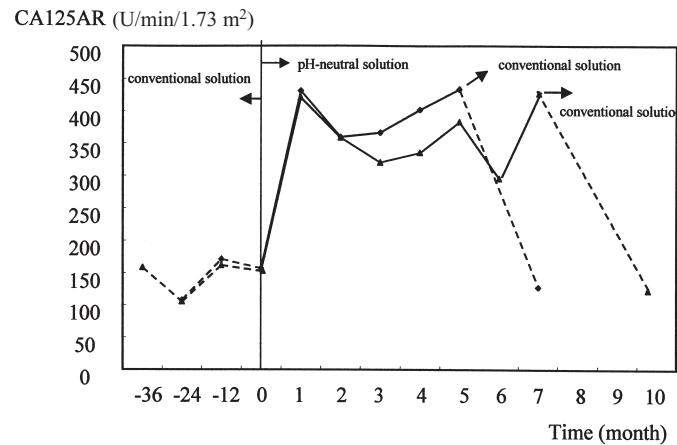


FIGURE 2 The pH-neutral peritoneal dialysis solution substituted for conventional PD solution was again changed to conventional solution. The appearance rate of cancer antigen<sup>125</sup> (CA125-AR), which increased with the use of pH-neutral solution, decreased with the use of conventional solution.

Because CA125 is produced by mesothelial cells, it may be a useful index for evaluating the mass of mesothelial cells in PD patients (4). However, the mass of mesothelial cells has been reported to decrease or not to be influenced with duration of PD (5). Moreover, other studies reported that some PD patients showed decreased CA125 levels from the early stage after introduction of PD (4). We encountered a PD patient in whom CA125-AR increased from the second week after substitution of the neutral PDS for the acidic PDS (Data not shown). Because mesothelial cells are regenerated at approximately 4-week intervals, it is doubtful whether such increases in CA125-AR reflect mesothelial cell proliferation. It was previously reported that CA125 production occurred during the G1 stage in cultured ovarian cancer cells (6). Therefore, CA125 production may similarly occur during G1 even in peritoneal mesothelial cells. Based on those findings, rapid increases in CA125 levels immediately after substitution of pH-neutral PDS for conventional PDS, and decreases in CA125 levels after secondary substitution of conventional PDS for pH-neutral PDS, may reflect changes in mesothelial cell viability. However, CA125-AR was slightly increased in PD patients with decreased peritoneal functions even when pH-neutral PDS was substituted for conventional PDS. That observation might be because the D/P<sup>o</sup>Cr obtained before substitution of pH-neutral PDS for conventional PDS was negatively

correlated with  $\Delta$ CA125-AR obtained 6 months after PDS substitution (Figure<sup>3</sup>). However, CA125-AR did not significantly change in 1<sup>st</sup> patient in whom PD had been recently initiated, even when pH-neutral PDS was substituted for conventional PDS, probably because peritoneal permeability was not increased and mesothelial cells were only slightly damaged. However, long-term follow-up is needed, because CA125-AR always remained at a lower level. Although mesothelial cell viability was increased after substitution of pH-neutral PDS for conventional PDS,

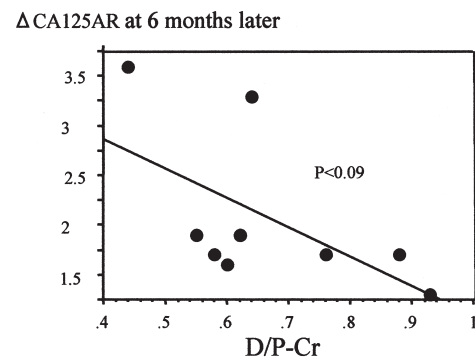


FIGURE 3 Relationship between change in the appearance rate of cancer antigen<sup>125</sup> ( $\Delta$ CA125-AR) and dialysate-to-plasma creatinine (D/P<sup>o</sup>Cr) 6 months later. As with  $\Delta$ CA125-AR, a negative trend of D/P<sup>o</sup>Cr was seen ( $p < 0.09$ ).

the level of increase might depend on the severity of peritoneal damage.

With regard to peritoneal permeability, none of %°area, %°absorption, or %°plasma loss changed significantly even after substitution of pH-neutral PD fluid for conventional PDS. Many previous studies reported no changes in peritoneal function even after substitution of pH-neutral PDS for conventional PDS (1,7). The GDPs contained in PDS produce AGEs (3,8), and AGE precipitation in the peritoneal capillaries accelerates microvascularization, thus increasing peritoneal permeability and enhancing the development of fibrosis. However, it takes a long time to regenerate damaged mesothelial cells even when pH-neutral PDS with fewer GDPs is substituted for conventional PDS.

The development of a two-bag system facilitated the use of pH-neutral PDS with higher biocompatibility as compared with conventional PDS. Although mesothelial cell viability was increased after substitution of pH-neutral PDS for conventional PDS, the level of the increase might differ depending on the severity of the peritoneal damage (8). In addition, the use of pH-neutral PDS did not improve the endothelial cell system. In the future, the development of a novel osmotic pressure—regulating substance substituting for glucose is essential to the development of PDS with higher biocompatibility.

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## Compliance in Automated Peritoneal Dialysis

*In peritoneal dialysis (PD), compliance with the dialytic prescription is an important element in achieving adequate dialysis. Using the questionnaire or inventory method, a rate of noncompliance between 10% and 20% has been reported for automated peritoneal dialysis (APD). The recent introduction of APD equipment capable of recording dialytic treatments (DTs) means that compliance can be assessed more precisely.*

*In the present study, the PDLINK software program (Baxter Healthcare Corporation, Deerfield, IL, U.S.A.) was used to retrospectively analyze 3 consecutive months of DTs in 19 APD patients (15 men, 4 women; age:  $67.9 \pm 10.2$  years; duration of PD:  $36.3 \pm 30.0$  months) who were treated with the HomeChoice Pro [HCpro (Baxter Healthcare Corporation, Deerfield, IL, U.S.A.)]. In 12 patients (63%), the treatment was self-administered; for the other 7 patients (37%), treatment was handled by a partner (spouse: 5; family member: 2).*

*Of 1673 recorded DTs, 20 (1.2%) were not performed. In the period taken into consideration (90 consecutive days), 9 patients underwent all the prescribed sessions, 4 patients missed 1 session, 3 patients missed 2 sessions, 2 patients missed 3 sessions, and 1 patient missed 4 sessions. No irregularities were observed in relation to the prescribed volumes, and session length was 60—120 minutes shorter in only 0.12% of the recorded sessions.*

*In conclusion, the HCpro system proved effective in assessing compliance. In our experience, noncompliance occurred in a lower percentage of cases than has previously been reported, notwithstanding the present method's greater sensitivity and lesser specificity.*

### Key words

Compliance, automated peritoneal dialysis, telemedicine

### Introduction

In peritoneal dialysis (PD), compliance with the dialytic prescription is important in achieving adequate dialysis. Several different methods of assessing compliance have been proposed, such as calculating the ratio between creatinine excreted and produced (1—5), the inventory method (6,7), and the questionnaire method (8,9). In automated peritoneal dialysis (APD), using the inventory method (6), which consists of calculating the association between prescribed and consumed material (assessed by two home visits, one approximately 1 month after the other), it has been found that 20% of patients may consume less than the prescribed quantity of material (by 10% or more). The questionnaire method, applied in the U.S. Renal Data System (USRDS) study of 1997 (9), consists of assessing, through an interview with the patient, the number of APD sessions missed during the last 2 weeks. That method has indicated that 10.8% of patients missed at least 1 session. However, though those methods may be highly specific, they are lacking in sensitivity. With the inventory, a low consumption can be concealed by eliminating material, and with the questionnaire, behavior that is perceived as incorrect may not be declared.

The present study aimed to determine dialytic compliance in APD with precision using the HomeChoice Pro system [HCpro (Baxter Healthcare Corporation, Deerfield, IL, U.S.A.)], with which dialytic sessions can be recorded.

### Patients and methods

We carried out a retrospective examination of all patients being treated by APD at our center between March and September 2001. We excluded from the study patients who have been in APD for less than 4 months, patients whose dialytic treatment had been performed by nurses from the center, and patients whose dialytic program envisaged 3—4 sessions per week. The remaining patients numbered 19 (15 men, 4 women). Their average age was  $67.9 \pm 10.2$  years, and they had been on PD for  $36.3 \pm 30$  months and on APD for  $27.3 \pm 22$  months. Table I shows the types

TABLE I Parameters of the dialytic prescriptions of the study patients

PD type	Patients (n)	Sessions/week	Partner (n) <sup>a</sup>	Hours/night <sup>b</sup>	Fill vol	Night vol	Day vol 1	Day vol 2
NTPD	1	6	0	9	2300	11500		
CCPD-1/NTPD-1	12	7	6	9.5±0.5	2350±294	12576±2175	1550±355	
CCPD-2/NTPD-2	6	7	1	9.2±0.4	2417±214	12202±1186	1800±253	1933±216

<sup>a</sup> Patients whose dialytic treatment was performed by a partner.

<sup>b</sup> Length of night sessions.

PD°= peritoneal dialysis; vol°= volume; NTPD°= nightly tidal peritoneal dialysis; CCPD°= continuous cycling peritoneal dialysis with one (-1) or two (-2) daytime exchanges; NTPD°= nightly tidal peritoneal dialysis with one (-1) or two (-2) daytime exchanges.

of treatment performed by the patients during the period of observation.

In 63% of the patients (Group°A; 12°patients; average age: 64.1±8.2°years), the dialytic treatment was self-administered, and in 37% (Group°B; 7°patients; average age: 74.4±10.4°years,  $p < 0.05$ ), treatment was handled by the spouse (26%) or another member of the family (11%). Only 2°patients were employed. No episodes of peritonitis were seen during the period, and only 1°patient was hospitalized (for 6°days).

All of the patients used the HCpro for APD treatment. The HCpro system records on cards all the data relating to the dialytic sessions. The data can be transferred to the center's computer by modem or manual download, and can then be read and analyzed using the PDLINK software program (Baxter Healthcare Corporation, Deerfield, IL, U.S.A.).

We retrospectively analyzed the records relating to the last consecutive 90°days of APD, comparing the dialytic prescription with the number of treatments recorded, their lengths, and their volumes. We also compared the results of the analysis to what the patients had themselves entered on their dialysis cards.

## Results

The number of treatments recorded was 1673.

### Number of sessions performed versus prescribed number

The difference between the number of sessions prescribed and recorded was 20 (1.2%). For 9°patients, the number of sessions recorded corresponded with the prescribed number. Four patients missed 1°session, three missed 2°sessions, two missed 3°sessions, and just one patient missed 4°sessions. In Group°A, 11 sessions were missed by 4°patients, and in Group°B, 9°sessions were missed by 6°patients. On the other hand, the cards completed by the patients showed a total of

only 6°missed sessions (5 in Group°A and 1 in Group°B; Table°II). No differences were recorded between patients using continuous cycling peritoneal dialysis with one daytime exchange (CCPD-1: 12°sessions missed by 8°patients) and CCPD with two daytime exchanges (CCPD-2: 4°sessions missed by 2°patients). The patient with 4°sessions missed (confirmed by the patient's card) was the only patient using nightly intermittent peritoneal dialysis (NIPD) 6°nights each week.

### Volumes used versus volumes prescribed

No differences were found between the volumes prescribed and those actually used for either the fill and total volumes or the nighttime dwell volume.

### Session length

The length of the nighttime dialysis was reduced in only 1°patient, twice by 1°hour (0.12% of all sessions). Differences of less than 60°minutes between the length of the prescribed and the actual nighttime dialyses can be attributed to the variability in drainage. The length of the daytime dwells was also in line with the divi-

TABLE II Patients divided according to the number of automated peritoneal dialysis sessions missed over 90°days

Missed DTs (n)	HCpro card <sup>a</sup>	Patient card <sup>b</sup>
0	9	16
1	4	2
2	3	0
3	2	0
4	1	1

<sup>a</sup> Number of patients who missed sessions, according to the electronic card records from the HomeChoice Pro cyclor (Baxter Healthcare Corporation, Deerfield, IL, U.S.A.).

<sup>b</sup> Number of patients who missed sessions, according to the manual cards completed by the patients.

DTs°= dialytic treatments.

sion suggested by the center. Table III shows the sessions divided on the basis of the difference between prescribed and actual length.

### Discussion

The recording of data using the HCpro has shown high sensitivity but limited specificity. In fact, a certain number of sessions performed may not be recorded on the card owing to temporary unavailability of the card or insufficient space to hold all of the treatments since the last download. That observation seems to be confirmed by the considerable difference between sessions not recorded on the card and sessions not recorded by the patient (20°sessions vs. 6°sessions). Despite that potential overestimate, the percentage noncompliance is decidedly lower than that described in papers on the subject.

Bernardini and Piraino (6) reported that 20% of patients using APD showed a difference of more than 10% between the material prescribed and used. The number of dialytic sessions missed over 90°days can also be considered to be at least 9. According to the USRDS data (9), 10.8% of patients admit to having missed at least one session over the previous 2°weeks, which would mean missing at least 6.5°sessions over a period of 90°days. In our study, no patient reached such a high percentage of noncompliance, and only 1°patient missed as many as 4°sessions. Compliance was excellent as regards length, and total as far as volumes were concerned.

The reasons for those results can be attributed to: (A)°the freedom of choice of dialytic treatment (APD was chosen on clinical grounds in only 2°cases); (B)°the home visits carried out as necessary; (C)°awareness of the recording, which can make the doctor—patient communication more explicit with regard to the countless personal problems that can be a source of noncompliance; (D)°the characteristics of our population (older and unemployed); and (E)°the optimization of the dialytic prescription not only on clinical grounds but also on personal grounds.

TABLE III Percentage of 1673 nighttime dialytic sessions in which treatment time was reduced (divided according to the number of minutes of reduction)

	Minutes of reduction				
	0—14	15—29	30—59	60—119	≥120
Sessions	6.63%	0.84%	0.36%	0.12%	0.00%

Noncompliance may be a problem in patients treated by a partner.

### Conclusions

The HCpro system proved effective in assessing compliance. In our experience, noncompliance occurred in a lower percentage of cases than has previously been reported, notwithstanding our method's greater sensitivity and lesser specificity. Our observations may be related to the ease with which the HCpro system assesses noncompliance, caters for identifying or modifying errors in the dialytic treatment, and optimizes that treatment.

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## Influence of the Preceding Exchange on Peritoneal Equilibration Test Results

*The present study evaluates the influence of the preceding exchange on peritoneal equilibration test (PET) results in patients on automated peritoneal dialysis (APD).*

*A standard PET was performed following a 24-hour CAPD period with a preceding long overnight dwell of 8°—10° hours (PET<sub>ST</sub>), and following the usual APD regimen with short overnight dwell (PET<sub>APD</sub>).*

*We evaluated 9 patients of mean age 59 ± 18° years. Mean time on peritoneal dialysis was 31 ± 17° months, and mean APD duration was 15 ± 11° months. Mean D/P creatinine at 4° hours was 0.77 ± 0.12 (PET<sub>ST</sub>) and 0.77 ± 0.13 (PET<sub>APD</sub>, p° = 0.901). Mean D/D<sub>0</sub> glucose was 0.33 ± 0.07 (PET<sub>ST</sub>) and 0.36 ± 0.09 (PET<sub>APD</sub>, p° = 0.347). A significant correlation was seen between the D/P creatinine ratios (r° = 0.946, p° < 0.001) for the two PET methods and the D/D<sub>0</sub> glucose ratios (r° = 0.554, p° = 0.017) for the two PET methods. Transport classification did not change in any patient.*

*The current data support the use of the PET for peritoneal membrane evaluation immediately after cyclor therapy in APD patients. We suggest that there is no need to change the dialysis regimen to a long dwell for the preceding exchange to evaluate peritoneal membrane characteristics when D/P creatinine and D/D<sub>0</sub> glucose ratios are measured.*

### Key words

Automated peritoneal dialysis, peritoneal transport

### Introduction

Peritoneal membrane characteristics can be evaluated using the peritoneal equilibration test (PET) introduced by Twardowski *et al* (1) for continuous ambulatory peritoneal dialysis (CAPD) patients. To assess peritoneal function, the dialysate-to-plasma creatinine ratio (D/P creatinine) and the ratio of dialysate glucose concentration divided by baseline glucose concentration (D/D<sub>0</sub> glucose) are measured. Based on the ratios

after a 4-hour dwell, the peritoneal transport type is classified as low, low-average, high-average, or high (1). The PET result can be used to individualize dialysis prescription, and helps in diagnosing ultrafiltration failure (1—3).

Recently, automated peritoneal dialysis (APD) has been prescribed as a treatment option, especially in patients with high peritoneal transport rates. The APD modality is performed overnight, using a cyclor to achieve short dwell times°(4).

The PET should be performed after a long night dwell of 8°—12° hours (1). Evaluating peritoneal membrane transport in APD patients requires changing the treatment prescription on the day before the diagnostic procedure, which was originally developed for CAPD patients. Information on the influence of the preceding exchange on PET results is scarce (5,6). The aim of the present study was to evaluate the influence of the preceding bag exchange dwell time on the PET results of patients on°APD.

### Patients and methods

The study was performed in the renal unit of Hospital S o Lucas (a university hospital in Porto Alegre, Brazil). We included 9 APD patients and performed two PETs. All patients had been on peritoneal dialysis treatment for at least 6° months. A standard PET was performed after a 24-hour CAPD period, with a preceding long overnight dwell of 8°—10° hours (PET<sub>ST</sub>). Membrane function was also assessed following the usual APD regimen, with short overnight dwells (PET<sub>APD</sub>).

Each PET was performed according to the previously described method (1). After complete drainage of the peritoneal cavity, 2°L of 2.5% glucose dialysate solution was infused intraperitoneally within 10° minutes. Dwell time was 4° hours. A blood sample was obtained at 2° hours. Dialysate samples were obtained at 0, 2, and 4° hours dwell time. Creatinine and glucose were measured in blood and dialysate at the various dwell times.

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The D/P creatinine ratio was performed at 0, 2, and 4° hours dwell, and D/D<sub>0</sub> glucose at 2 and 4° hours dwell. The peritoneal membrane transport characteristics of the patients were classified as high, high-average, low-average, and low as suggested by Twardowski<sup>(1)</sup>.

Results are presented as mean ± standard deviation. The paired Student *t*-test was used for comparison between the two PETs. The Pearson correlation coefficient was employed to evaluate the correlation between PET<sub>ST</sub> and PET<sub>APD</sub>. Data were processed and analyzed using the Excel and Oxstat<sup>®</sup>V software programs (Microsoft Corporation, Redmond, WA, U.S.A.).

### Results

We evaluated 9 patients (7° men, 2° women) of mean age 59 ± 18° years (range: 30°—78° years). Mean time on peritoneal dialysis was 31 ± 17° months (range: 7°—60° months), and mean APD duration was 15 ± 11° months (range: 0.5°—39° months). Table I shows the D/P creatinine and D/D<sub>0</sub> glucose for PET<sub>ST</sub> and PET<sub>APD</sub>. No significant difference was present.

The D/P creatinine was significantly correlated between the two PET results ( $r^2 = 0.946, p < 0.001$ ), as was the D/D<sub>0</sub> glucose ( $r^2 = 0.554, p < 0.017$ ).

In all cases, the peritoneal membrane classification was the same for PET<sub>ST</sub> and PET<sub>APD</sub>: 3° patients were classified as high transporters; 5° patients, as high-average transporters; and 1° patient, as a low-average transporter.

### Discussion

The present study shows that the PET results of patients on APD are similar, whether peritoneal function is evaluated following a 24-hour CAPD period with a

preceding long overnight dwell of 8°—10° hours, or following the usual APD regimen with short overnight dwells. The D/P creatinine and D/D<sub>0</sub> glucose ratios were similar at all time points, and the peritoneal transport classification profile was not different whether the PET was preceded by a short or long dwell.

The PET is usually performed after a preceding dwell of 8°—12° hours (1,3), and APD is performed overnight using short dwell times. In evaluating the peritoneal membrane in APD patients, the dialysis prescription is altered on the previous day, so that peritoneal function is characterized in a standardized way (1,3,7). The change is annoying and exposes patient to a different routine, and may therefore increase the risk of peritonitis. In addition, patients with high peritoneal solute transfer rates who are likely to have inadequate ultrafiltration on standard CAPD (7) may become fluid-overloaded.

Little information on the influence of the preceding exchange on PET results is available (5,6). Interference of a preceding exchange on PET results has been previously described. A preceding dry period significantly changes PET results: the D/P ratios from a PET performed after a dry period would overestimate peritoneal transport rates in CAPD patients (5). An icodextrin exchange preceding a PET also increases the D/P creatinine and glucose absorption (8). In our study, the only patient who was kept dry during the day had similar results on both PETs.

It has also been suggested that no significant difference exists between PET results performed after a preceding short or long dwell time when D/P ratios of small solutes (creatinine and glucose) are measured (5,6). However, differences were seen in the case of D/P protein and albumin (5). Our study examined permeability for glucose and creatinine, and it agrees with the results reported by Lilaj *et al*<sup>(5)</sup>.

The current data support the use of the PET for peritoneal membrane evaluation immediately after cycler therapy in APD patients. The data also suggest that, when D/P creatinine and D/D<sub>0</sub> glucose ratios are measured, changing the dialysis regimen to a long dwell for the preceding exchange is not necessary to evaluate peritoneal membrane characteristics.

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TABLE I Dialysate-to-plasma (D/P) creatinine and dialysate-to-instilled (D/D<sub>0</sub>) glucose ratios for standard and automated peritoneal dialysis (APD) peritoneal equilibration tests (PETs)

Ratio	Dwell time (hours)	PET (Mean ± SD)		p Value <sup>a</sup>
		Standard	APD	
D/P creatinine	0	0.217 ± 0.06	0.227 ± 0.09	0.764
	2	0.514 ± 0.09	0.482 ± 0.11	0.217
	4	0.766 ± 0.12	0.769 ± 0.13	0.901
D/D <sub>0</sub> glucose	2	0.607 ± 0.19	0.703 ± 0.19	0.331
	4	0.334 ± 0.07	0.360 ± 0.09	0.347

<sup>a</sup> By paired Student *t*-test.

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## Peritoneal Rest May Successfully Recover Ultrafiltration in Patients Who Develop Peritoneal Hyperpermeability with Time on Continuous Ambulatory Peritoneal Dialysis

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*Temporary transfer to hemodialysis, as a peritoneal rest, may be a rescue therapy to recover ultrafiltration (UF) in patients who develop peritoneal hyperpermeability as a complication of continuous ambulatory peritoneal dialysis (CAPD). However, peritoneal sclerosis has been reported after peritoneal pause.*

*Since the beginning of our CAPD program in 1985, 12°elective peritoneal pauses have been performed in 11°patients who developed type°I ultrafiltration failure (D/P<sub>240</sub> creatinine: 0.88°± 0.09) after 42°± 14°months on CAPD. Eight patients recovered UF and remained on CAPD with standard solutions for 10°± 9°months more (minimum: 5°months; maximum: 29°months). Only 3 of those patients were later switched to hemodialysis because of recurring UF failure. One patient remains on CAPD (62°months of follow-up). Four patients failed to respond and were permanently transferred to hemodialysis, without signs of developing encapsulating peritoneal sclerosis. The failed pauses were performed later after the detection of UF failure than were the successful ones (483°± 574°days vs. 54°± 52°days).*

*In our study, 8 of 12 peritoneal pauses (66.6%) successfully treated type°I UF failure and prolonged CAPD retention. If a pause is initiated soon after diagnosis of UF failure, results may improve further. We urge prospective studies to better determine the best and timely therapeutic approach in patients with loss of ultrafiltration.*

### Key words

Peritoneal rest, ultrafiltration failure, peritoneal transport

### Introduction

Cumulative long-term exposure of the peritoneal membrane to glucose solutions causes neoangiogenesis, interstitial fibrosis, and mesothelial loss (1,2). Functionally, those changes usually result in hyperpermeability with ultrafiltration loss. In rare cases, the patient also may develop a more serious and irreversible condition with peritoneal sclerosis.

When ultrafiltration failure occurs, patients usually are changed to automated peritoneal dialysis or permanently transferred to hemodialysis. Such a change has a negative effect in technique survival and financial expense, not to mention considerable psychological and social costs.

Strategies to prevent ultrafiltration failure are therefore mandatory (3). Structural abnormalities and transport hyperpermeability may sometimes be reversible if a timely intervention is proposed. That intervention may be either to stop hypertonic glucose solutions and to use alternatives such as icodextrin, amino acids, and neutral pH solutions, or to transfer temporarily to hemodialysis to assure a peritoneal rest.

This important clinical problem has been investigated with rat models that proved that peritoneal resting improves ultrafiltration by decreasing peritoneal thickening and hyperpermeability to glucose (4) and by restoring the surface layer and normal peritoneal transport (5).

De Alvaro *et al* (6) published a relevant clinical experience showing that peritoneal resting is beneficial in hyperpermeability and ultrafiltration failure. That study has been followed up only by anecdotal reports (7—12). Some investigators are particularly concerned that peritoneal rest may accelerate the progression to peritoneal sclerosis (13). To clarify those concerns, we analyzed our center's experience with

peritoneal rest in patients who developed persistent ultrafiltration failure.

### Patients and methods

Since the beginning of our continuous ambulatory peritoneal dialysis (CAPD) program in 1985, 12° peritoneal pauses have been performed in 11° patients (5° women, 6° men; 1° diabetic patient; 3° patients on CAPD as first treatment modality; previous time on hemodialysis:  $47 \pm 67$  months).

After  $42 \pm 14$  months on CAPD, 11° patients developed type°I ultrafiltration failure (D/P<sub>240</sub> creatinine:  $0.88 \pm 0.09$ ). In each case, a peritoneal pause (minimum: 30° days) was electively performed. Ultrafiltration failure was defined as a long-lasting decrease in ultrafiltration with an increased need for hypertonic solution, confirmed by a PET test. Temporary ultrafiltration failure associated with recent peritonitis or catheter-related problems was excluded.

### Results

Ultrafiltration was recovered in 8° patients: it increased from  $897 \pm 294$  mL in 24° hours, achieved with 2.54%  $\pm$  0.67% glucose solution before peritoneal resting, to  $1370 \pm 452$  mL in 24° hours, achieved with 1.79%  $\pm$  0.30% glucose solution after therapy. In PET analysis, D/P<sub>240</sub> creatinine changed from  $0.88 \pm 0.09$  to  $0.81 \pm 0.13$ .

The patients remained on CAPD with standard solutions for  $10 \pm 9$  months more (minimum: 5° months; maximum: 29° months). Only 3 of the patients were later switched to hemodialysis because of recurring ultrafiltration failure after the pause (at 12° months, 22° months, and 29° months respectively). The other causes of drop-out included a fatal cardiovascular event and three peritonitis episodes. One patient remains on CAPD (62° months follow-up).

Four patients failed to respond to the pause and were permanently transferred to hemodialysis, without signs of developing peritoneal encapsulating sclerosis. The failed pauses were performed later after the detection of ultrafiltration failure than were the successful ones ( $483 \pm 574$  days vs.  $54 \pm 52$  days). The reasons for the delay in implementing the strategy were either that the patients had no vascular access or refused earlier transfer to hemodialysis. Three of the patients had severe ultrafiltration failure, and even APD was supporting them inadequately when the pause was tried. One of them was efficiently switched

to CAPD with icodextrin and maintains the same schedule 12° months after peritoneal resting.

Therefore, 8 of 12 peritoneal pauses (66.6%) successfully treated type°I ultrafiltration failure and prolonged CAPD retention. The data suggest that if the pause is initiated soon after diagnosis, results may improve further.

### Discussion

The present study strongly emphasizes that peritoneal rest is a useful rescue strategy to recover ultrafiltration in patients with type°I ultrafiltration failure. More than one half of the patients were safely maintained on peritoneal dialysis after a peritoneal rest, returning to their baseline prescriptions.

It must be noted that the patients were not changed to the alternative solutions only recently more accessible in clinical practice. Strong investigational evidence exists that solutions that are more biocompatible may further reduce development of peritoneal lesions (14—16). Therefore, we believe that timely intervention with a peritoneal rest, followed by maintenance in CAPD with alternative solutions, may be able to achieve longer retention on peritoneal dialysis.

Because we all aim for safe strategies (keeping in mind the menace of peritoneal sclerosis), the peritoneal rest should be performed as soon as the changing profile of peritoneal permeability is documented. Longitudinal measurement in effluent of the appearance rate of cancer antigen 125, a marker of mesothelial mass, may be added information to help monitor membrane status (17,18). None of the patients in our study developed peritoneal sclerosis, although some of them had a delayed peritoneal rest.

We urge prospective studies to better determine predictive markers of ultrafiltration failure so that a timely therapeutic approach is viable. Peritoneal rest may be a successful therapy for ultrafiltration loss.

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