

*Original Article***The influence of automated peritoneal dialysis on the decrease in residual renal function**

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**Abstract**

**Background.** Automated peritoneal dialysis (APD) has been increasingly used in recent years. Our purpose was to investigate whether the good preservation of residual renal function (RRF) that has been reported in patients on continuous ambulatory peritoneal dialysis (CAPD) is also observed in APD.

**Methods.** RRF was determined and compared prospectively over 1 year in two groups of peritoneal dialysis (PD) patients: 18 consecutive new patients starting on APD (12 continuous cyclic peritoneal dialysis (CCPD) patients and six nightly intermittent peritoneal dialysis (NIPD) patients) and 18 selected patients who had started on CAPD at the same time and were matched for baseline characteristics. RRF was assessed on normalized creatinine clearance ( $\text{ml}/\text{min}/1.73 \text{ m}^2$ ) measured before the start of PD, at 6 months, and at 1 year. Wilcoxon's rank sum test was used to compare differences between the two groups.

**Results.** Creatinine clearance ( $\text{Cl}_{\text{Cr}}$ ) was 6.1  $\text{ml}/\text{min}$  in the APD group and 6  $\text{ml}/\text{min}$  in the CAPD group at the start of PD. The monthly rate of  $\text{Cl}_{\text{Cr}}$  decrease was significantly higher in the APD group:  $-0.28 \text{ ml}/\text{min}$  vs  $-0.1 \text{ ml}/\text{min}$  ( $P=0.04$ ) at 6 months and  $-0.26 \text{ ml}/\text{min}$  vs  $-0.13 \text{ ml}/\text{min}$  ( $P=0.005$ ) at 1 year. RRF decreased at the same rate in patients treated with NIPD or CCPD. The daily instilled volume of 3.86% glucose dialysis solution (l/day) was higher in APD patients than in CAPD patients: 2.5 vs 0 at 6 months and 1 year but there was no significant difference in ultrafiltration rate (l/day) between APD and CAPD patients at these timepoints: 0.53 vs 0.6 and 0.88 vs 0.7 respectively. There was no difference between the two groups in body weight and blood pressure, which remained stable in both groups throughout the study period.

**Conclusions.** RRF declined rapidly in APD patients whereas it was well preserved in CAPD patients. This may be explained by the less stable fluid and osmotic load together with the intermittent nature of APD and the larger use of hypertonic dialysate. RRF should be

closely monitored in APD patients in order to adjust PD prescriptions and maintain adequacy.

**Key words:** automated peritoneal dialysis; continuous ambulatory peritoneal dialysis; residual renal function

**Introduction**

Following the initial observations by Rottembourg [1], it is now recognized that residual renal function (RRF) is better preserved in end-stage renal disease patients on continuous ambulatory peritoneal dialysis (CAPD) than in those on haemodialysis. This finding has been recently reviewed and confirmed by Lameire [2].

Good preservation of RRF is one of the main advantages of peritoneal dialysis (PD). RRF plays a major role in maintaining water and electrolyte balance without stringent food and water intake restriction, in maintaining renal endocrine function, and in eliminating so-called middle molecules. Beside these clinical benefits, RRF is one of the factors that determine adequacy in PD patients. Consequently the length of time PD remains adequate depends on the rate at which RRF declines. The importance of RRF preservation in PD patients has been confirmed by the CANUSA study, which found a link between PD patient outcome and adequacy indices [3]. The change in these indices primarily resulted from a decrease in RRF over the course of that study. The importance of RRF has been recently emphasized by Bargman *et al.* who demonstrated that it is a predictor of patient survival on PD independently of PD dose [4].

Shortly after we expanded the use of automated peritoneal dialysis (APD) in our department, when second-generation home cyclers became available (1995), we had the impression that some of our APD patients had an unusually rapid decline in RRF. We therefore undertook this study to investigate whether the good preservation of RRF previously reported in patients on CAPD was also observed in patients on APD.

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## Subjects and methods

From November 1995 to April 1997 we recruited a total of 36 PD patients in a prospective study. RRF was determined and compared over 1 year of therapy in 18 consecutive new patients referred to our department to begin APD during this period (12 continuous cyclic peritoneal dialysis (CCPD) patients and six nightly intermittent peritoneal dialysis (NIPD) patients) and 18 selected new patients who had started on CAPD at the same time and were matched for baseline RRF and underlying renal disease (glomerulonephritis in seven patients, polycystic kidney disease in four patients, nephroangiosclerosis and hypertension in three patients, pyelonephritis in one patient, diabetes in two patients, and unknown nephropathy in two patients, in each group). Despite not being matched for sex, both groups had the same sex ratio (11 males and 7 females in each group). Age was  $50 \pm 15$  years (mean  $\pm$  SD) in the APD group and  $62 \pm 17$  years in the CAPD group. At the start of PD, furosemide (250–500 mg/day) was given to 17 patients in each group. Angiotensin-converting enzyme inhibitors (ACEI) were given to four patients in the APD group and two in the CAPD group.

Patient assignment to APD or CAPD was based upon their own choice after they had been fully informed about each of these modalities. RRF was assessed on 24-h  $Cl_{Cr}$  measured just before the start of PD, at 6 months and 1 year. Adequacy of PD was estimated at the same time-points by measuring weekly total Kt/V for urea and total  $Cl_{Cr}$ . Peritoneal Kt was estimated from 24-h dialysate urea excretion and the serum urea concentration. Renal Kt was estimated from the concurrent 24-h urinary urea excretion. Peritoneal  $Cl_{Cr}$  was estimated from the 24-h dialysate creatinine excretion and the serum concentration at the completion of collection. Residual and peritoneal clearances were normalized to 1.73 m<sup>2</sup> body surface area and expressed as ml/min and l/week respectively. Standard peritoneal equilibration test (PET), as described by Twardowski *et al.* [5], was also performed at the same time to estimate peritoneal permeability. PET was done during a 4-h dwell with a 2.27% glucose dialysis solution and results were given as the dialysate-to-plasma ratio for creatinine at 4 h.

Peritoneal  $Cl_{Cr}$ , urea Kt/V, and dialysate-to-plasma creatinine ratio were calculated using the computer-based kinetic modelling program PD Adequest™ version 1.4 [6]. Total daily dialysate volume, daily hypertonic dialysate volume, daily peritoneal ultrafiltration volume, body weight, and blood pressure were averaged from daily home data recorded over 1 month before clearance measurements.

All patients were treated with Dianeal<sup>R</sup> dialysis solutions in which glucose concentration was adjusted according to the patient's need for ultrafiltration. All APD patients used Home-Choice™ cyclers. Appropriate PD regimens were prescribed at the start of PD therapy and adjusted throughout the study period so as to achieve a Kt/V for urea of 2.1 or a total creatinine clearance of 70 l/week per 1.73 m<sup>2</sup>, as concluded in the CANUSA study. CAPD patients received three to four 1.5- to 2.5-l exchanges per day. APD patients had one 8- to 10-h nightly session with 5–10 exchanges using 1.5- to 2.0-l instilled volume and a dwell time of 45–75 min each time. CCPD patients had one or two additional 1.5- to 2.0-l exchanges daily, whereas NIPD patients had an empty peritoneal cavity during the daytime.

Differences in  $Cl_{Cr}$  values and differences in clinical and PD parameters between the two groups were calculated at

different time-points. These differences were expressed as median values and ranges and compared using the non-parametric Wilcoxon's rank sum test. Tests were two-tailed, and a *P* value <0.05 was considered significant.

## Results

Table 1 shows a significantly greater RRF decrease in APD patients than in CAPD patients at 6 months (*P*=0.04) and 1 year (*P*=0.005). At the end of the first year of treatment, median residual  $Cl_{Cr}$  had fallen by 57% in APD patients as compared with 24% in CAPD patients. In APD patients, RRF decreased at the same rate in the NIPD and CCPD patient subgroups.

Table 2 summarizes the time course of PD parameters over the study period. Total daily dialysate instilled volume and daily instilled volume of 3.86% glucose dialysis solution were greater in APD patients than in CAPD patients at 6 months and 1 year. There was no significant difference in daily ultrafiltration volume between the two groups at 6 months and 1 year. Weekly total  $Cl_{Cr}$  was significantly lower in APD patients than in CAPD patients (*P*=0.01). There was no difference in the 4-h dialysate to plasma creatinine ratio between the two groups at 6 months and 1 year. There was no difference between the two groups in body weight and blood pressure, which remained stable in both groups throughout the study period (Table 3).

## Discussion

The results of our 1-year study confirm that RRF decreases faster in patients on APD than in those on CAPD, as first reported by Hiroshige *et al.* [13], whose 6-month study suggested a negative influence of APD technique on RRF. The monthly rate of creatinine clearance decline in our APD patients was slightly higher than in their series:  $-0.40$  ml/min vs  $-0.31$  ml/min ( $Cl_{Cr}$  values are given as the mean so as to compare them with those reported by Hiroshige).

The rate of decline in  $Cl_{Cr}$  in our CAPD patients was comparable to that previously reported in the literature. This confirms that RRF is well-preserved in patients treated with this technique [1,2,10,12–14].

Creatinine clearance has been shown to overestimate GFR in end-stage renal failure patients because of an increased tubular secretion of creatinine, but it is well correlated to inulin clearance [7–9] and is much simpler to measure. Furthermore, most published studies of RRF have used this method to assess GFR in patients receiving maintenance therapy [1,2,10–14]. We therefore considered  $Cl_{Cr}$  to be the appropriate marker to compare our two groups of PD patients.

The observed difference in  $Cl_{Cr}$  decline between the APD and CAPD groups raises a number of questions, the first being whether or not this difference was a consequence of baseline clinical differences between the groups. Indeed, it would have been desirable to

**Table 1.** Comparison of residual  $Cl_{Cr}$  and rate of residual  $Cl_{Cr}$  decrease in APD and CAPD patients

Baseline		At 6 months		At 1 year	
APD	CAPD	APD	CAPD	APD	CAPD
Residual $Cl_{Cr}$ (ml/min/1.73 m <sup>2</sup> )					
6.1 (11–2.7)	6 (11–2.5)	3.5 <sup>a</sup> (8.5–0)	4.5 (11–2)	2.03 <sup>b</sup> (8.5–0)	4.6 (10–0)
Rate of residual $Cl_{Cr}$ decline (ml/min/month)					
		–0.28 <sup>a</sup> (–1.08 – +0.02)	–0.1 (–0.7 – +0.05)	–0.26 <sup>b</sup> (–0.65 – +0.02)	–0.13 (–0.47 – +0.08)

Values are medians (ranges); <sup>a</sup> $P=0.04$  and <sup>b</sup> $P=0.005$ , as compared with CAPD patients.

**Table 2.** Comparison of peritoneal dialysis parameters in APD and CAPD patients at 6 months and 1 year

PD modality	At 6 months		At 1 year	
	APD	CAPD	APD	CAPD
Total dialysate volume (l/day)	12.75 (8–16.5)	6 (6–8)	14.5 (8.1–19)	6.25 (6–9)
Hypertonic dialysate volume (l/day)	2.5 (0–3.8)	0 (0–2)	2.5 (0–3.8)	0 (0–2)
Ultrafiltration volume (l/day)	0.53 (0.1–1.5)	0.6 (0.3–1.8)	0.88 (0.1–1.4)	0.7 (0.2–2)
Total $Cl_{Cr}$ (l/week/1.73 m <sup>2</sup> )	72 (59–150)	83 <sup>a</sup> (60–141)	71.5 (56–150)	81 <sup>a</sup> (65–140)
Weekly urea Kt/V	2.2 (1.54–4.19)	2.18 (1.53–3)	2.29 (1.71–3.14)	2.17 (1.56–2.54)
4-h D/P creatinine	0.61 (0.51–0.94)	0.62 (0.51–0.86)	0.65 (0.48–0.99)	0.63 (0.42–0.76)

Values are medians (ranges); <sup>a</sup> $P=0.01$  as compared with CAPD patients.

**Table 3.** Comparison of body weight and blood pressure changes in APD and CAPD patients

PD modality	Baseline		At 6 months		At 1 year	
	APD	CAPD	APD	CAPD	APD	CAPD
Body weight (kg)	69.6 (45–95)	69 (47–83)	68.8 (45–95)	70.5 (47–83)	70.1 (45–98)	70.5 (47–83.5)
Systolic/diastolic blood pressure (mmHg)	140/80	140/80	130/80	145/90	140/80	145/80

Values are medians (ranges); no significant difference between the two groups.

determine the course of RRF decline in our patients prior to the start of dialysis, but this was impossible because the patients had either been late referrals or had been monitored on creatinine clearance calculated by the Cockcroft and Gault formula, which does not allow for inter-subject comparison. Furthermore, the comparison of baseline characteristics shows that the two groups were well-matched except for age, which was lower in the APD group than in the CAPD group. This was due to the fact that in our department most younger patients tend to chose APD because it allows them to remain active. Could this have introduced a selection bias by age? RRF would then be assumed to have declined more rapidly in younger patients simply because the earlier the onset of renal failure, the more

aggressive the underlying disease. Such a hypothesis has never been confirmed by previous studies. Iest *et al.* [11] reported that RRF was not affected by age in haemodialysed patients, and De Vecchi *et al.* [14] also reported that residual  $Cl_{Cr}$  was not affected by age after 1 year of CAPD, and moreover that elderly patients had a significantly lower RRF than did younger patients after 2 years of treatment. Furthermore, we compared the rate of RRF decline in four CAPD series of different ages (here again  $Cl_{Cr}$  values are given as the mean so as to compare them with those reported in the three other series): our CAPD group (mean age = 62), the series reported by Lysaght *et al.* ( $n=55$ , mean age 49) [12] and the two series reported by De Vecchi ( $n=86$ , mean age 51.8 and

$n=63$ , mean age 76.5 respectively) [14]. Regardless of age, the mean monthly rate of RRF decline was similar in all four series, including our own:  $-0.14$  ml/min,  $-0.12$  ml/min,  $-0.12$  ml/min and  $-0.16$  ml/min respectively. Such a comparison tends to demonstrate that age is not a determining factor in the rate of RRF decline.

The next question we may ask is whether or not the difference in RRF decline is a consequence of clinical conditions that may have developed during the study period and adversely affected RRF. All patients maintained a stable clinical course. No adverse event such as cardiac failure, uncontrolled hypertension, and active systemic inflammatory disease was seen. The use of high-dose furosemide probably did not affect the results of our study, since all but one patient in each group were given this drug. Moreover, whether routine furosemide helps preserve RRF remains speculative [2]. No patient was given ACEI after enrollment except those who had been treated with this medication before the start of PD therapy. Here again, the use of ACEI probably had no effect on the results of this study since the influence of this type of drug on RRF remains doubtful in CAPD patients [12]. One patient in the APD group had two episodes of peritonitis and one patient in the CAPD group had one episode. These episodes were treated as recommended for peritonitis related to peritoneal dialysis [15]. Neither of these two patients was given aminoglycosides. No patient received non-steroidal anti-inflammatory agents or any other nephrotoxic agent.

Perhaps then the APD technique itself contributed to the rapid RRF decline observed in our APD patients. A closer look at PD parameters shows that a greater daily hypertonic dialysate volume was prescribed to APD patients. The need for a greater hypertonic dialysate volume to increase ultrafiltration and prevent fluid overload became apparent early during treatment in many of these patients, even before their RRF had significantly decreased. Hence compensating the reduced urinary output resulting from the RRF decline cannot entirely explain the higher hypertonic dialysate volume requirement, which did not even lead to a significant difference in ultrafiltration between the two groups. This suggests that hypertonic solutions had a lower than expected yield in APD patients. Considering that the two groups showed no difference in peritoneal permeability that could have explained this finding, we may assume that the increased use of hypertonic solutions in APD patients is largely required by the technique itself. From our point of view, the supine position and the method of drainage often result in incomplete drainage, in turn followed by reabsorption of the remaining dialysate and ultrafiltrate. Consequently, the more rapid RRF decline in APD patients might be explained by a more intensive ultrafiltration associated with incomplete collection of the ultrafiltrate and hence a less stable fluid load. Another explanation might be that osmotic load varies more markedly with each nightly APD session because of the intermittent character of the technique. This is

true both in NIPD, where solute and fluid are removed only at night, and in CCPD therapy, where intensive night sessions are supplemented by one or two additional long exchanges. Greater variations in fluid and osmotic load may alter the haemodynamic status of these patients and potentially cause ischaemia, which further damages glomerular filtration. This hypothesis has been suggested previously to account for the better preservation of RRF in CAPD patients than in haemodialysed patients [12]. It may also be that glomerular filtration is affected by repeated exposure to a less biocompatible dialysis that would result from the higher exchange rate and hence the shorter time allowed for solute equilibration in APD.

Although the findings of our study need to be validated by further investigations, the observed rapid RRF decline in APD patients requires that we remain cautious when proposing this technique. Special attention should be paid to monitoring RRF in these patients in order to adjust PD prescriptions and maintain adequacy.

Patients who choose APD should be informed that their RRF may decline more rapidly and that consequently their PD regimen may need to be modified accordingly to lengthen nightly sessions and/or to include additional daytime exchange(s) that may impair their quality of life.

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