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Different treatment options in peritoneal dialysis

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Abstract

Patients with end-stage renal disease (ESRD) are placed on dialysis while they await kidney transplantation. The mortality rate among patients with ESRD is high. This review outlines the importance of preservation of residual renal function (RRF) and supports the idea of the integrated care approach to uraemia where patients start on peritoneal dialysis (PD).

Keywords: fluid state; sodium sieving; residual renal function; peritoneal transport characteristics; icodextrin

Introduction

Peritoneal dialysis (PD) is used in ∼25% of patients with end-stage renal disease (ESRD). With PD, the blood is cleansed by means of instillation of sterile dialysis fluid in the peritoneal cavity through a catheter, leading to an exchange of fluid and solutes between the peritoneal cavity and the peritoneal capillaries. There are different forms of PD. Continuous ambulatory peritoneal dialysis (CAPD) is performed manually, usually with daily exchanges of 2–2.5 l of dialysis fluid with an instillation time of 4–10 h. Automated peritoneal dialysis (APD) is performed automatically during the nighttime, usually with more rapid exchange cycles.

As in patients with ESRD, diuresis is often diminished or absent; fluid has to be removed by means of the dialysis technique. With PD, the excess fluid is removed by means of osmosis, evoked by the presence of glucose in the PD fluid.

However, many patients on CAPD are fluid-overloaded in the absence of any clinical signs. Subclinical overhydration due to an excess of extracellular water (ECW) is a major risk factor in the development of hypertension and left ventricular hypertrophy [1,2]. Changes in ECW are significantly related to changes in systolic blood pressure [3]. In patients with a negligible residual glomerular filtration rate (rGFR) (<2 ml/min), a higher ECW:height (l/m) ratio exists despite a higher peritoneal ultrafiltration (UF) volume leading to overhydration and inflammation [4].

Haemodialysis versus peritoneal dialysis

Although kidney transplantation is the preferred treatment method for patients with ESRD, most patients are placed on dialysis. Fenton *et al.* [5] found, in 1999, that the increased mortality on haemodialysis (HD) compared with APD and CAPD was concentrated in the first 2 years of follow-up. This has been confirmed by Heaf *et al*. [6] in 2002 by analysing the data from the Danish Terminal Uremia register. These data also showed a survival benefit for PD during the first 2 years of dialysis treatment and also that the change in dialysis modality was associated with increased mortality and the change from PD to HD with an accelerated mortality for the first 6 months. This may be due to unregistered differences in comorbidity at the start of treatment or may be causal due to better preservation of residual renal function (RRF).

Unadjusted death rates and relative risk of death among patients on HD compared with those on PD, according to time since the initiation of dialysis treatment (as-treated censoring), are given in Figure 2 [7].

This study supports the idea of the integrative care approach to uraemia, where patients start on PD and transfer to HD when PD-related mortality increases. RRF influences morbidity, mortality and quality of life in chronic dialysis patients. The NECOSAD Study Group concluded after analysing the decline rates of rGFR prospectively in HD and PD patients that rGFR is better maintained in PD patients than in HD patients (see also Figure 3). Baseline factors that were negatively associated with rGFR at 12 months were a higher diastolic blood pressure and a higher urinary protein loss. Both should be treated aggressively [8].

Another retrospective study by Lysaght *et al*. revealed that RRF was found to decline in both groups after the onset of therapy, but the rate of decline in the HD group was twice that in the CAPD group [9]. The better preservation of RRF in CAPD patients corresponded with greater cardiovascular stability compared to HD patients, independently of the membrane used. However, when using a

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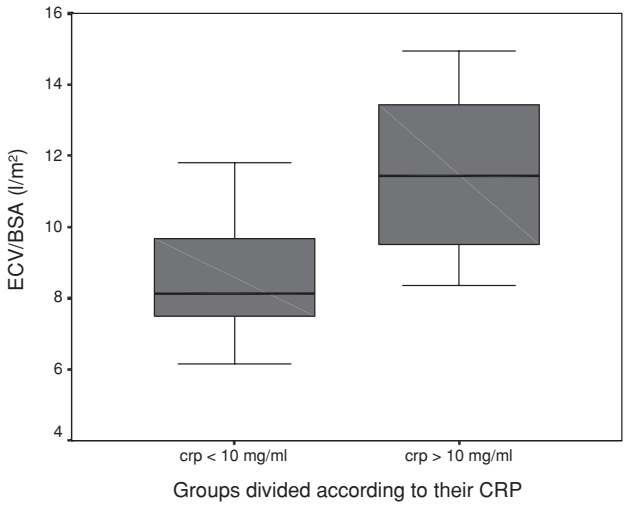

Fig. 1. rGFR is associated with fluid status in PD patients [13].

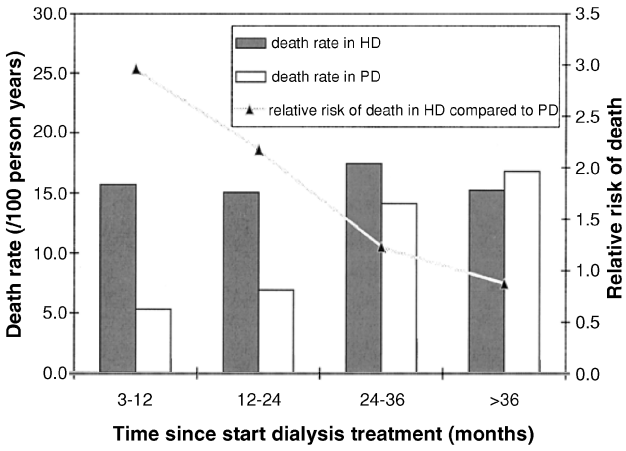

Fig. 2. Unadjusted death rates and relative risk of death among patients on haemodialysis (HD) compared with those on peritoneal dialysis (PD).

biocompatible membrane, the preservation of RRF is significantly higher. It should be avoided to start ESRD patients on HD prior to elective CAPD for better preservation of RRF [10]. The generation of nephrotoxic substances by the bioincompatible membrane results in faster decline of RRF. In principle, there is better preservation of RRF in PD compared to HD; however, one study found, when using a high-flux biocompatible membrane and ultrapure water, that RRF declines at an identical rate as in CAPD [11]. Further studies have to confirm this.

Risk factors for RRF loss in PD patients

RRF in ESRD is clinically important as it contributes to adequacy of dialysis, quality of life and mortality. Faster decline of rGFR was found to be associated with higher rate of peritonitis and the use of aminoglycoside antibiotics for the treatment of peritonitis. Also, blood pressure medications, large body mass index, diabetes mellitus, higher grades of left ventricular dysfunction and higher 24-h proteinuria were associated with faster decline of rGFR [12].

CAPD versus APD

Hufnagel *et al*. found in 1999 that the RRF declined rapidly in APD patients, whereas it was well preserved in CAPD patients. They concluded that this could be explained by the less stable fluid and osmotic load together with the intermittent nature of APD and the larger use of hypertonic dialysate [13]. This conclusion was based on their nonrandomized comparative study of 18 consecutive new patients starting APD [12 on continuous cyclic peritoneal dialysis (CCPD) and 6 on nightly intermittent peritoneal dialysis (NIPD)] and 18 CAPD patients, who were followed for 1 year, as reported by Fijter *et al*. [14]. Their prospective, randomized study comparing CAPD with Y-connector and APD revealed a significant decline in RRF over time in both groups. There was no significant difference between the dialysis modalities regarding RRF at any point of time during the follow-up [14]. In 2001, Holley *et al*. concluded in a retrospective study that modality of PD and patient demographic factors do not contribute to the rate at which RRF is lost in incident PD patients [15]. However, in 2004, Rodriguez-Carmona *et al*. found after 1 year of follow-up that UF and sodium removal rates were consistently lower in incident APD patients than in their counterparts undergoing CAPD.

Moreover, the RRF declined faster during APD than during CAPD therapy, although this difference may be partially counteracted by the detrimental effect of UF on RRF. Apart from a better control of systolic blood pressure in CAPD patients, these differences do not portend significant cardiovascular consequences during the first years of PD therapy [16].

In patients on CAPD, the fluid status is related to the peritoneal transport characteristics and the RRF. Patients with a so-called high transport status of the peritoneal membrane (i.e. a more permeable peritoneal membrane), characterized by a high dialysate to plasma (D/P) ratio of creatinine, have a low UF volume due to rapid dissipation of glucose from the PD fluid to the capillaries. In these patients, net fluid removal can be enhanced by the shorter duration of the dwell periods (i.e. the period during which the dialysis fluid resides in the peritoneal cavity) and dialysis solutions with higher tonicity. Hence, for patients with a high transport status, APD is generally preferred instead of CAPD, although there is not yet a proof of its superiority in terms of fluid removal and prevention of overhydration compared to CAPD.

Even in 'low transporters' (patients in which the permeability of the peritoneal membrane for solutes is lower), APD is frequently preferred because of social reasons (for example working or studying).

Fluid and sodium removal may differ between APD and CAPD. Although, as mentioned previously, the dissipation of the osmotically active glucose from the peritoneal cavity to the blood may be partly prevented by the more rapid exchange cycles with APD in high transporters, leading to enhanced fluid removal, in low transporters the use of APD

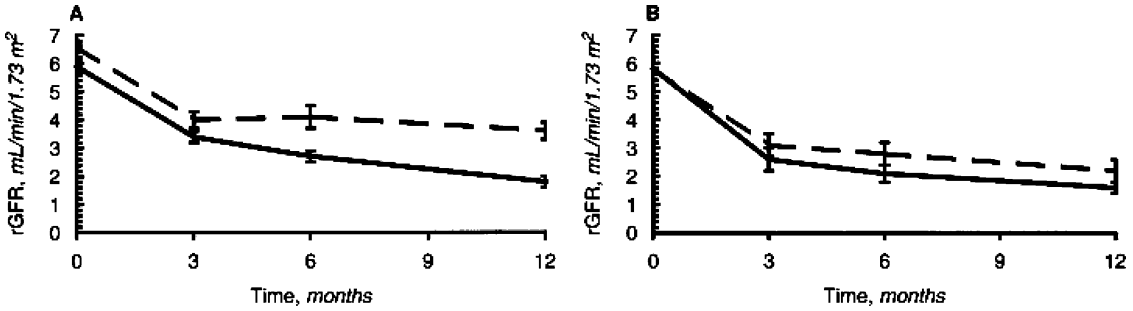

Fig. 3. Unadjusted (**A**) and adjusted (**B**) residual glomerular filtration rate (rGFR) values. SE at the start of dialysis treatment, and at 3, 6 and 12 months after the start of dialysis treatment. Symbols: (dashed lines) values in the PD patients; (solid lines) rGFR values in the HD patients [8].

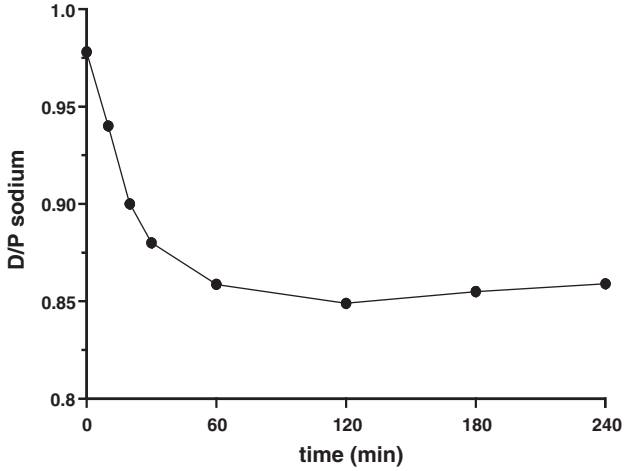

Fig. 4. Illustration of sodium sieving. For an explanation, see the text.

may be disadvantageous [16]. When the transport status of the peritoneal membrane is low, sodium sieving in APD is higher due to the shorter duration of the dwell periods.

Sodium sieving

As UF occurs early in the dwell, the dialysate sodium concentration drops due to sodium sieving by ultrasmall pores and serum sodium rises. Later in the dwell period, the UF lessens and sodium removal is increased by diffusion resulting in a drop in the serum sodium and a rise in the dialysate sodium. It should always be considered that, due to sodium sieving over the ultrasmall pores, fluid and salt removal are not always concordant [17].

A lower sodium removal is related to a higher systolic blood pressure and left ventricular hypertrophy [16]. Wang showed a significant lower UF volume and sodium removal [18] by performing peritoneal equilibration tests (PET) in patients with a high transport state of the peritoneal membrane. When in time the fluid balance worsens, the glucose polymer icodextrin can enhance UF in the long dwell [19]. In a trial to compare icodextrin versus 2.27% glucose, members of the icodextrin group lost weight, whereas the control group gained weight. Similar differences in total body water were observed, largely explained by reduced extracellular fluid volume in those receiving icodextrin, who also achieved better UF and total sodium losses and had better maintenance of urine volume [19] (see Table 1).

Table 1.

Change from baseline and between-group differences		Month 1	Month 3	Month 6
Ultrafiltration volume (ml)	Icodextrin	+166.8	+87.9	+193.4
	Glucose	−50.1	−311.1	−201.7
	Difference	216.9	399.0*	395.1
Dialysate sodium removal (mmol)	Icodextrin	+11.5	+0.9	+1.4
	Glucose	−11.4	−60.8	−25.0
	Difference	22.9	61.7*	26.4

*$P < 0.05$, EXTRANEAL versus 2.27% glucose [19].

For any degree of UF, sodium removal is better in CAPD than in APD. Icodextrin and longer nocturnal dwell times improve sodium removal in APD but this must be carefully monitored in patients on APD [20]. Konings *et al*. showed that use of icodextrin resulted in a significant reduction in ECW and left ventricular mass [21].

The European APD Outcome Study (EAPOS) showed that anuric patients also can successfully use APD. However, a baseline UF (<750 ml/24 h) is associated with worse patient survival [22]. Continuous exposure to bioincompatible PD solutions and episodes of peritonitis or haemoperitoneum cause acute and chronic inflammation and injury to the peritoneal membrane, which progressively undergoes fibrosis and angiogenesis and ultimately leads to UF failure [23].

Conclusions

Renal replacement therapy can no longer be seen as a separate entity of HD or PD or transplantation but should be seen as complementary therapy [24]. In ESRD it is a good option to start on PD. It is of utmost importance to measure RRF, because RRF influences morbidity, mortality and quality of life in chronic dialysis patients. Volume homeostasis is an important predictor of outcome in PD, because volume retention is driven by salt retention. Therefore, maintenance of salt balance should be of utmost concern. An important factor for this is dietary salt restriction [17]. Peritoneal

membrane function should be measured at least twice a year and should include a temporary drainage after 1 h for assessment of aquaporin function [25]. It is the opinion of the authors that too short dwells in slow transporters should not be used in APD. Icodextrin can be used in the long dwell when there is insufficient sodium removal due to sodium sieving.

Conflict of interest statement. None declared.

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