SHORT REPORTS

Does Loss of Residual Renal Function Lead to Increased Volume Overload and Hypertension in Peritoneal Dialysis Patients?

KEY WORDS: Bioelectrical impedance; peritoneal dialysis; glucose; icodextrin; extracellular water; intracellular water.

Peritoneal dialysis (PD) is a successful effective treatment for patients with chronic kidney disease, with > 300,000 patients treated worldwide. After peritonitis (1), many studies have shown that loss of residual renal function is the next most common cause of PD technique failure and transfer to hemodialysis (HD) (2,3). Without residual renal function, PD has to both achieve adequate solute clearances and prevent volume overload. Peritoneal dialysis patients have been reported to have increased extracellular water (ECW) (3), similar to that of midweek HD patients (4). Peritoneal dialysis patients who have lost residual renal function have been reported to have greater ECW expansion (5). As such, loss of residual renal function and fluid accumulation are a common scenario in PD patients transferring to HD (6,7). Earlier reports suggested that faster peritoneal small solute transporters failed to achieve adequate ultrafiltration, resulting in treatment modality failure and transfer to HD. However, the introduction of icodextrin has permitted patients with ultrafiltration failure on glucose-based peritoneal dialysates to continue on PD (8). Loss of residual renal function may therefore not necessarily determine transfer to HD, and other studies have reported that volume status can be maintained by adjusting PD prescriptions (9). Hence we wished to investigate whether PD patients who lost residual renal function became fluid overloaded, as measured by multi-frequency bioelectrical impedance assessments (MFBIA).

PATIENTS AND METHODS

We compared the first MFBIA after PD patients were documented to have become oligo-anuric (urine output < 100 mL/day) with a follow-up assessment. Ninety-four adult PD outpatients under the care of 2 tertiary university hospitals were studied between August 2008 and January 2012. All patients had MFBIA performed in a standardized manner (BCM Fresenius, Bad Homburg, Germany; InBody 720, Seoul South Korea), as part of established routine clinical care (10). We have previously derived equations comparing these devices (10) and assessed reproducibility (11). Relative ECW overhydration was calculated according to European Society

for Parenteral and Enteral Nutrition (ESPN) guidelines (12). Although both Baxter (Baxter Health Care, Deerfield, USA) and Fresenius PD systems were used, the majority of patients were treated with Baxter PD systems.

Patients attended for assessments of PD adequacy, with 24-hour effluent peritoneal dialysate and urine collections analyzed to determine urine volume and both peritoneal clearances and residual renal function, with calculation of normalized nitrogen appearance (nPNA), to assess dietary protein intake. Peritoneal transport was assessed using a 2-liter 22.7 g/L dextrose exchange.

Ethical approval was granted by the local ethical committee as audit and clinical service development. All patient data were appropriately anonymized and audit was conducted according to the UK NHS guidelines for clinical audit.

STATISTICAL ANALYSIS

Statistical analysis was by single or paired analysis, Student's *t*-tests, or Wilcoxon pair analysis, with appropriate correction for multiple analyses, and by Chi square test with Yate's correction (GraphPad Prism version 6.0, San Diego, USA). Data are presented as mean $\pm$ standard deviation, median (interquartile range) or as a percentage.

RESULTS

Ninety-four adult PD patients, median age 56.0 (47.3–66.6) years, 47.9 % male, 37.0% diabetic were studied (Figure 1). They had a median Stoke-Davies comorbidity score of 1 (0–3). Patients were predominantly from 3 major ethnic groups: 34% Caucasoid, 31.9% South Asian and 26.6% African/Afro-Caribbean. The median PD vintage at the time of oligo-anuria was 26.9 months (10.7–60.3), and the median time between assessments was 353 (301–388) days. About half (47.8%) of patients were using 7.5% icodextrin, 75.5% prescribed 22.7 or 28.6 g/L dextrose, and 51.1% prescribed 36.8 or 42.5 g/L dextrose dialysates when oligo-anuria was noted. On follow-up, more patients, 72.3% were prescribed 7.5% icodextrin ($\chi^2 = 10.74$, $p = 0.001$), whereas there was no significant increase in patients prescribed 22.7 or 28.6 g/L (80.9%; $\chi^2 = 0.49$, $p = 0.48$) or 36.8 or 42.5 g/L dextrose dialysates 59.6% ($\chi^2 = 1.05$, $p = 0.34$).

On follow-up peritoneal equilibrium testing (PET), the 4-hour dialysate to plasma creatinine ratio increased, but there was no difference in ultrafiltration volumes or in PD adequacy (Table 1).

There was no difference in weight or blood pressure, and indeed, on follow-up, fewer classes of antihypertensive

Figure 1 — Derivation of study cohort. Patient numbers on the left hand side from Royal London & St Bartholomew's Hospital and on the right hand side from the Royal Free Hospital. PD = peritoneal dialysis; MF-BIA = multi-frequency bioelectrical impedance assessments.

medications were prescribed (Table 2). Similarly, volume assessment by MFBIA showed no difference in ECW, or ECW/TBW (total body water) ratio or relative ECW overload.

DISCUSSION

We followed a cohort of almost 100 adult PD patients who had become oligo-anuric (daily urine output < 100 mL/day) for an average of 360 days. Although there was an increase in PET test 4-hour peritoneal dialysate effluent to serum creatinine, which has been previously reported to be associated with ultrafiltration failure and fluid retention (13), we did not observe any increase in ECW, either as absolute changes or as a ratio to TBW (14) or relative ECW overhydration (12). Over the course of follow-up, there were changes to PD prescriptions, and although the proportion of patients prescribed hypertonic glucose-containing dialysates did not significantly change, the major change was an increase in the use of 7.5% icodextrin. Previous reports have shown that the introduction of icodextrin can allow patients to be maintained on PD who otherwise would have been transferred to HD (8), and that icodextrin usage has been reported to reduce ECW expansion compared with glucose-containing dialysates (15). As such it is possible to alter PD prescriptions to avoid fluid retention in oligo-anuric PD patients despite an increase in transporter status. Similarly, despite the loss of residual renal function, there was no observed decrease in PD adequacy.

Although it has been suggested that PD becomes time limited once residual renal function has been lost, we have demonstrated in this observational cohort that despite loss of residual function, patients do not become volume overloaded or suffer a reduction in small solute clearances over an average 12-month follow-up. We accept that ours is a survivor cohort, as just over 66% of our patients remained on PD 12 months after becoming anuric, and changes in PD prescription were made, in particular increased usage of icodextrin, but even so this observational

TABLE 1
Peritoneal Dialysis Transport Testing (PET) and Dialysis Adequacy^a Upon Initial Oligo-Anuric Diagnosis and On Follow-Up

	Oligo-anuric	On follow-up ^{b,c}
4-hour D/P creatinine	0.69±0.13	0.75±0.09 (<i>p</i> =0.015)
PET UF volume (mL)	250 (100–400)	300 (175–400)
Weekly urine Kt/V _{urea}	0 (0–0.01)	0 (0–0.06)
Weekly peritoneal Kt/V _{urea}	1.9±0.41	1.88±.39
Total weekly Kt/V _{urea}	1.94±0.42	1.91±0.39
24-hour urine volume (mL)	30 (0–75)	0 (0–0) (<i>p</i> <0.001)
Creatinine cleared, urine	1.7 (0.67–1.01)	0 (0–0.6) (<i>p</i> =0.007)
Creatinine cleared, peritoneal	48.6±12.0	48.0±10.8
Creatinine cleared, total	51.2±11.7	50.0±11.8
24-hour peritoneal UF (mL)	928 (624–1,304)	888 (548–1,113)

PET = peritoneal dialysis transport testing; UF = ultrafiltration.

^a Peritoneal dialysis adequacy, measured as Kt/V_{urea} and liters of creatinine corrected for 1.73 m² and daily UF volume.

^b Mean follow-up time was 353 days.

^c Significant *p* values entered.

TABLE 2
Weight, Peripheral Blood Pressure, and Multifrequency Bioimpedance Assessments Upon Initial Oligo-Anuric Diagnosis and On Follow-Up

	Oligo-anuric	On follow-up ^{a,b}
Weight (kg)	69.3±14.5	69.3±15.4
SBP (mmHg)	138.9±29.1	134.9±26.3
DBP (mmHg)	81.3±17.3	78.6±15.6
MAP (mmHg)	100.6±19.6	97.4±7.6
BP meds	1 (0–2)	1 (0–1) (<i>p</i> =0.09)
ECW (L)	14.9±3.4	14.6±3.4
ECW/TBW	0.45±0.05	0.45±0.05
ECW-OH (L)	0.55 (–0.26–1.4)	0.4 (–0.22–1.4)

SBP = systolic blood pressure; DBP = diastolic blood pressure; MAP = mean arterial blood pressure; BP meds = number of different classes of antihypertensive medications prescribed; ECW = extracellular water, ECW/TBW = ratio ECW to total body water; ECW OH = relative ECW overhydration.

^a Mean follow-up was 353 days.

^b *p* values given if statistically significant.

cohort does not suggest that loss of residual renal function should necessarily trigger modality change to HD.

ACKNOWLEDGMENTS

SF has accepted monies from Fresenius AG for speaking engagements. Fresenius AG provided educational grants to the Royal London & St Bart's department of Renal medicine and supported the UCL Centre for Nephrology Dialysis course. Funding was provided by the Royal Free Hospital and The Royal London Hospital.

DISCLOSURES

The authors have no financial conflicts of interest to declare.

results of a double-blind randomized controlled trial. *J Am Soc Nephrol* 2003; 14(9):2338–44.

<http://dx.doi.org/10.3747/pdi.2014.00147>

Stanley Fan¹
Andrew Davenport^{2*}

Department of Nephrology¹
St. Barts & the London NHS Trust
Royal London Hospital, London, UK
UCL Center for Nephrology²
Royal Free Hospital
University College London Medical School
London, UK

*email: andrewdavenport@nhs.net

REFERENCES

1. Davenport A. Peritonitis remains the major clinical complication of peritoneal dialysis: the London, UK, peritonitis audit 2002–2003. *Perit Dial Int* 2009; 29(3):297–302.
2. Jager KJ, Merkus MP, Dekker FW, Boeschoten EW, Tijssen JG, Stevens P, et al. Mortality and technique failure in patients starting chronic peritoneal dialysis: results of The Netherlands Cooperative Study on the Adequacy of Dialysis. NECOSAD Study Group. *Kidney Int* 1999; 55(4):1476–85.
3. Bargman JM. The CANUSA study and the importance of residual kidney function in dialysis patients. *Kidney Int* 2010; 77(10):931.
4. Papakrivopoulou E, Booth J, Pinney J, Davenport A. Comparison of volume status in asymptomatic haemodialysis and peritoneal dialysis outpatients. *Nephron Extra* 2012; 2(1):48–54.
5. Fan S, Sayed RH, Davenport A. Extracellular volume expansion in peritoneal dialysis patients. *Int J Artif Organs* 2012; 35(5):338–45.
6. Davenport A, Willicombe MK. Hydration status does not influence peritoneal equilibration test ultrafiltration volumes. *Clin J Am Soc Nephrol* 2009; 4:1207–12.
7. Smit W, Schouten N, van den Berg N, Langedijk MJ, Struijk DG, Krediet RT; Netherlands Ultrafiltration Failure Study Group. Analysis of the prevalence and causes of ultrafiltration failure during long-term peritoneal dialysis: a cross-sectional study. *Perit Dial Int* 2004; 24(6):562–70.
8. Wilkie ME, Plant MJ, Edwards L, Brown CB. Icodextrin 7.5% dialysate solution (glucose polymer) in patients with ultrafiltration failure: extension of CAPD technique survival. *Perit Dial Int* 1997; 17(1):84–7.
9. Davenport A, Willicombe M. Comparison of fluid status in patients treated by different modalities of peritoneal dialysis using multi-frequency bioimpedance. *Int J Artif Organs* 2009; 32:779–86.
10. McCafferty K, Fan S, Davenport A. Extracellular volume expansion, measured by multifrequency bioimpedance, does not help preserve residual renal function in peritoneal dialysis patients. *Kidney Int* 2014; 85:151–7.
11. Davenport A, Agarwal B, Wright G, Mantzoukis K, Dimitrova R, Davar J, et al. Can non-invasive measurements aid clinical assessment of volume in patients with cirrhosis? *World J Hepatol* 2013; 5(8):433–8.
12. Kyle UG, Bosaeus I, De Lorenzo AD, Deurenberg P, Elia M, Gómez JM, et al.; Composition of the ESPEN Working Group. Bioelectrical impedance analysis-part II: utilization in clinical practice. *Clin Nutr* 2004; 23(6):1430–53.
13. Chung SH, Heimbürger O, Lindholm B. Poor outcomes for fast transporters on PD: the rise and fall of a clinical concern. *Semin Dial* 2008; 21(1):7–10.
14. Konings CJ, Kooman JP, Schonck M, Cox-Reijven PL, van Kreel B, Gladziwa U, et al. Assessment of fluid status in peritoneal dialysis patients. *Perit Dial Int* 2002; 22(6):683–92.
15. Davies SJ, Woodrow G, Donovan K, Plum J, Williams P, Johansson AC, et al. Icodextrin improves the fluid status of peritoneal dialysis patients: