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SHORT REPORTS

Increase in Extracellular Hydration Status After Initiating Peritoneal Dialysis Electively

Renal replacement therapy is designed to treat uremic symptoms and correct hypervolemia. We hypothesized that starting peritoneal dialysis (PD) should reduce overhydration, and we measured body composition and hydration status using bioimpedance in PD patients prior to training and then at the first assessment of peritoneal membrane function. We studied 100 consecutive patients with a planned start to PD, without peritoneal infections or mechanical catheter problems, mean age 54.7 ± 17.1 years, 57% male and 25% diabetic. Extracellular water (ECW) overhydration increased from -0.06 (-1.21 to 0.97) L to 0.96 (0.50 to 3.01) L, $p < 0.001$. Fat mass increased from 22.7 ± 11.1 to 23.7 ± 11.3 kg, $p = 0.007$). The change in ECW/total body water (TBW) was associated with age (β 0.065, $p < 0.001$), increasing comorbidity (β 1.107, $p = 0.005$), faster peritoneal protein transport (β 1.84, $p < 0.04$), and negatively with serum albumin (β -0.208, $p < 0.001$), and residual renal function (β -0.725, $p = 0.026$). Patients who had an increase in ECW/TBW had higher C-reactive protein (CRP) both before starting (16.8 ± 24.1 vs 7.7 ± 18.9 mg/L), and when established on PD (15.0 ± 31.8 vs 4.6 ± 5.1 mg/L), $p < 0.05$. Rather than a reduction in ECW hydration status, overhydration increased after starting PD. This was greater for older more comorbid patients and those with an inflammatory milieu and lower residual renal function. These factors should be considered when deciding upon initial PD prescriptions to limit ECW overhydration before information on peritoneal membrane function becomes available.

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

Peritoneal dialysis (PD) is designed to correct overhydration by removing excess fluid by ultrafiltration. Exposure to peritoneal dialysates potentially increases peritoneal capillary surface area, so clinical guidelines recommend delaying assessments of peritoneal membrane function for at least 6 weeks after starting PD, to allow for adaptation within the peritoneal cavity (1). We wished to determine whether initiation of PD improves hydration status.

STUDY DESIGN AND METHODS

We prospectively studied 100 consecutive patients attending for their first assessment of peritoneal membrane function, 6 – 8 weeks after training, and compared paired bioimpedance assessments. All patients started PD electively, none as an emergency, or urgent start, and no patient had suffered peritonitis or mechanical problems with their catheter. Ninety-eight patients used lactate- and glucose-containing dialysates, and 2 used neutral pH dialysates due to infusion pain. Icodextrin 7.5% was used as the day dwell for all patients using automated PD (APD) with a day dwell and as a night-time dwell for those treated by continuous ambulatory PD (CAPD) (Baxter Healthcare, Deerfield, Illinois, USA).

Serum biochemistry samples were analyzed using standard methods and 4-hour peritoneal equilibration tests (PET) used 2 liters of 2.27% dialysate. Peritoneal dialysis adequacy was calculated from 24-hour spent dialysate samples, and residual renal function (RRF) from 24-hour urine collections. Normalized protein nitrogen appearance rate (nPNA) was estimated from 24-hour urinary and peritoneal urea losses. Patient comorbidity used Stoke-Davies grading.

Multi-frequency bio-impedance analysis (MFBIA) used a standardized protocol (InBody 720 Body Composition Analysis, Biospace, Seoul, South Korea) (2). Volume status was determined by the ratio between extracellular and total body water (ECW/TBW ratio) (3), and by calculating ECW overhydration (4).

This audit fully complied with UK NHS clinical audit guidelines. Statistical analysis was by standard methods using GraphPad (GraphPad version 6.0, San Diego, CA, USA) and SPSS (SPSS version 22.0, Chicago, IL, USA), and statistical significance was taken at $p < 0.05$.

RESULTS

The mean patient age was 54.7 ± 17.1 years, 57% male, and 25% diabetic.

Extracellular water overhydration increased from a median of -0.06 L (-1.21 to 0.97) to 0.96 L (0.50 to 3.01), $p < 0.001$. Although there was no significant change in body weight, (75.5 ± 18.5 vs 75.2 ± 18.4 kg), there were falls in body cell mass (BCM) (33.5 ± 8.7 vs 32.7 ± 8.4 kg, $p = 0.031$) and ICW (23.64 ± 6.02 vs 23.21 ± 5.97 L, $p = 0.033$), but neither the fall in ECW (15.31 ± 3.96 vs 15.08 ± 3.78 L), nor skeletal muscle mass (28.5 ± 7.9 vs 28.0 ± 7.9 kg) were significant. There was a gain in fat mass (from 22.7 ± 11.1 to 23.7 ± 11.3, $p = 0.007$ kg), and percentage body fat (from 29.8 ± 10.9 to 30.9 ± 10.9%, $p = 0.013$). Serum albumin fell (39.0 ± 5.6 vs 37.5 ± 5.0 g/L,

$p < 0.001$), but there was no significant change in C-reactive protein (CRP); 12.8 ± 22 vs 10.3 ± 24 mg/L.

Patients were divided into those who had an increase in ECW/TBW and those who had either no change or a decrease in ECW/TBW (Table 1). Body composition was not different. Those with increased ECW/TBW had higher CRP. There were no differences in RRF, 24-hour ultrafiltration, serum albumin, comorbidity grades, diabetes, age, or sex, but there was a difference in ethnicity.

On univariate analysis, ECW/TBW was associated with age, comorbidity, serum CRP, PET creatinine transporter, serum creatinine, and negatively with serum albumin (Figure 1), nPNA, PET ultrafiltration volume, and RRF (Supplementary Table). On multivariable analysis the change in ECW/TBW was independently associated with age (β 0.065, $p < 0.001$), increasing comorbidity (β 1.107, $p = 0.005$), faster peritoneal protein transport (β 1.84, $p < 0.04$), and negatively with serum

TABLE 1
Patients with Increased ECW/TBW vs Patients with Stable or Falling ECW/TBW[a]

Variable	Increased ECW/TBW *n*=54	Stable or reduced ECW/TBW *n*=46	*P* value
Age, years	55±18	55±16	>0.05
Male sex	66.7%	45.7%	0.056
Diabetes mellitus	31.5%	17.4%	0.105
Caucasian	53.7%	30.4%	
Afro-Caribbean	24.1%	21.7%	
South Asian	14.8%	43.5%	0.035
Comorbidity[b] grade 0	40.7%	45.7%	
Comorbidity grade 1	42.6%	50%	
Comorbidity grade 2	16.7%	4.3%	0.32
Weight, kg pre-PD	74.7±17.0	76.7±20.5	>0.05
Weight, kg at PET	75.3±16.6	75.6±20.9	>0.05
ICW, liters pre-PD	23.59±5.97	23.25±6.26	>0.05
ICW, liters at PET	23.18±5.56	23.04±6.62	>0.05
ECW, liters pre-PD	15.10±3.90	15.14±4.15	>0.05
ECW, liters at PET	15.27±3.66	14.73±4.03	>0.05
TBW, liters pre-PD	38.70±9.77	38.40±10.33	>0.05
TBW, liters at PET	38.44±9.15	37.77±10.59	>0.05
Skeletal muscle mass pre-PD, kg	29.04±8.19	28.3±7.42	>0.05
Skeletal muscle mass at PET, kg	28.50±7.38	28.05±8.04	>0.05
Fat mass pre-PD, kg	22.27±11.48	23.83±10.92	>0.05
Fat mass at PET, kg	23.37±10.74	24.25±12.03	>0.05
Serum albumin, g/L pre-PD	39±6	39±5	>0.05
Serum albumin, g/L at PET	37±5	38±4	>0.05
CRP, mg/L pre-PD	16.78±24.10	7.67±18.9	<0.05
CRP, mg/L at PET	15.02±31.81	4.57±5.11	<0.05
Urine volume, mL/day	1399±907	1392±927	>0.05
RRF, mL/min/1.73 m^2	6.9 (3.2–9.9)	5.9 (3.2–9.3)	>0.05
Liters creatinine cleared/wk/1.73 m^2	70±49	82±70	>0.05
4-hour D/P creatinine	0.75±0.13	0.70±0.15	>0.05
4-hour D/P protein	0.11±0.07	0.12±0.19	>0.05
PET ultrafiltration volume, mL	300 (100–500)	200 (100–300)	<0.05
24-hour peritoneal ultrafiltration, mL	400 (82–794)	353 (78–739)	>0.05
APD dry day	16.7%	26.1%	>0.05
CAPD	24.1%	13.0%	>0.05
APD wet day	59.3%	60.9%	0.27
Frusemide dose pre-PD, mg/day	80 (0-80)	80 (0-80)	>0.05
Frusemide dose at PET, mg/day	250 (250–250)	250 (250–250)	>0.05

ECW = extracellular water; TBW = total body water; ICW = intracellular water; PD = peritoneal dialysis; PET = peritoneal equilibration test; CRP = C-reactive protein; RRF = residual renal function (combined urinary urea and creatinine clearance); APD = automated PD (over-night cycler); CAPD = continuous ambulatory PD; D/P = dialysate/plasma; SD = standard deviation; IQR = interquartile range.

[a] Comparison of patients with increase in ECW/TBW at the time of first peritoneal transport assessment compared with ECW/TBW prior to PD training compared with patients with stable or falling ECW/TBW.

[b] Stoke-Davies comorbidity grade.

Data expressed as mean±SD, median (IQR) or percentage.

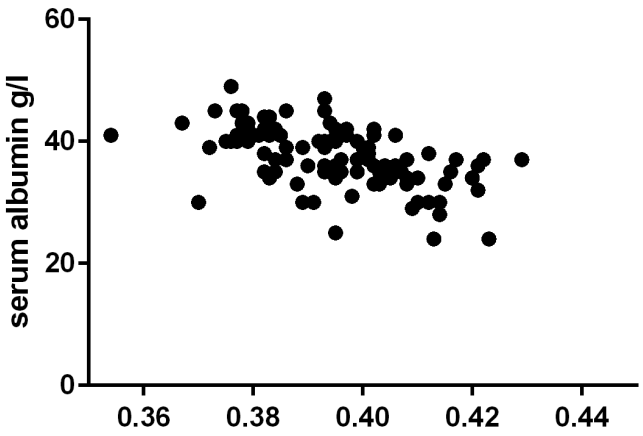

Figure 1 — Serum albumin and extracellular water (ECW)/total body water (TBW) ratio at time of first peritoneal membrane assessment. Pearson correlation r=-0.54, $p<0.001$.

albumin (β -0.208, $p < 0.001$), and RRF (β -0.725, $p = 0.026$) (Supplementary Table).

DISCUSSION

Dialysis is initiated to treat uremic symptoms and correct hypervolemia. One would expect that establishing patients on PD would result in an improvement in hydration and nutritional status. However, we found that patients electively starting PD, with no mechanical complications or peritoneal infections, had a relative increase in ECW hydration. This was associated with a fall in serum albumin, which could represent dilution due to ECW expansion (5), and an increase in fat mass potentially secondary to peritoneal glucose absorption. We divided patients into those with increased ECW/TBW or stable/fall in ECW/TBW (3), and those with increased ECW/TBW had higher serum CRP, and greater fall in albumin. Inflammation may increase extravascular albumin transfer and ECW expansion (6) and loss of BCM.

The ECW/TBW ratio was positively associated with age, serum CRP, faster peritoneal creatinine transport and comorbidity, and negatively with nPNA, serum albumin, and RRF. As such, an increased ECW/TBW ratio could be associated with both systemic and local peritoneal inflammation. Inflammation can increase large pore transport, and we observed a stepwise increase in ECW/TBW as 4-hour dialysate/plasma (D/P) protein increased. Residual renal function was negatively associated with ECW/TBW (7). However, ECW expansion does not necessarily correlate with plasma volume expansion, as this excess fluid is not readily accessible (8,9).

Our observational study can only report associations and not causality. Limitations to our study include no baseline assessment of RRF, however as these were stable patients starting PD it is unlikely that there would have been major changes in RRF in such a short time. Our study population predominantly used APD, and the shorter dwell time can lead to differences in water compared with sodium clearances with glucose dialysates. However, most APD patients also had a daytime icodextrin exchange.

Our study demonstrates that initiating PD is associated with a relative increase in ECW hydration. The change in ECW/TBW was greater in those patients who were older and more comorbid and had lower serum albumin, higher CRP, and faster peritoneal protein transport, suggesting that this is driven by an inflammatory phenotype, and greater for those with less RRF. These findings should be considered when first prescribing PD regimens for patients initiating PD.

DISCLOSURES

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