SHORT REPORTS

Clinical Experience Using Bioimpedance to Optimize Blood Pressure Control

KEY WORDS: Bioimpedance; blood pressure; body composition; overhydration; residual renal function.

The relationship between volume expansion and cardiac morbidity has been widely described, but an accurate assessment of fluid status based on the clinical parameters of peripheral edema, blood pressure, and central venous pressure remains a challenge (1). Equally, preserving urine output is of great importance (2), and without accurate measures of hydration status, there is a risk that aggressive fluid removal may precipitate dehydration and accelerate residual renal function (RRF) loss (3).

The Body Composition Monitor (BCM; Fresenius Medical Care, Bad Homburg, Germany) is a multi-frequency bioimpedance spectroscopy device that has been used in both the hemodialysis and peritoneal dialysis (PD) populations (4,5). We set out to describe the impact on RRF when the BCM is used to guide clinical management of patients deemed to be severely overhydrated. We also compared outcomes in the overhydrated patients with outcomes in other contemporaneously treated cohorts of patients (patients that were defined by the BCM to be euvolemic or dehydrated).

METHODS

Using the BCM, whole-body bioimpedance was measured in supine patients with PD fluid *in situ*. Euvolemia was considered to be a measurement between -1.1 L and $+1.1$ L, the 90th centile limits for a normal population. Individuals found to be significantly overhydrated (>2 L) were treated in a multidisciplinary clinic. The clinic focused on optimizing the dialysis prescription and advising on salt and fluid restriction (which often resulted in short-term changes to the dialysis prescription until patients achieved their target weight). Results of the BCM measurements were available to clinicians throughout the study period, although the clinicians used their clinical judgment to set target weights for patients who were

found to be either euvolemic or dehydrated. We compared patients who received active intervention (overhydrated patients) with those who were dehydrated ($n = 14$) or with uric euvolemic patients matched for age, sex, dialysis vintage, and ethnicity ($n = 13$).

Lean and fat tissue mass measured by bioimpedance were also recorded for nutrition status monitoring to detect any changes that might result from prescriptions for increased PD glucose. Subjective global assessment scores were also obtained at the time of the BCM measurements.

Prescribed antihypertensive drugs were recorded at each clinic visit, and we quantified the number of drugs prescribed with reference to the relationship between the prescribed dose and the maximum licensed dose for hypertension. Thus, ramipril prescribed at 10 mg daily was assigned a value of 1.0, but if prescribed at 5 mg daily, was assigned a value of 0.5. Blood pressure was measured at each clinic visit.

Residual renal function, defined using urine volume and the mean of urea and creatinine clearances normalized to 1.73 m² body surface area, was assessed every 3 months after baseline for patients who were overhydrated (standard practice for our unit was once every 6 months).

Statistical Analysis: Paired t-tests were used to compare intragroup changes, and one-way ANOVA was used to compare intergroup differences. A two-tailed p value less than 0.05 was considered to be statistically significant. Nonparametric analyses were performed using the Wilcoxon signed rank and Kruskal–Wallis tests.

RESULTS

Follow-up was completed for 13 of the 19 patients who were identified by the BCM as severely overhydrated. The reasons for drop-out were commencement on hemodialysis because of type 1 ultrafiltration failure [ultrafiltration less than 100 mL after 4 hours of a 3.86% glucose dwell ($n = 2$); transfer to hemodialysis after severe peritonitis ($n = 2$); death from congestive cardiac failure without achievement of BCM-defined euvolemia ($n = 1$); and failure to achieve euvolemia

despite a follow-up period of 6 months ($n = 1$). The remaining 13 patients achieved BCM-defined euvoolemia after a mean of 3.7 months. Of those 13 patients, 10 (77%) remained euvolemic for at least a further 3 months. Mean hydration status was $+0.5$ L at a mean of 9.4 months from baseline.

As shown in Table 1, use of antihypertensives declined after BCM-defined euvoolemia was achieved. Median (interquartile range) values fell from 1.00 (0.25 – 1.8) to 0.38 (0.0 – 1.08), $p < 0.05$, but blood pressure did not change significantly. The mean $\pm$ standard error of the arterial pressure was 100 ± 6 mmHg at baseline and 99 ± 6 mmHg at the end of follow-up.

Of the 13 patients that were severely overhydrated, only 1 had urine output of less than 100 mL daily. As in Table 1 shows, no statistically significant differences were observed in 24-hour urine output or weekly creatinine clearance at baseline and at the end of the study.

During follow-up, 4 patients switched their longest-dwell glucose bags to icodextrin (Extraneal: Baxter Healthcare, Compton, UK), and 2 patients switched from continuous ambulatory PD to automated PD. We estimated daily glucose absorption using the Renalsoft application (Baxter Healthcare) and found that absorption increased to 460 ± 58 kCal from 338 ± 43 kCal in 8 patients; although for the entire cohort, we observed no statistically significant change in mean glucose absorption. Of the 13 overhydrated patients, 5 achieved euvoolemia without any permanent change to their dialysis prescription.

Adverse Events: During follow-up, no adverse events that required medical admission were attributed to the change in fluid balance. One patient known to have cardiac failure (New York Heart Association class III) reported dizziness and hypotension at his euvolemic weight. He was managed as an outpatient with an increment to his target weight. In addition, as described earlier, 1 patient died with severe congestive heart failure (New York Heart Association class IV). Because of the severity of the cardiac failure and hypotension, he never achieved bioimpedance-defined euvoolemia.

Comparison with Dehydrated and Euvolemic Patients: We identified contemporary PD patients who were either consistently dehydrated ($n = 17$) or euvolemic ($n = 54$). Among them, 14 dehydrated and 42 euvolemic patients were uric (urine output > 100 mL daily). We then matched 13 uric euvolemic patients 1:1 to the overhydrated patients. Table 1 shows the demographics of the comparator cohorts. During a mean follow-up period of 7.6 ± 0.6 months, mean hydration status by BCM remained

similar: 0.1 ± 0.1 L to 0.2 ± 0.2 L, $p =$ nonsignificant. No statistically significant decline in RRF was observed, but the weekly creatinine clearance fell to 34 L from 43 L, and daily urine output fell to 760 mL from 950 mL.

Among dehydrated uric patients, the mean BCM reading was -2.6 , and these patients remained dehydrated during the study. Their BCM hydration was -2.4 ± 0.2 L after a follow-up period of 8.6 ± 0.5 months. These patients were found to have a statistically significant decline in renal function, with their weekly creatinine clearance falling to 24 L from 33 L ($p < 0.05$), although their decline in daily urine output did not reach statistical significance (to 550 mL from 700 mL, $p = 0.066$). In this group, prescription of antihypertensive drugs remained unchanged, as did blood pressure (Table 1).

Serum sodium and albumin have been shown to correlate with hydration status measured by bioimpedance methods. We observed no statistically significant differences between the overhydrated group and the euvolemic and dehydrated groups (Table 1). However, during the follow-up period, the overall group showed a small but statistically significant reduction in serum sodium (to 138.7 ± 0.5 mmol/L from 140.4 ± 0.6 mmol/L, $p < 0.001$). The clinical significance of that reduction is unclear, particularly given the lack of any significant differences between the 3 volume groups for change in sodium.

DISCUSSION

The algorithm used by the BCM machine to generate “overhydration” estimates has not been validated for PD patients. However, if the BCM were to provide accurate and precise estimates of hydration status, it would offer a significant advantage over current clinical methods of fluid assessment. Results from our study of severely overhydrated patients must be interpreted with great caution because of the small sample size. Nevertheless, it was reassuring that use of the BCM appeared to permit reductions in overhydration parameters without inducing clinical symptoms of dehydration or accelerated loss of RRF. Moreover, achieving BCM-defined euvoolemia resulted in a nearly 50% reduction in the use of antihypertensive medication.

Although the primary aim of the present report was to describe the effects of using the BCM to manage hydration status in PD patients deemed to be severely overhydrated, we tried to compare those patients with relevant cohorts of consistently dehydrated or euvolemic patients (defined by the BCM) treated contemporaneously. The comparator patients that were studied during the follow-up period were well matched for age, dialysis

TABLE 1
Comparison of Peritoneal Dialysis Patients Who Were Overhydrated (Corrected), Euvolemic, and Dehydrated^a

Variable	Overhydrated (corrected)			Study group Euvolemic			Dehydrated			
Patients (<i>n</i>)	13			13			14			
Age (years)	64±3			62±1			59±4			
Men (%)	85			85			29			
Diabetes mellitus (%)	62			23			29			
Dialysis vintage (years)										
Median	1.3			2.6			1.3			
Range	0.5–2.3			0.7–3.5			0.1–2.0			
Ethnicity (% white)	38			38			29			
	Baseline		Follow-up	Baseline		Follow-up	Baseline		Follow-up	<i>p</i> Value ^b
Time (months)	—		9.4±1.0	—		7.6±0.6	—		8.6±0.5	
Weight (kg)	82.7±4.6		83.8±5.1	73.8±4.3		75.4±4.8	82.6±4.0		85.3±4.2	NS
Hydration status (L)	+2.4±0.4		+0.5±0.2	0.1±0.1		0.2±0.2	−2.6±0.2		−2.4±0.2	<0.0001
Weekly CCr (L)	37±9	<—> <i>p</i> =NS	25±6	43±8	<—> <i>p</i> =NS	33.8±8	33±6	<—> <i>p</i> <0.05	24±6	NS
Daily urine output (mL)	550±130	<—> <i>p</i> =NS	480±130	950±190	<—> <i>p</i> =NS	760±170	700±150	<—> <i>p</i> =0.07	550±170	NS
Systolic BP (mmHg)	146±10	<—> <i>p</i> =NS	145±8	137±6	<—> <i>p</i> =NS	149±7	140±5	<—> <i>p</i> =NS	137±6	NS
Diastolic BP (mmHg)	76±5	<—> <i>p</i> =NS	76±3	81±2	<—> <i>p</i> =NS	86±3	84±3	<—> <i>p</i> =NS	82±3	NS
MAP (mmHg)	100±6	<—> <i>p</i> =NS	99±4	100±3	<—> <i>p</i> =NS	107±4	103±3	<—> <i>p</i> =NS	100±4	NS
α-HT drugs										
Median	1.00	<—>	0.38	0.25		0.5	0.25		0.25	
Range	0.25–1.8	<i>p</i> <0.02 ^c	0.0–1.08	0.25–0.5		0.25–0.5	0.03–1.0		0.13–0.88	<0.02 ^d
Serum										
Albumin (mmol/L)	37.5±1.7	<—> <i>p</i> =NS	38.3±1.1	39.1±1.1	<—> <i>p</i> =NS	37.6±1.0	40.7±1.0	<—> <i>p</i> =NS	40.1±0.9	NS
Sodium (mmol/L)	138.8±1.1	<—> <i>p</i> =NS	137.7±0.8	142.2±1.0	<—> <i>p</i> <0.05 ^d	139.8±1.0	140.2±0.8	<—> <i>p</i> <0.05 ^d	138.9±0.9	NS

CCr = creatinine clearance (normalized to 1.73 m² body surface area); BP = blood pressure; MAP = mean arterial pressure.

^a Unless otherwise noted, values are expressed as mean ± standard error of the mean or as median (1st – 3rd quartile).

^b One-way analysis of variance, comparing the change between the 3 columns.

^c By Wilcoxon signed rank test.

^d By Kruskal–Wallis test.

^d If Bonferroni correction is applied, result is deemed statistically nonsignificant.

vintage, and ethnicity. However, the higher incidence of diabetes mellitus in the overhydrated patients is striking, and a causal link is possible. Diabetes may be associated with a greater incidence of ischemic heart disease and cardiac failure, and hyperglycemia can cause thirst.

It is more difficult to explain why women predominated in the dehydration cohort. That observation raised concern that perhaps the BCM's algorithm underestimates total body water in women, particularly given that the clinicians looking after these patients did not think that they were hypovolemic, requiring active treatment to increase hydration. However, it is particularly pertinent that these patients showed a decline of RRF that reached statistical significance in the case of creatinine clearance. Although the euvoletic and overhydrated groups were of similar size, the changes in RRF in these latter cohorts were not statistically significant. Perhaps the BCM accurately diagnosed dehydration that was not clinically evident, and that dehydration led to greater RRF decline.

We reiterate that great care must be taken when drawing conclusions from the present study. The short follow-up period also negates our ability to report on cardiovascular outcomes other than blood pressure. However, one of the strengths of the study is that we intervened only in very overhydrated patients, meaning that, to achieve BCM-defined euvolectmia, large changes in extracellular water were induced. Despite those large changes, we observed no evidence suggesting that the patients became dehydrated, and importantly, we were able to maintain euvolectmia in most of them.

We suggest that multi-frequency bioimpedance is safe and effective in the PD setting to improve fluid overload and optimize blood pressure control.

DISCLOSURES

SLF has received lecture fees from Fresenius Medical Care and Baxter Health Care. The Renal Unit at The Royal London and St. Bartholomew's Hospitals have received research and educational grants from both companies.

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