Lowering Postdialysis Plasma Sodium (Conductivity) to Increase Sodium Removal in Volume-Expanded Hemodialysis Patients: A Pilot Study Using a Biofeedback Software System

Jaimi Manlucu, MD, FRCPC, Kerri Gallo, RN, CNS, Paul A. Heidenheim, MSoc, and Robert M. Lindsay, MD, FRCPC, FRCP(Edin), FRCP(Glasg)

Background: Extracellular fluid expansion is common in hemodialysis patients. Aggressive fluid removal may lead to intradialytic complications. High dialysate sodium concentrations may lessen complications, but may increase extracellular volume. We hypothesized that decreasing plasma sodium concentration during dialysis will increase sodium removal and decrease extracellular volume.

Study Design: Pilot clinical trial.

Setting & Participants: 16 patients with end-stage kidney disease treated using thrice-weekly hemodialysis at a university teaching hospital hemodialysis unit.

Intervention: Stepwise decrease in postdialysis plasma sodium level (calculated as end-of-session plasma conductivity) over 4 phases effected by dialysate conductivity measurement cells and a biofeedback software system (Diacontrol; Hospal, www.hospal.it) that allowed alteration of dialysate inlet conductivity and calculation of plasma conductivity.

Outcomes: Decrease in postdialysis plasma sodium (conductivity) levels, sodium removal, redistribution of body water, and effect of these on interdialytic weight gain and blood pressure.

Measurements: Plasma sodium and conductivity values (the latter measured in millisiemens per centimeter); ionic mass balance (sodium removal); bioelectrical impedance analysis measurements of body-water compartments and phase angle; interdialytic weight gain; and blood pressure.

Results: Plasma sodium concentrations at the end of dialysis were decreased from 137.8 (phase 1) to 135.6 mmol/L (phase 4) and end-of-session plasma conductivity values were decreased from 14.0 (phase 1) to 13.5 mS/cm (phase 4; all mean values). Ionic mass balance increased from 383 to 480 mmol. Extracellular water was significantly decreased, phase angle was increased, and blood pressure and interdialytic weight gain were decreased. Plasma sodium levels correlated significantly with plasma conductivity; thus, changes in postdialysis plasma sodium levels can be inferred from changes in end-of-session plasma conductivity values.

Limitations: Small number of patients. No information for dietary sodium intake.

Conclusion: To decrease extracellular volume, it may be necessary to add diffusive to convective sodium losses.

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INDEX WORDS: Plasma conductivity; sodium balance; body-water compartments; blood pressure; interdialytic weight gain; hemodialysis.

Editorial, p. 1

Salt and water balance influences outcomes of patients with chronic kidney disease on maintenance hemodialysis therapy.[1-3] Persistent salt and volume overload limit quality of life and influence cardiovascular morbidity and mortality. Unfortunately, aggressive removal of interdialytic sodium and water load may result in intradialytic hemodynamic instability.[4-6] Dialysate sodium concentration has a major influence on the mass of sodium removed. Currently, common clinical practice is to prescribe universal default dialysate sodium for all patients despite variability in individual patient's sodium intake. Furthermore, "high" sodium dialysate levels often are used to provide hemodynamic stability during treatments.[7] However, these may be of a sodium concentration greater than the patient's own plasma water sodium concentration, causing sodium diffusion into the patient. During the

From the Division of Nephrology, Department of Medicine, London Health Sciences Centre, and The University of Western Ontario, London, Ontario, Canada.

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Address correspondence to Robert M. Lindsay, MD, FRCPC, FRCP(Edin), FRCP(Glasg), Rm A2-345, London Health Sciences Centre, 800 Commissioners Rd E, London, Ontario, Canada N6A 4G5. E-mail: robert.lindsay@lhsc.on.ca

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time this state persists, net sodium loss is effected solely by convection and is dependent on the volume of ultrafiltration possible. These factors help maintain a long-term state of sodium and fluid excess. Individualized dialysate sodium concentrations may be a solution.

Advancements in dialysis technology now make this feasible. Software in dialysis machines equipped with conductivity measurement cells has the ability to alter the dialysate inlet conductivity and can measure effective ionic dialysance (a surrogate for effective solute clearance) and ionic mass balance (a surrogate for sodium loss or gain).[8,9] Plasma conductivity (a surrogate for plasma sodium concentration) also can be determined when ionic dialysance, dialysate inlet and outlet conductivities, and dialysate and ultrafiltration flow rates are known. Through serial plasma conductivity monitoring and appropriate adjustments in dialysate conductivity, the Diacontrol (Hospal, www.hospal.it) version of such software makes it possible for a physician or nurse to set desired postdialysis plasma conductivity.

With the use of Diacontrol, we carried out a pilot study to examine the potential efficacy and safety of individualized serial decreases in postdialysis plasma conductivity and their effects on ionic mass balance, interdialytic weight gain, blood pressure control, and body-water distribution between intra- and extracellular compartments. We hypothesized that progressively decreasing postdialysis plasma conductivity to levels less than those found at the start of the dialysis treatment will increase ionic mass balance (implies sodium removal) by adding a diffusive component to removal by convection (ultrafiltration). This may be sufficient to decrease extracellular volume, interdialytic weight gain, and blood pressure.

METHODS

Setting and Patients

Sixteen patients with end-stage renal failure receiving maintenance out-patient hemodialysis treatments 3 times weekly at the Adam Linton Dialysis Unit, Victoria Hospital, London Health Sciences Centre, London, Canada, were studied. All had a well-functioning dialysis blood access (arteriovenous fistula, graft, or cuffed tunneled central catheter). All were chosen because of known stability during dialysis treatments and the ability to give informed consent. No patient was enrolled in another research study that required a set hemodialysis regimen. Demographics of these patients are listed in Table 1. This study was approved by The University of Western Ontario Research Ethics Committee (no. 12008E). All patients gave signed informed consent.

Table 1. Demographics of Study Patients With Number of Antihypertensive Medications Used

Characteristic	No. of Patients
Sex	
Men	11
Women	5
Cause of ESRD[a]	
Diabetic nephropathy	5
Hypertensive nephrosclerosis	3
Glomerulonephritis	1
Renovascular disease	1
Immunoglobulin A nephropathy	1
Multiple myeloma	1
No. of BP medications prescribed[b] prestudy	
0	3
1	7
2	4
3	2
4	0
No. of BP medications prescribed[b] poststudy	
0	3
1	8
2	2
3	2
4	1

Note: Average age of study patients was 63 ± 11 (SD) years.

Abbreviations: BP, blood pressure; ESRD, end-stage renal disease.

[a]Cause missing for 4 patients.

[b]Number of antihypertensive medication pills per day per patient.

Intervention

Each patient was followed up over a 7-week period in which target postdialysis (end-of-session) plasma conductivity gradually was decreased in the following stages: (1) phase 1 (week 1): no target set; patients dialyzed against a standard default dialysate sodium concentration of 140 mmol/L throughout; (2) phase 2 (weeks 2 and 3): end plasma conductivity targeted to equal the first plasma conductivity calculated using Diacontrol software (18 minutes into dialysis); (3) phase 3 (weeks 4 and 5): end plasma conductivity targeted to be 0.1 mS/cm less than the first value (measured at 18 minutes); and (4) phase 4 (weeks 6 and 7): end plasma conductivity targeted to be 0.2 mS/cm less than the first value (measured at 18 minutes).

In choosing these postdialysis conductivities, patient safety was the first consideration. By phase 4, the target could lead

to a postdialysis plasma sodium level of approximately 135 mmol/L. In previous studies, Lambie et al[10] and Selby et al[11] had safely decreased postdialysis plasma conductivity to similar levels. The study protocol determined that if intradialytic hypotension requiring intervention occurred in any patient, that individual would have the postdialysis plasma conductivity target increased by 0.1 mS/cm and remain at that level for the study duration.

Dialysis was conducted using Integra Dialysis Machines (Gambro Inc, www.gambro.com) fitted with the Diacontrol system. All machines were capable of downloading data to the Exalis data retrieval system (Gambro Inc). Exalis recorded all plasma conductivities, dialysate conductivities, ionic mass balances, and machine parameters during the course of each dialysis treatment. Data recorded manually from dialysis records included pre- and postdialysis weights (kilograms); interdialytic weight gain (kilograms); predialysis systolic, diastolic, and mean arterial blood pressures (millimeters of mercury); intradialytic events (eg, hypotension [decrease in systolic blood pressure $\geq$20 mm Hg), cramps, etc) requiring intervention (eg, stopping ultrafiltration, placing patient in Trendelberg position, and/or giving intravenous saline); and changes in antihypertensive medication.

Bioelectrical impedance analysis (BIA) measurements of body composition were made during weeks 1 and 7 using a single-frequency analyzer (Bioelectrical Body Composition Analyzer Quantum II; RJL Systems, www.rjlsystems.com). BIA is based on the measurement of resistance and reactance when a constant alternating electrical current is applied to a patient. Empirical equations are used to predict total-body water from resistance and total-body cell mass from the ratio of resistance to reactance. Measurements were made before the dialysis treatment with patients recumbent for at least 10 minutes before measurement. Parameters of interest included total-body water volume, extracellular water volume, extracellular water as a percentage of total-body water, and the ratio of extracellular water to intracellular water volume. The BIA system software provided both actual and "desired" values based on resistance and reactance values measured using body electrodes. Phase angle also was measured using BIA. This, an estimate of cellular health, is measured as the linear relationship between resistance and reactance. A high phase angle value represents large quantities of metabolically active cells and lean body mass, which are highly conductive (low resistance) because of high levels of water and conducting electrolytes.

Blood samples were obtained before dialysis, at 18 minutes, and at the end of dialysis from the dialysis arterial blood tubing for the laboratory measurement of plasma sodium on 1 of 3 dialysis treatments in phase 1 and 2 of 6 dialysis treatments in phase 4. These were drawn to compare plasma sodium levels with plasma conductivities (thereby confirming the accuracy of the ionic dialysance monitor [Diascan, Hospal]) and assess plasma sodium profiles across dialysis during these phases.

Objectives and End Points

The primary objectives of this study were determining whether a decrease in postdialysis plasma conductivity (sodium): (1) can be achieved using Diacontrol and whether it is associated with increased ionic mass balance (ie, sodium removal) by dialysis; (2) is related to redistribution of body water by examining extracellular water as a percentage of total-body water volume and extra- to intracellular water volume ratio; and (3) is related to a change in phase angle (a BIA-derived variable related to body cell mass).

The primary end points were postdialysis plasma conductivity, ionic mass balance, extracellular water as a percentage of total-body water volume, extra- to intracellular water volume ratio, and phase angle.

Secondary objectives were to examine: (1) the effects of Diacontrol use on blood pressure control and interdialytic weight gain and (2) the safety of Diacontrol use.

Statistical Methods

Initially, descriptive statistics were run on all parameters to identify outliers, patterns of missing data, and the skewness of the distributions of variables measured at the interval/ratio level. No extreme outliers were found. One patient died during the course of the study and consequently was missing the bulk of follow-up data; this patient was excluded from all further analysis, leaving a sample of 15. Several variables were highly skewed; hence the decision to use nonparametric statistical methods when appropriate.

Comparisons between study phases were performed using both paired-samples *t* test and nonparametric Wilcoxon test. Correlational analyses used the Pearson bivariate correlation coefficient and rank-order correlations, and regression analysis was a linear regression using the block-entry method. Graphical analyses were achieved using a scatter plot, and a cluster error bar graph was used to illustrate selected phase comparisons.

All analyses were performed using Statistical Package for the Social Sciences (SPSS), version 15.0, release 15.0.0 (SPSS Inc, www.spss.com).

RESULTS

All 15 patients tolerated the individualized gradual decrease in postdialysis target plasma conductivity with very minimal symptoms during the 7-week period**.** There were 4 episodes of intradialytic hypotension (decrease in systolic blood pressure $>$20 mm Hg) during the entire study period, none of which required intervention. The primary end points of interest were the decrease in plasma conductivity, changes in total ionic mass balance, and BIA measurements (quantifying body-water distribution and phase angle). Changes in interdialytic weight gain and blood pressure also were of interest.

Plasma Conductivity

Significant decreases in postdialysis plasma conductivity were noted through all experimental phases. This was most marked in phase 4, decreasing by a mean of 0.473 mS/cm in compari-

Table 2. Plasma Conductivities and Ionic Mass Balance Values During the Course of the Study

	Phase				
	1	2	3	4	P^a
Plasma conductivity (mS/cm)					
At 18 min	13.96 ± 0.36	13.97 ± 0.23	13.82 ± 0.29	13.793 ± 0.2086	0.03
Postdialysis	14.02 ± 0.05	13.87 ± 0.11	13.73 ± 0.21	13.547 ± 0.0516	<0.001
Ionic mass balance (mmol)	382.60 ± 112.66	400.60 ± 105.08	420.60 ± 121.74	480.27 ± 145.62	0.005

Note: Plasma conductivity (millisiemens per centimeter) correlates with plasma sodium (millimoles per liter) and ionic mass balance represents sodium loss by dialysis.

[a]Phase 1 versus phase 4, nonparametric Wilcoxon signed-rank test.

son to phase 1 ($P < 0.001$). However, significant decreases were not observed in the 18-minute plasma conductivities until phase 4**,** decreasing from 13.96 ± 0.36 in phase 1 to 13.79 ± 0.21 by phase 4 ($P = 0.05$; Table 2). Moreover, comparing sodium profiles between phases 1 and 4 at various points during the course of an average dialysis session (ie, predialysis, at 18 minutes, and postdialysis), mean sodium levels generally were lower in all stages, but only statistically significant postdialysis ($P = 0.001$; Fig 1).

Diascan-measured plasma conductivity values showed a strongly significant ($r^2 = 0.69$; $P < 0.001$) linear correlation with plasma sodium levels, as shown in Fig 2.

Ionic Mass Balance

There was a steady increase in total ionic mass balance during the 4 phases of the study, just missing statistical significance in phase 3 ($P = 0.05$), but reaching significance in phase 4 ($P < 0.01$; Table 2). This indicates a progressive increase in total sodium removal with each downward increment in postdialysis target conductivity. By phase 4, nearly 100 mmol more sodium was removed per dialysis session, with a 0.2-mS/cm decrease in end-dialysis plasma conductivity compared with baseline (phase 1).

Bioelectrical Impedance Analysis

There were no significant differences in total-body water or extracellular water volumes observed during the study period (Table 3). However, the distribution of water over compartments was altered significantly. A direct comparison of phase 1 and phase 4 results showed a statistically significant decrease in the relative volume of water distribution in the extracellular compartment. This is illustrated best by the decrease in extracellular water as a percentage of total-body water volume (51.8% ± 4.72% vs 49.3% ± 5.31%; $P < 0.001$) and the extra- to intracellular water volume ratio (1.09 ± 0.21 vs 0.99 ± 0.21; $P < 0.001$). Also worthy of note is that the calculated mean "desired" values for extracellular water as a percentage of total-body water volume and extra- to intracellular water volume

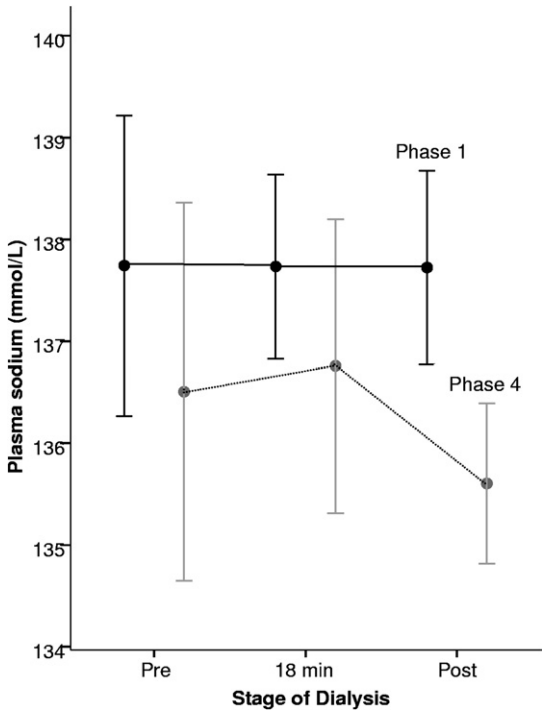

Figure 1. Mean plasma sodium values obtained before the dialysis session (pre), at 18 minutes, and postdialysis for dialyses conducted during phases 1 and 4 of the study (n = 142). Error bars are standard deviations.

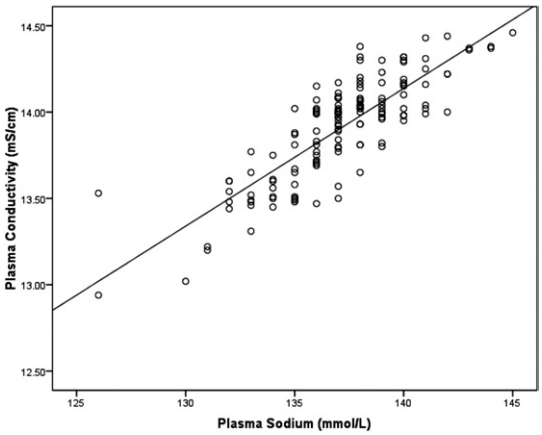

Figure 2. Plasma conductivities versus plasma sodium concentrations measured at the same time. Plasma conductivities were obtained from dialyses in phases 1 and 4 of the study; plasma sodium concentrations are those shown in Fig 1 (n = 142). The regression equation is PC = 2.967 + 0.080 × Na, where PC is plasma conductivity and Na is plasma sodium. The proportion of variation in plasma conductivity explained by serum sodium is 68.8% (adjusted).

ratios (39.9% and 0.66, respectively) were much lower than those measured in any phase of the study. This reflects the persistent state of extracellular volume overload in these patients. A statistically significant increase in phase angle was observed between phase 1 and phase 4 (3.74° ± 1.0° vs 4.45° ± 1.4°; $P < 0.001$) without an associated decrease in actual postdialysis weight or total-body water volume. Phase angles in healthy individuals range from 6°-9° (Third National Health and Nutrition Examination Survey [NHANES III]).

Weight Gain

Although no significant patient weight changes were detected during the course of the study, interdialytic weight gain was significantly decreased by phase 4 ($P < 0.05$; Table 4). This correlated well with the decrease in postdialysis conductivities and increase in ionic mass balance (Table 2).

Blood Pressure

Systolic and mean arterial blood pressures progressively decreased during the phases of the study, attaining statistical significance by phase 4 (Table 4). There were no significant changes in number of blood pressure medications or dosages during the course of the study (Table 1).

DISCUSSION

Persistent volume overload in patients with end-stage renal failure is common and is one of the primary determinants of cardiovascular morbidity and mortality.[1-3,12] This fluid-overloaded state is caused by salt and water retention. Unfortunately, salt and water removal by hemodialysis is limited by the rate of intravascular refilling; thus, cramping and symptomatic hypotension are common.[4-6] Shortening hemodialysis treatment times and the common clinical practice of universal rather than individual sodium prescriptions may be "salt-loading" such patients further. This pilot study is designed to assess the safety and efficacy of serial decreases in postdialysis plasma conductivities using Diacontrol. Diacontrol is software available on Integra Physio dialysis machines that will allow postdialysis plasma conductivities to be set by the physician: the required dialysate sodium time profile is determined automatically by a biofeedback loop between dialysate conductivity (measured continuously) and plasma conductivity measured every

Table 3. BIA Measurements of Body-Water Compartments During the First and Last Week of the Study

			%ECW		ECW/ICW	
	TBW (L)	ECW (L)	Actual	Desired	Actual	Desired
Phase 1	43.75 ± 11.67	21.85 ± 5.31	51.81 ± 4.72	39.80 ± 2.66	1.09 ± 0.21	0.66 ± 0.08
Phase 4	44.08 ± 12.01	21.51 ± 4.99	49.33 ± 5.31	39.88 ± 2.61	0.99 ± 0.21	0.66 ± 0.07
P[a]	0.2	0.3	0.001	0.7	0.001	0.3

Abbreviations and definitions: BIA, bioelectrical impedance analysis; ECW, extracellular water volume; %ECW, extracellular water as a percentage of total-body water volume; ECW/ICW, ratio of extracellular water to intracellular water volume; TBW, total-body water volume.

[a]Phase 1 versus phase 4, nonparametric Wilcoxon signed-rank test.

Table 4. Patient Weights, Interdialytic Weight Gains, and Blood Pressures During the Course of the Study

	Phase				
	1	2	3	4	*P*[a]
Predialysis					
Weight (kg)	82.03 ± 26.40	83.90 ± 29.43	82.11 ± 28.05	81.26 ± 25.97	0.4
SBP (mm Hg)	146.80 ± 26.87	153.57 ± 27.17	142.89 ± 21.81	135.60 ± 18.65	0.02
DBP (mm Hg)	78.67 ± 12.23	80.57 ± 17.90	75.89 ± 7.94	74.93 ± 9.29	0.04
MAP (mm Hg)	101.38 ± 16.19	104.91 ± 20.57	98.22 ± 11.90	95.15 ± 11.15	0.04
Interdialytic weight gain (kg)	2.77 ± 1.63	3.25 ± 1.47	2.73 ± 1.20	2.13 ± 0.96	0.04
Postdialysis weight (kg)	79.85 ± 26.05	80.77 ± 28.59	79.13 ± 27.40	79.11 ± 25.35	0.8

Abbreviations: DBP, diastolic blood pressure; MAP, mean arterial blood pressure; SBP, systolic blood pressure.
[a]Phase 1 versus phase 4, nonparametric Wilcoxon signed-rank test.

15 minutes by the Diascan module standard on the Integra Physio machine.

Lambie et al[10] showed that in comparison to a standard sodium prescription, serial manual decreases in dialysate conductivity were safe and well tolerated and resulted in improved interdialytic weight gain and blood pressure control. They used Diascan and were able to monitor plasma conductivity and confirmed that lower plasma conductivities led to increased ionic mass balance. They also showed that these values were directly reflective of plasma sodium levels and total sodium removal, respectively. Lambie et al[10] did not use Diacontrol.

This study of Diacontrol efficacy was able to show not only that targeted plasma conductivities could be achieved safely, but also that individualized serial decreases in this value result in increased total salt removal. This resulted in a relative decrease in extracellular water volume and translated into improvements in blood pressure control and interdialytic weight gains.

A previous study by Selby et al[11] also used Diacontrol. They also decreased postdialysis plasma conductivity to a mean of 13.5 mS/cm in 10 patients in a similarly timed stepwise fashion. In contrast to our study, they showed no increase in ionic mass balance by doing so. Furthermore, there were no changes in blood pressure, interdialytic weight gain, or extracellular water volume measured using BIA. The reason for the differences is not obvious. There were differences between the 2 studies. The dialysate used by Selby et al[11] contained 138 mmol/L of sodium, and ours contained 140 mmol/L. Their target postdialysis plasma conductivities were 13.7, 13.6, and 13.5 mS/cm per 2-week period; ours were from 14.0 to 13.5 mS/cm. Thus, it is possible that our patients were more salt loaded than theirs at the beginning of the study and hence more likely to benefit. Patients in the Selby et al[11] study had pre- and postdialysis extracellular water volumes of 0.21 ± 0.04 L/kg; ours had a mean of 0.26 L/kg (calculated from data in Tables 3 and 4), which might support this possibility, accepting that BIA measurements were not made using identical methods or devices. The ionic mass balance values of Selby et al[11] were 390-411 mmol during the course of their study, very similar to our values of 382-420 mmol during phases 1 to 3. Only by phase 4 did our ionic mass balance increase significantly to 480 mmol. Our study also did not show a decrease in actual extracellular water volume, but did in the distribution of body-water compartments. The major thrust of the study by Selby et al[11] was to compare progressive conductivity decreases between Diacontrol and standard dialysis. Their findings were that Diacontrol had no advantage over standard dialysis. The latter was able to decrease extracellular water volume significantly by being able to decrease postdialysis plasma conductivity to 13.2 mS/cm; Diacontrol has a limit on lower conductivity settings.

The increase in total salt removal (ionic mass balance) achieved in this study is caused by 2 factors. First, adjusting the dialysate sodium prescription to patients' initial plasma sodium concentration decreases the potential for salt loading, which will occur in individuals presenting with plasma sodium concentrations lower than a universally prescribed dialysate sodium level (of-

ten 140 mmol/L). Because of Diacontrol's inability to calculate plasma conductivity before 18 minutes, there may have been an element of salt loading during that period in our study patients. Second, decreasing plasma conductivity during the course of dialysis will cause diffusive clearance of sodium in addition to the usual convective clearance driven by ultrafiltration.

The increase in ionic mass balance was well tolerated, likely because the decreases in target postdialysis plasma conductivity were small (<0.2 mS/cm), gradual (over 2-week blocks), and adjusted according to each individual's plasma conductivity early in dialysis. The increase in total salt removal (ionic mass balance) did not reach statistical significance until phase 4. However, by this stage, an average increment of nearly 100 mmol of sodium compared with baseline was removed per dialysis session, with only a 0.2-mS/cm target decrease in plasma end-conductivity. This suggests that even more sodium removal may be possible with a longer study period and further decreases in end plasma conductivities. However, when a target postdialysis plasma conductivity is established, ionic mass balance likely will return to baseline levels (unless dietary sodium changes) and stabilize again. The increase in the diffusive component of ionic mass balance caused by the decrease in postdialysis plasma conductivity is going to be offset by the decrease in the convective component of ionic mass balance as interdialytic weight gain decreases. The patient thus achieves a new steady state with lower total-body sodium levels. How long it takes to reach this new steady state is uncertain from these studies because the ionic mass balance values listed in Table 2 were derived from the average ionic mass balance value per patient per dialysis session. The study of Lambie et al[10] suggested that this might be as little as 1 week. The baseline (phase 1) ionic mass balance value of approximately 380 mmol most likely is equal to the average sodium dietary intake for the period between 2 dialyses, assuming the absence of residual renal function. Unfortunately, dietary sodium intake was not monitored to confirm this, which is a limitation of the study.

Although no significant changes were observed in pre- and postdialysis weights throughout the study, there was a significant decrease (albeit small) in interdialytic weight gain detected by phase 4. Mean pre- and postdialysis weights decreased by 0.77 and 0.74 kg, respectively. This is similar to the mean 0.64-kg decrease in interdialytic weight gain. This was associated with the decrease in end plasma conductivities and increase in ionic mass balance, supporting a direct relationship between weight (presumably primarily water) gain and total-body sodium. Because serum osmolality stimulates thirst and is determined primarily by sodium, it would be reasonable to infer that the increased salt removal may have led to a decrease in water consumption. Some studies have found a significant decrease in thirst associated with lower dialysate conductivity.[13] Our participants did not volunteer a change in thirst. No valid objective assessment of thirst was made, which is an additional limitation of this study.

Hemodialysis patients previously have been reported to persistently have expanded extracellular water volumes and increased extra- to intracellular water volume ratios, measured using BIA.[14] This clearly is supported by our bioimpedance data. The calculated mean "desired" or "ideal" values for these parameters were much lower than measured values throughout study. Although no significant differences in total-body water or extracellular water volumes were observed during the study period, the distribution of water over compartments was altered. During 7 weeks, a statistically significant contraction in relative extracellular fluid volume was noted, as illustrated by the decrease in extracellular water as a percentage of total-body water volume and extra- to intracellular water volume ratio. This shows that a modest decrease in individualized target end conductivity can significantly increase total salt removal and shrink the extracellular fluid compartment during a relatively short period. This promises greater outcomes over a longer study period and perhaps lower target plasma conductivities.

An intriguing finding was the significant increase in phase angle between the initial and final phases of the study (3.74° ± 1.0° vs 4.45° ± 1.4°; $P < 0.001$). Similar values for phase angle in the hemodialysis population have been reported by Chertow et al,[15] who also reported that low phase angles are associated with an increased risk of mortality.[16] As mentioned, phase

angle largely represents the quantity of metabolically active cells and lean body cell mass, which contains large amounts of water and conducting electrolytes. Therefore, one possible explanation for redistribution of fluid between compartments (represented by the decrease in extracellular water volume without an associated decrease in postdialysis weight or total-body water volume) may be an increase in body cellular mass. This would suggest that individualized sodium prescriptions not only may improve clinical outcomes through the benefits of decreased extracellular fluid volumes, but also may improve cellular health. This concept certainly warrants further investigation.

Associated with the relative contraction of the extracellular water compartment, there was a decrease in systolic and mean arterial blood pressures. This reached statistical significance only by phase 4. It was not associated with an increase or decrease in blood pressure medication. Additional larger and longer studies are needed to see whether such medication can be eliminated.

In conclusion, salt and volume overload with its cardiovascular sequelae plagues the dialysis population, committing patients to a restrictive low-salt diet, fluid restrictions, and the need for antihypertensive medication. Attempts to remove salt and water using dialysis ultrafiltration may lead to intradialytic complications. It is likely that "desalting" a dialysis patient using ultrafiltration (convection) alone is impossible; sodium removal by diffusion is necessary. Our study, along with those of Lambie et al[10] and Selby et al,[11] suggest that individualized gradual decreases in end dialysis plasma sodium concentrations may begin to address this issue. Technological advances such as Diacontrol may help make this clinically feasible and practical. It also is possible that simply individualizing dialysate sodium concentrations to ensure that diffusion occurs may be equally safe and efficacious using standard dialysis. Further studies clearly are indicated.

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