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Clinical consequences of an individualized dialysate sodium prescription in hemodialysis patients

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Clinical consequences of an individualized dialysate sodium prescription in hemodialysis patients.

Background. Predialysis plasma sodium (Na^+) concentration is relatively constant in hemodialysis (HD) patients, and a higher dialysate Na^+ concentration can promote an increase in the interdialytic fluid ingestion to achieve an individual's osmolar set point, and individualization of dialysate Na^+ concentration may improve interdialytic weight gain (IDWG), blood pressure (BP), and HD-related symptoms.

Methods. Twenty-seven nondiabetic, non-hypotension prone HD patients were enrolled in a single-blind crossover study. Subjects underwent nine consecutive HD sessions with the dialysate Na^+ concentration set to 138 mEq/L (standard Na^+ HD), followed by nine sessions wherein the dialysate Na^+ was set to match the patients average pre-HD plasma Na^+ measured three times during the standard Na^+ phase multiplied by 0.95 (individualized dialysate Na^+ HD). Dry weight, dialysis prescription, and medications were not modified during the six weeks of the study.

Results. Pre-HD Na^+ was similar in both periods of the study (standard Na^+ HD, 134.0 ± 1.4 mEq/L; individualized Na^+ HD, 134.0 ± 1.5 mEq/L; $P = 0.735$). There was a significant decrease in interdialytic weight gain (2.91 ± 0.87 kg vs. 2.29 ± 0.65 kg; $P < 0.001$), interdialytic thirst scores, and episodes of intradialytic hypotension in the individualized Na^+ period compared with the standard phase. Pre-HD BP was lower in individualized Na^+ HD in patients with uncontrolled BP at baseline ($N = 15$), but not in those with controlled BP at baseline ($N = 12$) (ΔBP $-15.6/-6.5$ mm Hg in uncontrolled vs. ΔBP $+6.4/+4.5$ mm Hg in controlled, $P = <0.001$ for systolic BP and $P = <0.001$ for diastolic BP).

Conclusion. An individualized Na^+ dialysate based on predialysis plasma Na^+ levels decreases thirst, IDWG, HD-related symptoms, and pre-HD BP (in patients with uncontrolled BP at baseline).

Key words: dialysis solutions, sodium, renal dialysis, weight gain, blood pressure, hypertension, thirst.

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Interdialytic weight gain (IDWG) is a major concern in chronic hemodialysis (HD) treatment [1, 2]. Large IDWG leads to expansion of extracellular volume, which is the major determinant of hypertension in HD patients [3]. Furthermore, an excessive IDWG may lead to patient discomfort during HD because brisk ultrafiltration rates are required in order to get the patient to his or her estimated dry weight during the relatively short period of a conventional HD session [4].

Current HD practices include setting the dialysate sodium concentration to levels as high as 144 mEq/L to prevent HD complications related to rapid osmolar shifts during HD, and indeed, the use of high dialysate sodium concentrations is effective in preventing such complications [5]. However, predialysis plasma sodium concentration is constant in HD patients, and these patients seem to have an individual osmolar set point [6]; consequently, the use of a dialysate Na^+ concentration higher than plasma could contribute to an increase in the interdialytic fluid ingestion in the attempt to achieve this set point [7].

Control of dialysate sodium has been extensively used in patients who have frequent hypotension during HD. In most studies, the sodium dialysate concentration is set to a high concentration at the beginning of HD and is gradually decreased, a procedure called sodium profiling [8]. However, little data exist in stable, non-hypotension prone patients [9]. In these patients, the benefits of higher dialysate sodium are often not necessary, and they may suffer from complications of high sodium dialysis, such as increased thirst, IDWG, and hypertension [10]. Because lower dialysate sodium dialysis was safely and effectively used in the past [10], and there is evidence to suggest that it is well tolerated in patients undergoing high efficiency dialysis [11, 12], we designed a study to investigate the short-term consequences of an individualized dialysate Na^+ prescription based on pre-HD plasma sodium concentration on HD treatment parameters and complications.

METHODS

Thirty-seven patients on HD for at least three months were enrolled from a single dialysis unit. All patients were receiving thrice weekly HD with volumetric dialysis machines (SPS 1550; Baxter, Deerfield, IL, USA) using bicarbonate-based dialysate and cellulose acetate dialyzers (CA-150, CA-170, CA-210; Baxter). They were in stable clinical condition, stable prescribed dry weight, mean dialysis prescription (Kt/V) ≥1.2, and residual daily urine output <500 mL/day. Diabetic patients were not included in the study in order to avoid possible effects of poor glucose control on measurements of plasma sodium. The study protocol was approved by the ethics committee of the State University of Rio de Janeiro, and all subjects gave written informed consent.

Study design

This was a prospective, nonrandomized, single-blind, crossover trial. The study was performed in two different phases, with each subject used as his/her own control. Dry weight, dialysis prescription, and medications were not modified during the entire study except for the dialysate sodium concentration.

In the first phase, patients were submitted to nine consecutive HD sessions with a standard dialysis prescription of blood flow ≥300 mL/min and dialysate flow of 500 mL/min. The standard dialysate composition was: bicarbonate 33 mEq/L, potassium 2.0 mEq/L, calcium 3.5 mEq/L, magnesium 1.0 mEq/L, chloride 109.5 mEq/L, and acetate 3.0 mEq/L. The dialysate sodium concentration was fixed at 138 mEq/L, which is the standard concentration used in our dialysis facility. The pre and post-HD plasma sodium concentration was determined for each patient in three different dialysis sessions using a direct ion selective electrode method (AVL 9180; AVL Medical Instruments, Schaffhausen, Switzerland). The sodium concentration of the dialysate was determined by the same method, and was shown to be quite constant (130.1 ± 0.6 mEq/L). Dialysate conductivity (13.7 ± 0.2 ms/cm) was used as reference for dialysate sodium concentration.

In the second phase of the study, patients were subjected again to nine consecutive HD sessions, but the dialysate Na^+ concentration was set to the mean of the pre-HD Na^+ concentration multiplied by the Donnan coefficient of 0.95 (individualized Na^+). Only 27 of the 37 patients had a mean pre-HD Na^+ lower than the measured standard dialysate Na^+ concentration. Because the measured dialysate Na^+ concentration at a prescribed dialysate Na^+ concentration of 138 mEq/L was 130.1 ± 0.6 mEq/L, only patients in whom measured plasma Na^+ multiplied by 0.95 was lower than 130 mEq/L were included in the study analysis, and the remaining 10 subjects were excluded. Patients were not aware of the modification in the dialysate Na^+ concentration. Due to a limitation in the machines used, wherein the dialysate Na^+ can only be adjusted to even numbers (138, 136, 134 mEq/L, etc.), the prescribed gradient was 1 mEq/L above the target in nine patients, and 1 mEq/L below in six patients. Sodium concentration of the dialysate with −2 and −4 decrease from the standard concentration was proportional to the reduction (128 ± 1 mEq/L and 126 ± 1 mEq/L, respectively).

Pre-, intra-, and post-HD BP were measured using a mercury sphygmomanometer. Auscultatory measurements followed standard clinical guidelines using Korotkoff I and V sounds to indicate systolic and diastolic BP, respectively. Subjects were classified as having "controlled" or "uncontrolled" BP based on the average pre-HD systolic BP on the three dialysis sessions of the third week of the first phase of the study (on standardized dialysate Na^+). "Uncontrolled BP" was defined as pre-HD systolic BP >150 mm Hg or diastolic BP >85 mm Hg regardless of the use of antihypertensive drugs. These values have been shown to have the best composite predictive ability for hypertension in HD patients (true positive rate of 81% to 82% and false positive rate of 33% to 39% using an average 44-hour ambulatory BP >135/85 as the gold standard) [13]. Similarly, "controlled BP" was defined as pre-HD BP ≤150/85 mm Hg, also regardless of medication use. Differences in BP control were based on the average BP for the three HD sessions of the last week of each phase of the study.

Estimated dry weight was determined through standard clinical criteria. Ultrafiltration (UF) and IDWG were determined based on changes in body weight before and after each HD session (UF), or between the end of HD and return to the next session (IDWG). In order to allow for better interpretation of clinical indices, we corrected the UF to pre-HD weight, and the IDWG to the estimated dry weight, thus obtaining measures that were more relevant to each specific patient.

Dialysis-related hypotension and symptoms (headache, cramps, nausea, and vomiting) were recorded and analyzed as the number of occurrences during each study phase. Hypotensive episodes were defined as rapid changes in BP (within 15 minutes) accompanied by symptoms requiring nursing interventions, or a brisk fall in BP >40 mm Hg systolic or >20 mm Hg diastolic within a 15-minute period regardless of symptoms or interventions. Interdialytic thirst scores (nil, mild, moderate, and severe) were obtained by a written questionnaire answered by the patients after each phase of the study.

Statistical analysis

We used paired Student *t* tests to compare continuous variables between each study phase, and two-sample Student *t* tests were used to compare hypertensive and

normotensives subjects. Chi-square tests were used to compare categorical variables. Pearson correlation coefficients and simple linear regression were used to study the relationship between different continuous variables. P values <0.05 were considered statistically significant. We used the statistical package SPSS/PC (SPSS, Inc., Chicago, IL, USA) for all calculations.

RESULTS

Twenty-seven (13 males and 14 females) out of 37 patients had a mean predialysis plasma sodium concentration adjusted by the Gibbs-Donnan factor lower than the standard dialysate sodium concentration. The mean age was 46 ± 14 years and subjects were on dialysis for a median time of 17 months (range 3 to 153 months). Racial distribution was 18 caucasian (67%) and nine black (33%). Hypertension was the presumed cause of the end-stage renal disease in 19 patients (70%), chronic glomerulonephritis in six (22%), tubulointerstitial disease in one (1%), and unknown in one patient (1%). Twenty-three patients (85%) were taking antihypertensive medications (mean 2.1 ± 0.6 drugs; range 1 to 3 drugs). Based on the criteria of Agarwal and Lewis [13] described above, 12 subjects were classified as having controlled BP, and 15 as having uncontrolled BP. Twenty-three patients (85%) were receiving erythropoietin (6000 ± 3328 U/wk); mean hematocrit was 34 ± 5%. The average duration of each HD session was 4.1 ± 0.3 hours.

Predialysis plasma Na^+ was similar in both periods of the study (Table 1). The coefficient of variation of pre-HD sodium concentration was 0.5% and 0.7% in the standard and individualized phases, respectively. Postdialysis plasma Na^+ decreased significantly in the individualized Na^+ HD, and the dialysate Na^+ concentration was reduced by 3 ± 1 mEq/L (Na^+ gradient) during the individualized phase. In fact, as a matter of protocol, there was no gradient in the individualized phase of the study. There was a significant decrease in IDWG, IDWG/estimated dry weight ratio, UF, and UF/pre-HD weight ratio in the individualized Na^+ HD (Table 1).

There were no significant differences in pre- and post-HD blood pressure levels for the group taken as a whole (Table 1). However, when we categorized patients as having controlled or uncontrolled BP, it became apparent that uncontrolled patients had a significant reduction in systolic BP during the individualized Na^+ phase (ΔBP −15.6/−6.5 mm Hg, $P < 0.001$ for systolic BP and $P = 0.079$ for diastolic BP), whereas controlled subjects had a net, not statistically significant, increase in BP (ΔBP +6.4/+4.5 mm Hg, $P = 0.296$ for systolic BP and $P < 0.001$ for diastolic BP). These differences of response between subjects with controlled and uncontrolled BP were clinically and statistically different (Table 2). Figure 1 depicts individual responses in controlled BP and uncontrolled BP subjects. No differences in achieved weight were noted between groups. In fact, both groups had a minimal increase in post-HD weight as the study progressed (controlled BP patients gained 0.3 ± 0.3 kg, uncontrolled BP patients gained 0.2 ± 0.3 kg, $P = 0.40$). Significant changes in IDWG occurred in patients with uncontrolled BP (standard Na^+, 3.12 ± 1.00 kg; individualized Na^+ 2.42 ± 0.71 kg; $P < 0.001$), as well as in those with controlled BP (standard Na^+, 2.65 ± 0.63 kg; individualized Na^+ 2.14 ± 0.55 kg; $P = 0.007$). There were no differences in post-HD blood pressure levels in either group.

The correlation between IDWG and the gradient between dialysate and plasma Na^+ concentration in the standard Na^+ phase of the study was not significant. However, the correlation was significant when the IDWG was adjusted to the estimated dry weight (Fig. 2).

Table 1. Plasma Na^+ concentration, dialysis parameters, and blood pressure in the standard Na^+ HD and in the individualized Na^+ HD

	Standard Na^+	Individualized Na^+	P
Pre HD Na^+ *mEq/L*	134.0 ± 1.4	134.0 ± 1.5	0.725
Post HD Na^+ *mEq/L*	135.9 ± 2.0	133.1 ± 2.6	<0.001
IDWG *kg*	2.91 ± 0.87	2.29 ± 0.87	<0.001
IDWG %	4.73 ± 1.19	3.75 ± 0.97	<0.001
UF *kg*	2.89 ± 1.01	2.37 ± 0.68	<0.001
UF %	4.59 ± 1.10	3.73 ± 0.88	<0.001
Pre HD SBP *mm Hg*	147 ± 19	146 ± 19	0.554
Pre HD DBP *mm Hg*	85 ± 13	85 ± 12	0.938
Pre HD PP *mm Hg*	63 ± 12	60 ± 13	0.305
Post HD SBP *mm Hg*	124 ± 15	123 ± 17	0.701
Post HD DBP *mm Hg*	73 ± 11	74 ± 9	0.605
Post HD PP *mm Hg*	50 ± 10	48 ± 12	0.239

UF, ultrafiltration; UF%, ultrafiltration/predialysis weight; IDWG, interdialytic weight gain, IDWG%, IDWG/estimated dry weight; SBP, systolic blood pressure; DBP, diastolic blood pressure; PP, pulse pressure. Mean ± SD of nine consecutive dialysis sessions.

Table 2. Differences in achieved blood pressure between patients with controlled and uncontrolled BP in standard Na^+ HD and individualized Na^+ HD

	Controlled BP	Uncontrolled BP	P
Number of patients	12	15	
Pre-HD SBP 1 *mm Hg*	130 ± 11	165 ± 15	<0.001
Pre-HD DBP 1 *mm Hg*	73 ± 10	95 ± 8	<0.001
Post-HD SBP 1 *mm Hg*	118 ± 13	132 ± 16	0.019
Post-HD DBP 1 *mm Hg*	71 ± 9	78 ± 11	0.081
Pre-HD SBP 2 *mm Hg*	136 ± 16	149 ± 18	0.059
Pre-HD DBP 2 *mm Hg*	78 ± 11	89 ± 8	0.009
Post-HD SBP 2 *mm Hg*	121 ± 16	127 ± 18	0.369
Post-HD DBP 2 *mm Hg*	72 ± 9	78 ± 10	0.114
Δ pre-HD SBP *mm Hg*	6.4 ± 12.8	−15.6 ± 14.2	<0.001
Δ pre-HD DBP *mm Hg*	4.5 ± 8.1	−6.5 ± 7.9	<0.001
Δ post-HD SBP *mm Hg*	2.8 ± 12.6	−4.5 ± 15.6	0.221
Δ post-HD DBP *mm Hg*	1.4 ± 11.1	−0.4 ± 11.6	0.824

SBP, systolic blood pressure; DBP, diastolic blood pressure; Δ BP, BP at the end of individualized Na^+ HD phase minus BP at the end of the standard Na^+ HD phase (see **Methods** for details). "Controlled BP" were subjects with pre-HD BP ≤150/85 mm Hg during the control phase of the study, regardless of use of antihypertensive drugs. "Uncontrolled BP" subjects were those with BP >150/85 mm Hg.

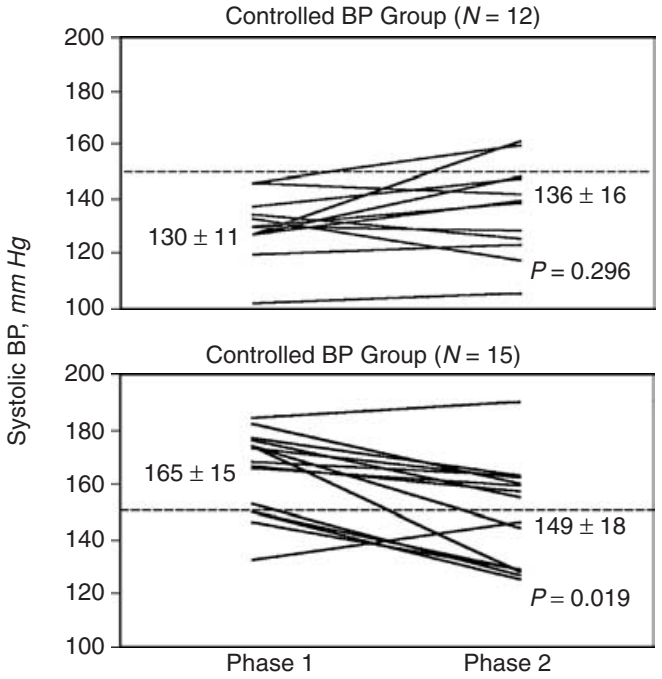

Fig. 1. Individual behavior of systolic BP in during control (phase 1) and intervention (phase 2) periods according to BP control status. "Controlled BP" were subjects with pre-HD BP ≤150/85 mm Hg during the control phase of the study, regardless of use of antihypertensive drugs. "Uncontrolled BP" subjects were those with BP >150/85 mm Hg. The hatched line indicates 150 mm Hg, which was the cutoff used to indicate BP control based on pre-dialysis BP. Phase 1, standard dialysate Na^+ (138 mEq/L); phase 2, individualized dialysate Na^+.

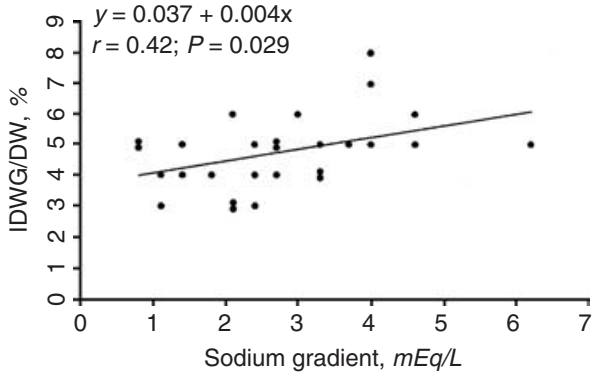

Fig. 2. Correlation between the difference between dialysate and plasma sodium (sodium gradient) and the interdialytic weight gain adjusted to the estimated dry weight (IDWG/DW) in the standard dialysate Na^+ (138 mEq/L) phase of the study.

The plasma free water deficit at the end of the standard HD sessions was determined by the formula:

$$\text{Free water deficit} = \frac{\text{Post-HD } Na^{\pm}\text{-Pre-HD } Na^{\pm}}{\text{Pre-HD } Na^{+}} \times \text{total body water}^{*}$$

(*by the Watson formula) [14].

The mean postdialysis plasma free water deficit in standard Na^+ HD was 0.56 ± 0.47 L.

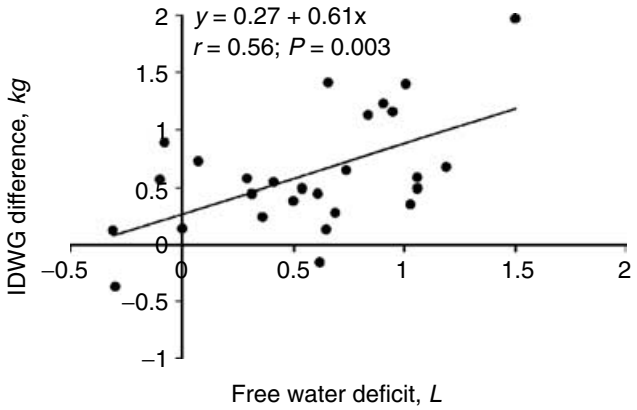

Fig. 3. Correlation between the free water deficit in standard dialysate Na^+ (138 mEq/L) phase and the difference between the interdialytic weight gain in standard dialysate Na^+ and in individualized Na^+ (IDWG difference).

Table 3. HD-related hypotension, symptoms and interdialytic thirst scores in standard Na^+ HD and individualized Na^+ HD

	Standard Na^+	Individualized Na^+	*P* value
Hypotension	23 (9%)	6 (2%)	<0.001
Cramps	12 (5%)	5 (2%)	0.072
Headaches	11 (5%)	3 (1%)	0.010
Nausea/vomiting	0 (0%)	0 (0%)	–
Interdialytic thirst			
Nil	0 (0%)	4 (15%)	0.043
Mild	1 (4%)	17 (63%)	<0.001
Moderate	11 (41%)	5 (18%)	0.07
Severe	15 (55%)	1 (4%)	<0.001

There was a significant correlation between the calculated free water deficit in standard Na^+ HD and the difference between the IDWG in standard Na^+ HD and individualized Na^+ HD (Fig. 3).

Dialysis-related hypotension and related symptoms were reduced in the individualized sodium phase of the study (Table 3). Thirst scores were also significantly reduced.

As an "intention-to-treat" analysis, we also reviewed the data from the group of 10 patients who were not part of the main analysis because their plasma Na^+ was not lower than the dialysate Na^+ concentration. This subanalysis showed no significant differences in any of the study variables between the early and latter three-week periods of the study. One could also look at this analysis as one to confirm the absence of temporal confounding, as it demonstrates the stability of this group of patients throughout both phases of the study without any intervention being applied.

DISCUSSION

In this study we analyzed the short-term consequences of an individualized dialysate Na^+ prescription in a population of nondiabetic, nonhypotension prone, stable HD

patients. The short-term duration permitted us to leave unchanged important parameters, such as estimated dry weight and the dosage of vasoactive drugs, and thereby link the observed differences exclusively to the dialysate sodium changes. The main findings of our study were a reduction in IDWG, ultrafiltration, interdialytic thirst, and an improvement in predialysis BP in hypertensive patients.

Flanigan [10] has emphasized the importance of sodium balance during the dialysis treatment, and the importance of its ionic activity rather than its total concentration in the fluid and electrolyte movement between plasma and dialysate. We, therefore, determined the plasma and dialysate direct sodium concentration by direct potentiometry. Direct potentiometry permits the determination of sodium concentration in undiluted samples, and is not influenced by abnormal levels of plasma proteins and lipids. Furthermore, the method measures noncomplexed, free sodium concentration, which represents those sodium molecules available for diffusion [10]. For this reason, it is proposed that sodium levels determined by direct potentiometry be referred to as the concentration of ionized sodium rather than total sodium concentration [15]. To avoid clinical confusing interpretation the results are usually related to flame photometry results by a conversion factor [16].

The difference in sodium concentration between plasma and dialysate noted by us and others [7, 17] occurs because plasma water constitutes only 93% of total plasma, whereas it is 100% of total dialysate volume. In vivo, this concentration difference is compensated by the Gibbs-Donnan effect. Otherwise, the dialysate should have a concentration approximately 6 to 7 mEq/L higher to result in an isonatremic dialysis [10, 17]. The Gibbs-Donnan effect in hemodialysis occurs because plasma proteins, which are negatively charged and not diffusable through the dialysis membrane, create an electric field that attracts sodium, reducing the plasma diffusable sodium by 4% to 5% [17]. In our study, low dialysate Na^+ values (130 mEq/L) were observed when dialysate Na^+ concentration was measured by direct ionometry because the values were adjusted to the volume of plasma water by the instrument. As it imitates what happens in HD, we applied a theoretical Gibbs-Donnan effect of 0.95 to plasma Na^+ concentration to better estimate the actual gradient between dialysate and plasma. Some direct ionometry-based electrolyte analyzers provide configurations that allow the determination of sodium values in aqueous solutions, including dialysate, without a correction for the plasma water volume. In such cases, the Gibbs-Donnan correction is not needed for plasma sodium, and a dialysate to plasma sodium gradient may be established directly. It is known that direct ionometry sodium determination in aqueous solutions may be affected by pH and substances such as glucose [18], but we do not believe these interactions had an impact in our observations.

Other methods may be used to establish the actual pre-HD dialysate to plasma sodium gradient. Dialysate conductivity reflects ionic activity and mirrors dialysate Na^+ concentration when multiplied by 10 [19]. On-line dialysate and plasma conductivity can be measured in HD patients and reflects diffusible particles, mainly sodium. In machines equipped with conductivity monitors, this technique may be used to estimate the dialysate to pre-HD plasma sodium gradient, and has the advantage of allowing adjustments and matching during the dialysis session [20].

Our results showed that predialysis sodium concentration was constant when the dialysate was set to a standard concentration, and remained at the same level when the dialysate sodium concentration was individualized. This is in agreement with previous studies showing that the predialysis sodium concentration is constant independently of the sodium gradient established between blood and dialysate in the previous session [6]. This "set point" dictates the interdialytic fluid intake to bring one's osmolality back to its set point; if the post-HD Na^+ is higher, greater IDWG will inevitably occur. Our data substantiate this assertion.

We found a significant correlation between the dialysate to plasma Na^+ gradient and IDWG adjusted to the estimated dry weight in the standard dialysate Na^+ phase of the study. These data are in agreement with the findings of Levin et al [7], who found the same significant correlation between the dialysate to blood Na^+ gradient and the absolute interdialytic weight gain. Furthermore, when we estimated the free water deficit generated by the dialysate to plasma Na^+ gradient in standard Na^+ HD, we found a significant correlation between this gradient and the difference between the IDWG in standard Na^+ HD and individualized Na^+ HD. These analyses show that part of the interdialytic fluid ingestion is destined to supply the free water deficit generated by the higher dialysate sodium concentration. In fact, when we adjusted the dialysate Na^+ concentration to the predialysis plasma Na^+ concentration we observed a significant reduction in interdialytic thirst scores, IDWG, and, concomitantly, in ultrafiltration requirements. The decrease in the rate of fluid removal during the HD session is the most likely cause of the observed reduction in the HD hypotension episodes.

The main concern with the method of individualized dialysate Na^+ prescription is that, in attempting to reach an isonatric HD, it could result in hyponatremia and hyposmolality-related complications because of the lack of sodium diffusion and the concomitant sodium losses by ultrafiltration. Indeed, postdialysis Na^+ plasma concentration was significantly reduced in the individualized Na^+ HD. However, convective sodium losses are lower

than expected in HD, and were partially compensated by the reduction in the ultrafiltration and were well tolerated. Besides, predialysis sodium remained unchanged despite the decrease in IDWG, probably related to a decrease in interdialytic fluid ingestion. Therefore, we believe that the adjustment in the sodium prescription based on predialysis values may be used safely. Another possible problem is that patients who are prone to intradialytic hypotension may not tolerate this technique. We did not include these patients in our study, and caution must be exercised when extending our results to this specific group of patients.

It could be anticipated that decreased IDWG and a more negative Na^+ balance could lead to better BP control; however, it is well known that there is a lag period between changes in Na^+ balance and volume status and achievement of BP control [21], so we were surprised with our findings of improved BP control in hypertensive patients after only three weeks of intervention. Several previous studies have addressed this issue in different ways [12, 22–24]. Flanigan et al and Song et al have demonstrated that the use of Na^+ profiling with high time-averaged dialysate Na^+ leads to higher BP carefully documented by ambulatory BP monitoring [22, 23]. Alternatively, Krautzig et al [12] and Ferraboli et al [abstract; Ferraboli R et al, *J Am Soc Nephrol* 13:211A, 2002] showed that lowering the dialysate sodium concentration to 135 mEq/L can be a successful intervention to improve BP control, a finding that was not corroborated by Kooman et al [24]. We did not find a significant difference in blood pressure levels between the two phases of the study when analyzing the group as a whole. However, stratified analyses according to BP control demonstrated that uncontrolled BP subjects had a significant improvement in BP control, whereas controlled BP patients remained with stable BP levels. Similar findings were reported by Flanigan et al in their study of different sodium modeling approaches, who observed a rise of BP in their normotensive patients, whereas hypertensive patients had a usual fall in BP, especially those who were not under pharmacologic treatment [22]. Presence or absence of drug treatment did not alter our results; only the presence of uncontrolled BP was a predictor of a BP-lowering response to individualized dialysate Na^+ in our study.

It does not seem that our results were caused by the observed changes in IDWG, as there were no significant changes in achieved weight, and both controlled BP and uncontrolled BP patients had a significant decrease in IDWG in the individualized Na^+ HD. Individualized dialysate prescriptions lead to a decrease in ionic mass transfer to the patient [19], so it is possible that the individualized prescription led to a more favorable sodium balance and lower peripheral resistance, as has been suggested in patients undergoing daily nocturnal hemodialysis [25, 26]. Any further discussion on mechanisms to explain our observations would be merely speculative.

Our study has several limitations that merit discussion. First is the exclusion of hypotension-prone patients, which certainly limits the ability to generalize our results as discussed above. Second is the fact that we did not employ randomized block assignment to our study design, a technique that would have strengthened our methodology. While this is a limitation, we are reassured by the lack of temporal changes in the group of 10 subjects excluded from analysis due to baseline plasma Na^+, an observation that makes us confident that the differences observed in the individualized group were indeed related to the intervention, and not due to temporal changes as confounders. Third is the issue related to the adjustment of the prescribed individualized Na^+ to the characteristics of our dialysis machines, which accept adjustments in dialysate Na^+ only in even numbers. However, our analysis of the average difference did not show a bias in either direction, and we believe that this does not detract from our results. Last is the fact that we did not use ambulatory BP monitoring, which is a more precise method to estimate BP in dialysis patients, as established by our own group [27]. While this is a limitation, the careful protocol observed in the determination of peridialysis BPs makes our results as reproducible as possible.

CONCLUSION

An individualized dialysate Na^+ concentration was associated with a decrease in interdialytic thirst, IDWG, dialysis hypotension and related-symptoms, and better BP control in stable chronic HD patients. Long-term studies are necessary to observe if these short-term benefits are sustained.

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