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Original Investigation

Comparison of Prescribed and Measured Dialysate Sodium: A Quality Improvement Project

Ambreen Gul, MD,[1] Dana C. Miskulin, MD,[2] Susan S. Paine, MPH,[1] Sriram S. Narsipur, MD,[3] Leonard A. Arbeit, MD,[4] Antonia M. Harford, MD,[5] Daniel E. Weiner, MD,[2] Ronald Schrader, PhD,[1] Bruce L. Horowitz, MD,[5] and Philip G. Zager, MD[1,5]

Background: There is controversy regarding the optimal dialysate sodium concentration for hemodialysis patients. Dialysate sodium concentrations of 134 to 138 mEq/L may decrease interdialytic weight gain and improve hypertension control, whereas a higher dialysate sodium concentration may offer protection to patients with low serum sodium concentrations and hypotension. We conducted a quality improvement project to explore the hypothesis that prescribed and delivered dialysate sodium concentrations may differ significantly.

Study Design: Cross-sectional quality improvement project.

Setting & Participants: 333 hemodialysis treatments in 4 facilities operated by Dialysis Clinic, Inc.

Quality Improvement Plan: Measure dialysate sodium to assess the relationships of prescribed and measured dialysate sodium concentrations.

Outcomes: Magnitude of differences between prescribed and measured dialysate sodium concentrations.

Measurements: Dialysate sodium measured pre- and late dialysis.

Results: The least square mean of the difference between prescribed minus measured dialysate sodium concentration was −2.48 (95% CI, −2.87 to −2.10) mEq/L. Clinics with a greater number of different dialysate sodium prescriptions (clinic 1, n = 8; clinic 2, n = 7) and that mixed dialysate concentrates on site had greater differences between prescribed and measured dialysate sodium concentrations. Overall, 57% of measured dialysate sodium concentrations were within ±2 mEq/L of the prescribed dialysate sodium concentration. Differences were greater at higher prescribed dialysate sodium concentrations.

Limitations: We only studied 4 facilities and dialysate delivery machines from 2 manufacturers. Because clinics using premixed dialysate used the same type of machine, we were unable to independently assess the impact of these factors. Pressures in dialysate delivery loops were not measured.

Conclusions: There were significant differences between prescribed and measured dialysate sodium concentrations. This may have beneficial or deleterious effects on clinical outcomes, as well as confound results from studies assessing the relationships of dialysate sodium concentrations to outcomes. Additional studies are needed to identify factors that contribute to differences between prescribed and measured dialysate sodium concentrations. Quality assurance and performance improvement (QAPI) programs should include measurements of dialysate sodium.

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INDEX WORDS: Prescribed dialysate sodium; measured dialysate sodium; ordered dialysate sodium; delivered dialysate sodium; quality assurance; quality improvement; hemodialysis; renal replacement therapy (RRT).

There is controversy regarding the optimal dialysate sodium concentration, with some investigators suggesting the use of individualized dialysate sodium prescriptions to achieve a zero sodium predialysis gradient between dialysate and serum.[1,2] Recently, the chief medical officers of 14 US dialysis providers suggested that dialysate sodium prescriptions should range from 134 to 138 mEq/L.[3] They stated that use of these dialysate sodium concentrations may reduce thirst, interdialytic weight gain, and systolic blood pressure,[1,4,5] with subsequent beneficial effects on left ventricular morphology.[5] In contrast, DOPPS (Dialysis Outcomes and Practice Patterns Study) and other investigators have reported

From [1]Dialysis Clinic, Inc, Albuquerque, NM; [2]Tufts Medical Center, Boston, MA; [3]State University of New York, Syracuse; [4]State University of New York, Stony Brook, NY; and [5]University of New Mexico Health Sciences Center, Albuquerque, NM.

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Address correspondence to Philip G. Zager, MD, University of New Mexico, Department of Internal Medicine, 1500 Indian School Rd NE, Ste 200, Albuquerque, NM 87102. E-mail: pzag@unm.edu

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only modest increases in interdialytic weight gain and blood pressure with higher prescribed dialysate sodium concentrations.[6-8] Additionally, they observed an association between lower dialysate sodium concentration and increased incidence of hospitalization and death.[7,9] Therefore, these investigators have questioned the recommendations by the chief medical officers[10] and urged caution in recommending the use of lower dialysate sodium concentrations.[11]

None of the mentioned studies considered that there might be significant differences between prescribed and measured dialysate sodium concentrations. However, if there were significant differences, it is possible that the delivered dialysate sodium concentration differed significantly from that prescribed, which may have introduced significant biases. To our knowledge, only a single study has examined the difference between prescribed and measured dialysate sodium concentrations. In that study, investigators analyzed dialysate samples from 72 hemodialysis patients in a single unit in Austria. Although the mean difference between measured and prescribed dialysate sodium concentrations was close to zero (−0.1 mEq/L), the standard deviation was large (±2.5 mEq/L). Only 37.5% of dialysate sodium measurements were within ±1 mEq/L of the prescribed dialysate sodium concentration. Higher measured minus prescribed dialysate sodium concentration gradients were observed among patients dialyzed with Nikkiso versus Fresenius dialysate delivery machines.

The present quality improvement project was undertaken to explore how closely the delivered dialysate sodium concentration matched the prescribed dialysate sodium concentration (ie, the dialysate sodium concentration ordered by the physician). To accomplish this, we assessed the difference between prescribed and delivered dialysate sodium concentrations in maintenance hemodialysis patients receiving thrice-weekly dialysis at 4 outpatient dialysis facilities in the United States. We hypothesized that prescribed dialysate sodium concentrations would be within ±2 mEq/L of measured dialysate sodium concentrations.

METHODS

Participating Clinics

The project was undertaken as a quality improvement initiative at 4 dialysis facilities, 2 in New York and 2 in New Mexico. Each facility is operated by Dialysis Clinic, Inc (DCI), the largest not-for-profit provider in the United States. This project is part of the DCI Corporate Quality Management program, which has been approved by the University of New Mexico's Institutional Review Board (number 13-597). Because this was conducted as a quality improvement initiative and no patient-specific data were obtained, informed consent was not obtained. Data from patient treatments in the 4 clinics were included in the quality improvement project unless patients were dialyzed with a variable dialysate sodium concentration. Predialysis dialysate sodium samples were studied in 333 patient treatments, whereas dialysate sodium was measured again in the last 10 minutes in 234 patient treatments in clinics 1, 2, and 3. Dialysate orders were input into the machine by a dialysis technician and checked by a second technician and a nurse to ensure accuracy. The online clearance monitoring feature, which quantifies sodium dialysance while transiently varying the conductivity of the dialysate, was turned off during the project.

Practices at Participating Dialysis Units

Dialysis Machines

Clinics 1 and 2 used Fresenius models 2008K and 2008K^2 (Fresenius Medical Care), whereas clinics 3 and 4 used Gambro Phoenix machines (Gambro Inc). The number of times a given machine was studied ranged from 1 to 5. The median number of treatments for which a machine was examined was 3, and 66% of machines were examined 3 or more times. In all DCI clinics, dialysate delivery machines are serviced in accordance with manufacturer's recommendations.

Dialysate Concentrates

At each facility, dialysate acid concentrate was distributed from a central delivery system. Clinics 1 and 2 used Fresenius Granuflo Dry Acid (Fresenius Medical Care), which was mixed from dry concentrate by an automated process using the Granuflo Dissolution Unit versions 1 and 2, respectively. Acid concentrates were mixed weekly at clinic 1 and daily at clinic 2 using the manufacturer-approved procedures. Prior to transfer to a storage tank, specific gravity was measured using a hydrometer to ensure that the measured specific gravity is within the range recommended by the manufacturer.[12] The expected sodium concentration in the acid concentrate was 100 mEq/L.

The bicarbonate concentrate used in clinics 1 and 2 was Fresenius NaturaLyte. Briefly, bicarbonate concentrate was mixed twice daily to minimize the risk for bacterial growth and change in pH due to evaporation of carbon dioxide. The final mixed bicarbonate concentrate was checked for pH (mean, 8 ± 0.5 [standard deviation]), specific gravity (1.058 ± 0.002), and conductivity (70 ± 2 mS).[13] The expected sodium concentration in the bicarbonate concentrate was 37 mEq/L.

Clinics 3 and 4 used premixed acid concentrates obtained directly from the manufacturer (Rockwell Medical Technologies). These units used bicarbonate cartridges by Gambro (Gambro Inc).

Dialysis Machine Calibration

In each facility, the conductivity meters of the machines were validated prior to each shift using an external handheld conductivity meter (pHoenix Dialysate Meter by Mesa Labs). The external handheld conductivity meters were calibrated daily using a standard solution in accord with manufacturer recommendations and dialysis unit protocols. Dialysate conductivity measurements by the external meter were within ±0.2 mS/cm (0.02 S/m) and within ±0.3 mS/cm (0.03 S/m) of the prescribed dialysate conductivity in clinics 1 and 2 and clinics 3 and 4, respectively. Conductivity of 1 mS/cm (0.01 S/m) approximates a sodium concentration of 10 mEq/L in a protein-free solution.[14]

Sample Collection

Dialysate concentrates were set to achieve the prescribed dialysate sodium concentration and the machines were started 30 or more minutes prior to collection of the samples. Dialysate sodium samples were collected from the arterial dialyzer port, which is located after the dialysate concentrate has passed through the pressure pump but before it enters the dialyzer. Predialysis samples (n = 333) were obtained in each of the 4 clinics. Late dialysis dialysate sodium samples (n = 234) were collected in clinics 1, 2, and 3 during the last 10 minutes of the treatment. Samples were shipped overnight to the DCI Central Laboratory in Nashville, TN,

Table 1. Clinic Practices

Clinic	No. of Patients	Machines	Machines Sampled	Acid Concentrate	Base	Mix Method
1 and 2	72 (clinic 1); 79 (clinic 2)	Fresenius 2008K and 2008K[2]	24 (clinic 1); 26 (clinic 2)	Fresenius Granuflo	Fresenius Naturalyte	Staff mix
3 and 4	83 (clinic 3); 99 (clinic 4)	Gambro Phoenix	33 (clinic 3); 27 (clinic 4)	Rockwell premix with Rockwell Dri-State	Gambro BiCart Cartridge	Premix

Note: N = 333.

where sodium was measured using an indirect ion-selective electrode method on a Roche/Hitachi analyzer (Roche Diagnostics). The interassay coefficient of variation for measurement of dialysate sodium was 0.5%.

Statistical Analysis

We used a linear mixed model (Proc Mixed in SAS, version 9.3; SAS Institute Inc) to assess differences between prescribed and measured dialysate sodium concentrations. The outcome variable was prescribed minus measured dialysate sodium concentration, a single fixed effect was clinic, and random effects modeled the repeated measures for dialysis machines. In a separate analysis, we fit a random intercept logistic regression model (Proc GlimMix in SAS, version 9.3) to estimate the proportion of patient treatments in which measured dialysate sodium was within ±2 mEq/L of the prescribed dialysate sodium concentration with the binary outcome variable (inclusion of measured dialysate sodium concentration in the interval) and the identical model as before. In these models, we calculated least squares means for the differences between prescribed and measured dialysate sodium concentrations within clinics, adjusting for the repeated measures on machines. A single anomalous difference (of 17 mEq/L) was deleted from both analyses.

RESULTS

The machines and concentrates used at each clinic and the number of machines sampled (Table 1) and distribution of dialysate sodium prescriptions (Table 2) are shown. Clinics 1 and 2 used more individualized prescriptions, with 8 and 7 different dialysate sodium concentrations prescribed, respectively (Table 2). In contrast, 99% of patients at clinic 3 were dialyzed with a dialysate sodium concentration of 134 mEq/L, and 96% of patients at clinic 4 were treated with a dialysate sodium concentration of 140 mEq/L.

Differences in measured dialysate sodium concentrations from samples obtained predialysis versus in the last 10 minutes of the treatment are depicted in the Bland-Altman plot in Fig 1A. Despite some scatter, most values, except the highest dialysate sodium values, were centered around zero, indicating good agreement. Differences between prescribed and measured dialysate sodium concentrations in samples obtained predialysis (Fig 1B) and in the last 10 minutes of the treatment (Fig 1C) are depicted in Bland-Altman plots. In Fig 1B and C, differences in the mean values are below zero and the standard deviations are wide, indicating poor agreement between the prescribed and measured dialysate sodium values. However, in Fig 1C, agreement between the prescribed and measured high values was better in samples obtained late in dialysis than in predialysis samples (Fig 1B).

Differences between the prescribed and measured dialysate sodium concentrations by clinic are shown in Table 3. Mean and median differences between prescribed and delivered dialysate sodium concentrations were less than zero in each clinic, indicating that the measured dialysate sodium concentration was usually higher than the prescribed dialysate sodium concentration. The magnitude of the differences varied significantly by clinic ($P < 0.001$), with the greatest differences between prescribed and measured dialysate sodium concentrations in clinics 1 and 2 (Table 3), which used Fresenius machines, mixed concentrates on site, and had a large variety of dialysate sodium prescriptions. Specifically, least squares mean differences were larger at clinics 1 and 2 (−3.27 [95% CI, −4.02 to −2.53] and −3.77 [95% CI, −4.49 to −3.05] mEq/L, respectively) compared with clinics 3 and 4 (−1.44 [95% CI, −2.10 to −0.78] and −1.78 [95% CI, −2.4 to −1.10] mEq/L, respectively). The magnitude of the differences

Table 2. Distribution of Prescribed Dialysate Sodium by Dialysis Facility

	Prescribed Dialysate Sodium, mEq/L										
Clinic	130	132	133	134	135	136	137	138	139	140	142
1	2.8	2.8	1.4	—	20.8	11.1	4.2	12.5	—	44.4	—
2	2.5	—	—	—	8.9	1.3	1.3	38.0	—	46.8	1.3
3	—	—	—	98.6	—	—	2.4	—	—	—	—
4	—	—	—	—	—	—	4.0	—	—	96.0	—
All	1.2	0.6	0.3	24.3	6.6	2.7	3.0	11.7	—	49.3	0.3

Note: Values are given as percentage.

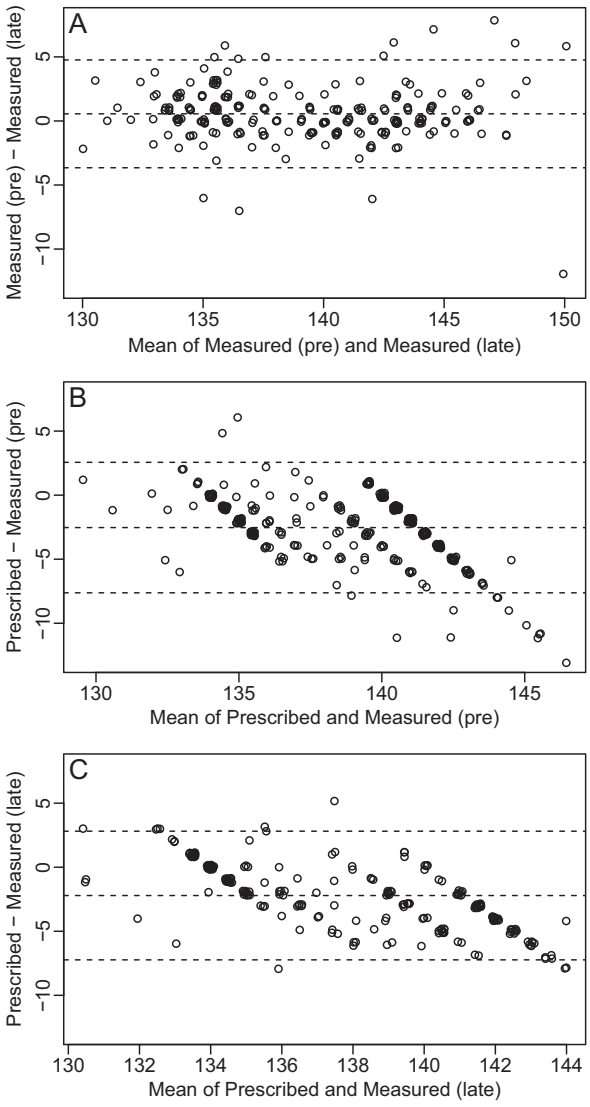

Figure 1. Distribution of the differences between prescribed and measured dialysate sodium concentrations across clinics. Bland-Altman plot of (A) pre- and late dialysis measured dialysate sodium concentrations, (B) prescribed and measured predialysis dialysate sodium concentrations, and (C) prescribed and measured late dialysis dialysate sodium concentrations.

ranged from −13 mEq/L to +6 mEq/L. Measured dialysate sodium concentrations were within 2 mEq/L of prescribed dialysate sodium concentrations in 47%, 25%, 71%, and 77% of treatments at clinics 1, 2, 3, and 4, respectively. In the present study, differences between prescribed and measured dialysate sodium concentrations were not greater on later versus first shifts (data not shown).

DISCUSSION

The present quality improvement project demonstrates significant differences between prescribed and measured dialysate sodium concentrations. The magnitude of these differences varied by clinic, with measured dialysate sodium concentrations exceeding the prescribed dialysate sodium concentrations by >3 mEq/L in 2 clinics. The range of the difference between measured and prescribed dialysate sodium concentrations was wide, varying from −13 mEq/L to +6 mEq/L. Given the overall positive bias, such that measured dialysate sodium concentrations were often higher than prescribed, net transfer of sodium from dialysate to the patient likely exceeded that which would have been expected based on the dialysis prescription. If there were similar differences between prescribed and measured dialysate sodium concentrations in studies designed to assess the relationship of dialysate sodium concentration and clinical outcomes, they may have led to unrecognized bias.[1,7,15-21]

There were several practices that differed across the participating dialysis units that may have contributed to the variation in differences between prescribed and measured dialysate sodium concentrations. Acid and bicarbonate concentrates were mixed on site in clinics 1 and 2 using automated systems in accordance with manufacturer recommendations. Manufacturers are allowed a margin of error up to 2.5%,[14] which corresponds to ±3.4 mEq/L for a prescribed dialysate sodium concentration of 135 mEq/L and ±3.5 mEq/L for a prescribed dialysate sodium concentration of 140 mEq/L. Another possible source of error is batch-to-batch variability, which was likely greater when mixing was done on site as opposed to using concentrates premixed by the manufacturer.[22] Accordingly, results of the present study suggest that use of premixed acid and bicarbonate concentrates may decrease the magnitude of differences between prescribed and measured dialysate sodium concentrations. The better agreement between high (dialysate sodium ≥ 145 mEq/L) prescribed and measured dialysate sodium concentrations observed in samples obtained during the last 10 minutes of dialysis versus the predialysis samples suggests that these dialysates may need adequate time to equilibrate. Direct measurement of concentrate conductivity may identify significant differences across batches, reflecting significant variability in concentrate preparation even when the process is largely automated. Processes to standardize and validate the methods for concentrate preparation are in place in all units, but these need to be reviewed periodically to maintain quality control, minimize the introduction of errors, and ensure that errors are identified and corrected immediately.

Differences in dialysate preparation and dialysate delivery machines may both have contributed to the variation in magnitude of the differences between prescribed and measured dialysate sodium concentrations across facilities. There are inherent differences in

Table 3. Difference in Prescribed and Measured Dialysate Sodium by Clinic

Clinic	No. of Patients	Prescribed − Measured, mEq/L[a]	Proportion of Observations Between −1 and 1 mEq/L	Proportion of Observations Between −2 and 2 mEq/L
1	72	−3.27 (−4.02 to −2.53)	31.6% (18.1% to 49.2%)	46.6% (29.9% to 64.1%)
2	79	−3.77 (−4.49 to −3.05)	10.4% (4.5% to 22.2%)	25.2% (13.8% to 41.5%)
3	83	−1.44 (−2.10 to −0.78)	46.3% (31.1% to 62.2%)	70.5% (55.0% to 82.4%)
4	99	−1.78 (−2.47 to −1.10)	48.9% (33.0% to 65.0%)	77.4% (62.9% to 87.3%)
All	333	−2.48 (−2.87 to −2.10)	34.2% (26.7% to 42.6%)	57.0% (48.0% to 65.5%)

Note: All models are adjusted for the random effect of machine.
[a]Values are given as least squares means (95% confidence interval).

the controls and processes by which acid and base concentrates are proportioned by the Fresenius and Gambro machines to achieve the desired conductivity. Sodium is the most abundant ion in dialysate, so conductivity often parallels dialysate sodium concentrations; 1 mS/cm (0.01 S/m) conductivity approximates 10 mEq/L of sodium.[14,23-25] The conductivity alarm range, outside of which an alarm is triggered, is ±0.5 mS/cm[26] (0.05 S/m) for Fresenius machines and ±5% for Gambro machines.[27] With either machine, the dialysate sodium concentration may differ significantly from that ordered before the machine alarms. The conductivity alarms can be easily widened during the treatment with Fresenius machines, whereas this is more difficult with the Gambro machines. Although alarm ranges were not knowingly altered in this study, it may occur in practice and could lead to even greater discrepancies between the prescribed and delivered dialysate sodium concentrations.

Both the Fresenius and Gambro machines have feedback control systems that allocate precise volumes of concentrates and water into the machine to achieve the ordered conductivity. Fresenius machines allocate the volumes of the concentrates based on the conductivity calculated by the machine from the initial dialysate sodium orders entered into the machine. In contrast, concentrate proportioning in the Gambro machines is controlled by alteration in the pump speed based on the conductivity measured by the acid and bicarbonate conductivity control sensors, respectively.[28]

The Fresenius machines are sensitive to the pressure in the loop through which the concentrates travel from the central delivery system tanks to the dialysate delivery machines, which should not be >2 psi (>1.37896 Pa).[26] If the pressure exceeds this value, extra concentrate may be pumped into the balancing chamber. Normally if the resulting conductivity is outside the accepted error range, this should set off the conductivity alarm.[26] In contrast, concentrate proportioning in the Gambro machines is not affected by high pressure in the loop.[27]

Improper calibration of dialysis machines is another potential source of error. Conductivity measurement is verified prior to the start of each shift using external meters, which are calibrated against standard solutions on a daily basis. The range of acceptable error is from ±0.2 mS/cm (0.02 S/m) to ±0.3 mS/cm (0.03 S/m), corresponding to dialysate sodium concentrations of approximately ±2 to 3 mEq/L.

Differences between prescribed and measured dialysate sodium concentrations were smaller in units using one predominant prescribed dialysate sodium concentration (>95% of patients) compared with units in which dialysate sodium concentration was more individualized. However, units with individualized dialysate sodium concentrations also used concentrates mixed on site and Fresenius dialysis machines. Therefore, we were unable to determine the relative impact of multiple dialysate sodium prescriptions, mixing dialysate on site, and type of dialysate delivery machine. Between treatments, hemodialysis machines do not automatically reset the dialysate sodium concentration. In daily practice in units in which a low dialysate sodium concentration is followed by a high dialysate sodium prescription, there may not be adequate time for the new dialysate prescription to fully equilibrate. Moreover, failure to reset the machine may occur and lead to even greater discrepancies in prescribed versus measured dialysate sodium concentrations. However, in the present study, differences between prescribed and measured dialysate sodium concentrations were not greater on later versus first shifts. With each new dialysate prescription, the pump speed (Gambro) or volume partitioned by the diaphragm pumps (Fresenius) must be adjusted. Failure to do so is another source of potential error.

In the present study, dialysate sodium values were measured using an indirect ion-selective electrode method, which is widely used across clinical laboratories. This method measures sodium activity rather than concentration. Because there is no protein in the dialysate, the reflective coefficient of sodium approaches unity and the Gibbs-Donnan effect is minimal. When measuring serum sodium, it is usual to correct for hyperglycemia to account for movement of water from the intracellular into the extracellular fluid. This does not occur in dialysate, and moreover, the dialysate glucose concentration was only 100 mg/dL.

With the newest indirect ion-selective electrode methods, sodium activity approaches sodium concentration in a protein- and glucose-free aqueous solution. These indirect readings are calibrated against reference values to yield a concentration.[29] La Milia et al[30] compared plasma and dialysate sodium concentrations measured by flame photometry, direct ion-selective electrodes, and indirect ion-selective electrodes in peritoneal dialysis patients. They obtained similar results with all 3 measurement techniques. In another study, there were small but consistent differences between results obtained with flame photometry and the indirect ion-selective electrode methods.[31] However, sodium measurements in peritoneal dialysate fluid are affected by hypertonic dialysate due to very high glucose concentration. Some authorities recommend direct potentiometry as the best method to determine dialysate sodium concentration because it allows sodium determination in undiluted samples.[18] Others consider the indirect method to provide an accurate assessment of dialysate sodium concentration.[2]

The present study has several strengths. To our knowledge, it is the largest study to examine the difference between prescribed and delivered dialysate sodium concentrations. The project was conducted in 4 different facilities, which used dialysate delivery machines and dialysate concentrates obtained from different manufacturers. All dialysate sodium concentrations were measured in a central laboratory. The study also has several limitations. We studied only 4 dialysis facilities, all operated by the same provider. Because multiple factors differed across these facilities, we were unable to quantitate the contribution of each factor to the observed disparities.

In summary, the present study demonstrated that there were often significant differences between prescribed and measured dialysate sodium concentrations. There was a positive bias, with measured dialysate sodium concentration often higher than that prescribed. The magnitude of these errors varied by clinic. It will be difficult to resolve the ongoing controversy regarding the optimal dialysate sodium concentration for hemodialysis patients unless we put in place the requisite quality control processes necessary to minimize differences between prescribed and delivered dialysate sodium concentrations. Therefore, consideration should be given to monitoring differences between prescribed and measured dialysate sodium concentrations as part of routine practice. Further research is needed to identify system processes that will minimize these differences.

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