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Dialysate Sodium: Choosing the Optimal Hemodialysis Bath

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Fluid overload in patients undergoing hemodialysis contributes to cardiovascular morbidity and is a major cause of hospitalizations. It is often addressed by reinforcing the importance of a low-salt diet with patients and challenging estimated dry weights. More recently, interest has shifted toward the dialysate sodium prescription as a strategy to improve fluid overload and its adverse sequelae. The availability of high-flux high-efficiency dialysis in conjunction with the need to ensure its tolerability for patients has resulted in an increase in dialysate sodium prescriptions from 120 to ≥140 mEq/L. However, we are now tackling the unforeseen consequences associated with high dialysate sodium prescriptions. High dialysate sodium concentration is associated with high interdialytic weight gain, a commonly used surrogate for hypervolemia contributing to hypertension. The association between mortality and high dialysate sodium concentration remains controversial with conflicting data. It is clear that fluid management in the diverse end-stage renal disease population is extremely complex and more clinical trials are needed. In the meantime, while patients require treatments and clinical decisions need to be made, this review article attempts to summarize the current evidence for individualized dialysate sodium prescriptions based on patients' volume status, comorbid conditions, plasma sodium level, and hemodynamic response to dialysis therapy.
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INDEX WORDS: Dialysate sodium; fluid overload; hemodialysis; sodium gradient; inter-dialytic weight gain; dry weight; target weight; intra-dialytic hypotension; review.

Note from Editors: This article is part 4 of a 4-part series of invited In Practice reviews highlighting issues related to the composition of dialysate.

CASE PRESENTATION

A 72-year-old African American woman with end-stage renal disease (ESRD) secondary to diabetes mellitus started hemodialysis (HD) therapy 15 months ago. Despite dietary education to limit sodium intake to <2 g/d and adherence to dialysis therapy and antihypertensive medications, her blood pressure remained uncontrolled with an average pre-HD measurement of 169/86 mm Hg. Dry weight was 93.0 kg and average interdialytic weight gain (IDWG) was 3.0 kg. She received dialysis for 180 minutes through an arteriovenous graft. Ultrafiltration was limited by cramps and intradialytic hypotension. Her average plasma sodium level over a 3-month period was 139 mEq/L. She dialyzed with a dialysate sodium concentration of 140 mEq/L. On routine clinical assessment, her lungs were clear and she had no lower-extremity edema. The patient was not interested in increasing her treatment time to optimize ultrafiltration, blood pressure control, and intradialytic adverse events.

INTRODUCTION

HD, a life-sustaining therapy for patients with ESRD, is currently used by close to 400,000 patients in the United States and accounts for almost 90% of the ESRD population.[1] Many aspects of the delivery of ESRD care have evolved and improved since the introduction of the Medicare Act in 1973. However, the scarcity of evidence from randomized clinical trials as a foundation of practice is surprising and often troubling. The focus on small-solute clearance as defined by Kt/V over the past 2 to 3 decades has overshadowed other critical issues, including fluid control. While achieving euvolemia through fluid removal during dialysis has always been part of the therapy, it is becoming center stage[2] in a concerted effort to ameliorate fluid-associated comorbid conditions, including hypertension and left ventricular hypertrophy. Multiple strategies are recommended to control volume overload. Efforts to optimize estimated dry weight, better termed "target weight," even in the absence of clinical symptoms of hypervolemia[3] have been helped by newer devices that monitor changes in relative blood volume.[4] In addition, efforts continue to educate patients on the benefits of low salt intake as the standard of care.[5] Achieving normovolemia is paramount to blood pressure control and prevention of its long-term consequences. High salt intake has always been recognized as a culprit for worse cardiovascular outcomes in patients with chronic kidney disease, including those with ESRD,[6-9] but the difficulty implementing long-lasting lifestyle changes such as a low-salt diet is well recognized. Therefore, new emphasis has been directed toward the subject of

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dialysate sodium prescription as a way to affect both salt and fluid balance.

In this review, we examine the historical evolution of dialysate sodium prescription since the inception of dialysis therapy and the changes made in response to the availability of advanced technology. The evidence for dialysate sodium prescription appears to heavily rely on practice patterns combined with evidence from mostly observational studies. Thus, the clinician is often left with the responsibility to prescribe without being able to rely on evidence-based guidelines. This article aims to support these clinical decisions with a review of the current literature and resulting recommendations.

HISTORICAL SUMMARY OF DIALYSATE SODIUM USE

Dr Willem J. Kolff, a pioneer of dialytic therapy, advocated use of a dialysate solution containing 126.5 mEq/L of sodium[10] since the 1940s because he realized that hypertension and thirst were much easier to control[11] (Table 1).

Disequilibrium Syndrome and Osmotic Ultrafiltration (1960s)

In the early 1960s, when HD became a reality for the treatment of uremia and ESRD, use of very low dialysate sodium concentration was a common practice to treat hypertension. However, it was associated with complications. Initial observations reported periods of disorientation and convulsions, mostly seen in patients treated with a dialysate sodium concentration $<$ 120 mEq/L,[12] and a new clinical disorder called dialysis disequilibrium syndrome was described.[13] This syndrome included self-limited symptoms such as headache, nausea, vomiting, blurry vision, disorientation, restlessness, tremors, and seizures occurring during or soon after HD, mainly in patients new to dialysis therapy.[14] While the pathogenesis of this syndrome is not completely understood, experimental models suggest that the cerebral edema associated with rapid decrease of urea in uremic animals is probably a result of idiogenic osmols and not due to changes in sodium concentration.[15]

The first dialytic treatments used dialyzers unable to resist high transmembrane pressures. Therefore, fluid removal was performed by "osmotic ultrafiltration" using high dialysate glucose concentrations (1.36-2.72 g/dL) to create an osmotic gradient.[10] These supraphysiologic glucose concentrations increased dialysate osmolality, counteracting the low sodium concentration.[10] The development of dialyzers capable of tolerating higher pressures allowed the change to "hydrostatic ultrafiltration" (fluid removal by increasing transmembrane pressures)[10,16] and led to the reduction of high glucose dialysate concentration to 182 mg/dL.[10] This, together with efforts to prevent disequilibrium syndrome, coincided with the first increase in dialysate sodium concentration. In 1963, 80% of European dialysis centers used a dialysate sodium concentration of 130 mEq/L.[10]

Acetate and Treatment Time (1970 to early 1980s)

In 1964, acetate was used as the dialysate buffer of choice instead of bicarbonate to eliminate the need for an extra pump.[17] However, with the introduction of increased-efficiency dialyzers in the late 1960s, symptoms resembling disequilibrium syndrome, including nausea, headache, weakness, fatigue, and muscle cramps, although milder, emerged again.[14] Later, acetate was identified as the culprit for many of these symptoms, resulting in the reintroduction of bicarbonate dialysis.[18-20]

HD treatments were initially performed for more than 24 hours every 5 to 7 days.[21-23] With increasing hypertension, fluid overload, and neuropathy among patients with ESRD, the frequency was changed to 12 to 20 hours twice weekly,[21,24] before a thrice-weekly 8- to 10-hour dialysis schedule became standard in home hemodialysis programs.[24] Over time, larger dialyzers with newer membranes led to shorter dialysis schedules. The long-term feasibility of

Table 1. Dialysate Sodium History

	Milestones	Na_d (mEq/L)	Dialysate Buffer	Time (h)	Frequency
Kolff, 1940	Acute	126.5	Bicarbonate	>24	On demand
Scribner, 1960	Maintenance		Bicarbonate	76	Every 5-7 d
1960s		~130	Bicarbonate	12-20	2×/wk
1964	Home HD		Acetate	8-10	3×/wk
1970		~135	Acetate		
1973	Short HD	137	Acetate	3-4	3×/wk
1980s		134-136	Bicarbonate	3-4	3×/wk
1990-2000		138-141	Bicarbonate	3-4	3×/wk
2010-2015		136-149	Bicarbonate	3-4	3×/wk

Abbreviations: HD, hemodialysis; Na_d, dialysate sodium.