Management of Severe Hyponatremia with Continuous Renal Replacement Therapies

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Introduction

For most American Society of Nephrology (ASN) Kidney Week attendees, case-based clinical nephrology talks are one of the most exciting venues. The Nephrology Quiz and Questionnaire (NQ&Q) is the essence of clinical nephrology and represents what drew all of us into the field of nephrology. This year’s NQ&Q in “The Big Easy” (city of New Orleans), with full-house audience, was no exception. The expert discussants prepared vignettes of puzzling cases, which illustrated some topical, challenging, or controversial aspect of the diagnosis or management of key clinical areas of nephrology. These eight interesting cases were presented and eloquently discussed by four our expert ASN faculty. Subsequently, each discussant prepared a manuscript summarizing a case discussion, which serves as the main text of this article. (Mark A. Perazella and Michael Choi, comoderators).

Patient A

A 72-year-old woman with hypertension and stage 4 CKD (baseline creatinine 2.4–2.8 mg/dl) is admitted to the hospital with malaise and confusion. Approximately 10 days before, her primary care practitioner had increased enalapril to 20 mg twice daily (from 10 mg twice daily) and added furosemide 20 mg twice daily to get better control of BP. At that visit, her serum sodium was 124 mEq/L, and creatinine was 3.0 mg/dl. Over the next week, she has become lethargic with decreased urine output and confused. At the urging of her daughter, she has been drinking excessive amounts of fluid (>2 L/d) over the past week. On presentation, she was not oriented to person or place, and her vital signs were notable for an elevated respiratory rate and an oxygen saturation of 82% on room air but otherwise normal. Physical examination revealed jugular venous distention, bibasilar rales, and an S4 on cardiac examination. Blood chemistries were notable for the following: sodium 112 mEq/L, potassium 6.8 mEq/L, chloride 80 mEq/L, bicarbonate 16 mEq/L, BUN 93 mg/dl, and creatinine 3.6 mEq/L.

Question

Which of the following would be your next step in management of this patient?

A. 0.9% Saline infused at 125 ml/min
B. Hemodialysis with a custom sodium dialysate of 130 mEq/L
C. Continuous venovenous hemofiltration with a custom replacement solution
D. Tolvaptan 30 mg/d

Discussion

The correct answer for this patient would be item C. This patient presents with acute on CKD along with oliguria, volume overload, severe hyponatremia, and hyperkalemia along with metabolic acidosis. Another important aspect of her history includes the observation that at least some component of her hyponatremia is chronic on the basis of baseline plasma sodium of 124 mEq/L. Thus, the clinical imperative in treating this patient is to correct the metabolic disarray, while at the same time, avoiding over-rapid correction of her serum sodium. Recent guidelines stress that, in a patient such as this, to avoid the development of osmotic demyelination syndrome, the rate of correction of her serum sodium should be no >6 mEq/L per day (1). Of note, the patient presented with confusion, which may be multifactorial, but it certainly raises the question of hyponatremia-associated encephalopathy. In this case, 100 ml of hypertonic (3%) sodium chloride could be administered intravenously to more rapidly raise the plasma sodium value a few milliequivalents per liter (2). However, given this patient’s signs of volume overload as well as other metabolic derangements, careful monitoring would be required to avoid worsening of her volume status. In this case, it was felt that emergent initiation of continuous RRT (CRRT) would be the best treatment option. Tolvaptan would be ineffective with this degree of AKI and would not address the other metabolic issues.

Continuous Dialysis for the Correction of Hyponatremia

CRRT has advantages in its ability to correct plasma sodium values in a predictable and slow manner (3,4). Compared with standard hemodialysis machines, where the lowest dialysate sodium concentration is 130 mEq/L (due to constraints from the conductivity
alarm), CRRT solutions can be customized to any desired sodium level, allowing for personalized therapy (5). To operationalize these advantages and prescribe CRRT to target an increase in serum sodium no >6 mEq/L per day, the clinician has two options: either (1) customize the CRRT circuit or (2) customize CRRT solutions. Within these groupings, there are many ways to achieve this goal, and this approach is one methodology.

**Method 1: Customizing the CRRT Circuit**

The CRRT circuit has the advantage that the clinician can control numerous parameters and concentrations of replacement and dialysis solutions to achieve a goal. In this patient, our goal is to treat hyponatremia, hyperkalemia, and AKI.

(1) Continuous venovenous hemofiltration. We need to decide on a dose of renal replacement, and data support targeting a total effluent flow rate of 20–25 ml/kg per hour; if we assume a body weight of 80 kg, then total effluent flow should be 1600–2000 ml/h (typically, effluent flow rates may be higher to account for interruptions in therapy) (6). The blood flow rate will be set at 200 ml/min, and replacement fluid will be delivered prefiltre at 2000 ml/h (Figure 1A). The filtration fraction, which should ideally be <25% to lower the risk of filter clotting, is 19% (assuming a hematocrit in the normal range). As shown in Figure 1A, typical replacement solution has a sodium concentration of 140 mEq/L. With this prescription, the sodium concentration at the end of the circuit can be determined by total sodium in circuit (per hour)/total therapy fluid amount (per hour). In this case, (replacement sodium concentration × rate) + (dialysate sodium concentration × rate)/total fluid amount. Substituting the treatment values, (140 mEq/L × 2 L)/2 L = 140 mEq/L. Obviously, we do not want the sodium at the end of the circuit to be this high, which would translate into raising the plasma sodium to this level as

![Figure 1. Schematic representation of continuous RRT (CRRT) and correction of hyponatremia. (A) Continuous venovenous hemofiltration (CVVH). (B) Continuous venovenous hemodialfiltration (CVVHDF). Ca, calcium; CaCl2, calcium chloride; Cl−, chloride; D5W, 5% dextrose in water; iCa2+, ionized calcium; Gluc, glucose; K+, potassium; HCO3−, bicarbonate; Mg, magnesium; PF, post filter; Na+, sodium; Qb, blood flow rate; Qd, dialysate fluid rate; Qr, replacement fluid rate; V, venous. Modified from Ashita Tolwani, with permission.](image-url)
well. To lower the circuit sodium concentration, additional replacement fluid can be added, such as 5% dextrose in water (D5W). If D5W was added as a postfilter replacement, then the resulting circuit sodium would be lowered as follows: (140 mEq/L × 2 L) + (0 mEq/L × 0.4 L)/(2 L + 0.4 L), which equals 116.7 mEq/L, a value close to that desired. With this additional fluid, the dose increases to 30 ml/kg per hour, and the filtration fraction increases to 23%. After the plasma sodium increases to 117 mEq/l, the postfilter replacement solution can be changed using this method to target the plasma sodium to whatever is desired by either decreasing the rate of the D5W postfilter replacement solution or changing the solution to D5 0.25 NaCl or D5 0.5 NaCl.

(2) Continuous venovenous hemodiafiltration. In this case, commercial dialysate solutions are used, which have a sodium concentration of 140 mEq/L, and the circuit may include citrate anticoagulation, which has a sodium concentration of 224 mEq/L (ACD solution; Baxter). Walking through this prescription, (1) dose of 20–25 ml/kg per hour or 1600–2000 ml/h, (2) blood flow rate of 200 ml/h, (3) dialysate solution (Figure 1B) with sodium concentration of 140 mEq/L (Prismasate), and (4) anticoagulation with ACD (Baxter) and sodium concentration of 224 mEq/L at 300 ml/h. The sodium at the end of the circuit will be quite high, and thus, D5W replacement fluid must be added (650 ml/h). With this prescription, the sodium at the end of the circuit is (224 mEq/L × 0.3 L) + (140 mEq/L × 2 L) + (0 mEq/L × 0.65 L)/(0.3 L + 2 L + 0.65 L) = 117.7 mEq/L. Thus, the addition of D5W replacement solution allows the calibration of the dialysis circuit sodium concentration to any desired value.

Method 2: Customizing Dialysis Solutions
An alternative methodology involves adding various volumes of sterile water to commercial dialysis solutions to achieve a desired final sodium concentration. For instance, if a 5-L bag of replacement solution has a sodium concentration of 140 mEq/L, then the addition of 1 L of water would result in a final sodium solution of the replacement solution of 116.7 mEq/L. Of note, the addition of D5W also lowers the potassium from 4 to 3.33 mEq/L. The downsides of this approach include the requirement for a compounding pharmacist and the added expense and potential for an error in making these changes. A nomogram for these additions of sterile water to commercial dialysis solutions can be found in ref. 3.

Summary
Unstable patients with hyponatremia and AKI represent challenging clinical circumstances. CRRT offers the advantage of allowing a personalized approach to therapy, whereby a desired sodium correction can be determined and prescribed through customized replacement solutions or altering the circuit. Frequent determinations of the patient’s plasma sodium level should occur, and the prescription should be altered accordingly. Although the above methods are on the basis of mathematical determinations of the CRRT circuit sodium concentration, it should be noted that these methods have not been validated in clinical trials. That being said, in CRRT, patients reach a steady state where the serum electrolyte concentrations of sodium, potassium, chloride, magnesium, and calcium approximate the CRRT circuit therapy fluid concentrations of these same solutes.

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Disclosures
None.

References

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