1-1-2014

Treatment of severe hyponatremia in patients with kidney failure: Role of continuous venovenous hemofiltration with low-sodium replacement fluid

Lenar Yessayan
Henry Ford Health

Jerry Yee
Henry Ford Health, JYEE1@hfhs.org

Stan Frinak
Henry Ford Health, Sfrinak1@hfhs.org

Balazs Szamosfalvi
Henry Ford Health, bszamos1@hfhs.org

Recommended Citation

Yessayan L, Yee J, Frinak S, Szamosfalvi B. Treatment of severe hyponatremia in patients with kidney failure: Role of continuous venovenous hemofiltration with low-sodium replacement fluid. American Journal of Kidney Diseases 2014; 64(2):305-310.

AJKD

Acid-Base and Electrolyte Teaching Case

Treatment of Severe Hyponatremia in Patients With Kidney Failure: Role of Continuous Venovenous Hemofiltration With Low-Sodium Replacement Fluid

Lenar Yessayan, MD, Jerry Yee, MD, Stan Frinak, MSEE, and Balazs Szamosfalvi, MD

Patients with hypervolemic hyponatremia and kidney failure pose a special therapeutic challenge. Hemodialysis to correct volume overload, azotemia, and abnormal electrolyte levels will result in rapid correction of serum sodium concentration and place the patient at risk for osmotic demyelination syndrome. We present a patient with acute kidney injury and severe hypervolemic hypotonic hyponatremia (serum sodium < 100 mEq/L) who was treated successfully with continuous venovenous hemofiltration. This teaching case illustrates the limitations of hemodialysis and demonstrates how to regulate the sodium correction rate by single-pool sodium kinetic modeling during continuous venovenous hemofiltration. Two methods to adjust the replacement fluid to achieve the desired sodium concentration are outlined.

Am J Kidney Dis. 64(2):305-310. © *2014 by the National Kidney Foundation, Inc.*

INDEX WORDS: Hyponatremia; treatment; continuous venovenous hemofiltration (CVVH); hemodialysis.

INTRODUCTION

In patients with chronic severe symptomatic hyponatremia and concomitant kidney failure, hypertonic saline should be used until resolution of the symptoms. Thereafter, the goal should be gradual correction of serum sodium level, by not more than 8-10 mEq/L over 24 hours.[1] In those who require hemodialysis, rapid correction of serum sodium concentration [Na^+] could ensue and put the patient at risk for osmotic demyelination syndrome.[2,3] Management using continuous renal replacement therapy also is challenging due to the lack of commercially available hypotonic dialysate or replacement fluids. This teaching case presents a patient with acute kidney injury and severe hyponatremia (serum [Na^+] < 100 mEq/L) treated with continuous venovenous hemofiltration (CVVH) in which gradual correction of serum [Na^+] was achieved using hypotonic replacement fluid composed of successively higher [Na^+].

CASE REPORT

Clinical History and Initial Laboratory Data

A 54-year-old woman presented to the emergency department with confusion, decreased responsiveness, and generalized weakness for 24 hours. She had nausea and decreased oral intake for a few weeks, with reduced urine output for a few days. Her medical history was significant for uncontrolled hypertension and alcohol abuse. Blood pressure was 246/115 mm Hg, heart rate was 106 beats/min, respiration rate was 21 breaths/min, and pulse oximetry was 94% on room air.

The patient's physical examination revealed bilateral basilar rales. Serum laboratory studies showed the following values: sodium, 96 mEq/L; potassium, 5.6 mEq/L; chloride, 64 mEq/L; bicarbonate, 16 mEq/L; serum urea nitrogen, 51 mg/dL; creatinine, 9.9 mg/dL; phosphorus, 8.1 mg/dL; serum osmolality, 226 mOsm/kg; and brain natriuretic peptide, 2,800 pg/mL. Arterial blood gas analysis showed pH 7.36, $Paco_2$ of 27.9 mm Hg, Pao_2 of 57.5 mm Hg, and bicarbonate level of 15.4 mEq/L. Urine sediment showed few granular casts. Urine osmolality was 157 mOsm/kg, sodium was 40 mEq/L, and creatinine was 33 mg/dL, with fractional sodium excretion of 12.5%.

Additional Investigations

Computed tomography of the brain demonstrated no intracranial pathology. The radiograph of the chest showed mild to moderate cardiomegaly with pulmonary vascular congestion.

Diagnosis

Acute kidney injury and severe hypervolemic hypotonic hyponatremia was diagnosed. Acute tubular necrosis was the presumptive cause of the acute kidney injury.

Clinical Follow-up

Treatment goals were identified to include gradual correction of hyponatremia, alleviation of congestive heart failure, and management of hyperkalemia, azotemia, and hyperphosphatemia. The patient began CVVH using a modified hypotonic replacement fluid. Standard fluid bags (NxStage PureFlow dialysate solution RFP 401; NxStage Medical Inc) were diluted by the addition of pure water to 112 mEq/L at the start of CVVH, 120 mEq/L 24 hours later, and 128 mEq/L 56 hours after initiating CVVH. CVVH was performed for a total of 72 hours at a rate of correction recommended by therapeutic guidelines[4] (Fig 1). Mentation improved without neurologic sequelae. On hospital day 2, an ultrasonogram showed bilateral hydronephrosis, which was treated by bilateral nephrostomy tube insertions on day 4 that produced complete recovery of kidney function. The patient was essentially anuric (urine < 100 mL/d) until bilateral nephrostomy placement.

From the Division of Nephrology and Hypertension, Henry Ford Hospital, Detroit, MI.

Received September 12, 2013. Accepted in revised form January 13, 2014. Originally published online May 2, 2014.

Address correspondence to Lenar Yessayan, MD, Division of Nephrology and Hypertension, Henry Ford Hospital, 2799 West Grand Blvd, Detroit, MI 48202. E-mail: lyessay1@hfhs.org

0272-6386/$36.00

http://dx.doi.org/10.1053/j.ajkd.2014.01.451

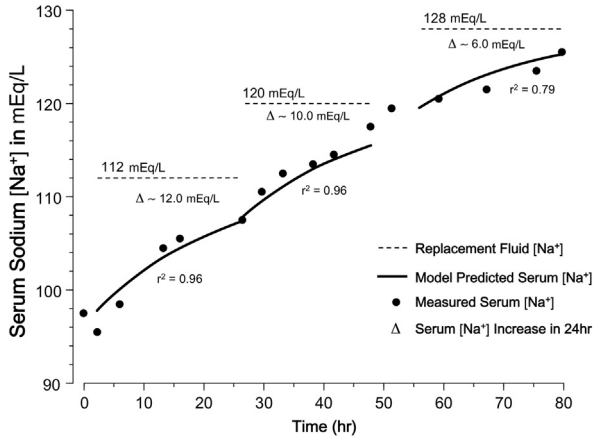

Figure 1. Serum sodium concentrations at baseline and during continuous venovenous hemofiltration (CVVH) while using successively higher replacement fluid concentrations. The r^2 denotes the coefficient of determination between predicted and measured serum sodium levels for each 24-hour CVVH period.

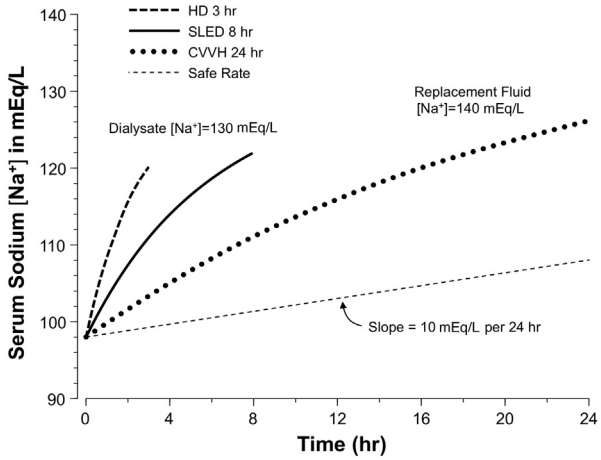

Figure 2. The expected serum sodium change during hemodialysis (HD), sustained low-efficiency dialysis (SLED), and continuous venovenous hemofiltration (CVVH) with noncustomized fluid bags. For HD, treatment time is 3 hours, dialysate sodium is 130 mEq/L, blood flow rate is 200 mL/min, and approximate delivered urea clearance is 180 mL/min (10.8 L/h). For SLED, treatment time is 8 hours, dialysate sodium is 130 mEq/L, dialysate flow is 100 mL/min, blood flow rate is 200 mL/min, and approximate delivered urea clearance is 78 mL/min (4.7 L/h). For CVVH, treatment time is 24 hours, replacement fluid sodium is 140 mEq/L, blood flow rate is 300 mL/min, replacement fluid is 1.2 L/h, and approximate delivered urea clearance is 1.2 L/h.

The final diagnosis was obstructive acute kidney injury due to cervical cancer.

DISCUSSION

Management of hypotonic hyponatremia should be based on its presumed duration and severity. In acute hyponatremia, free water movement into brain cells results in varying degrees of cerebral edema.[5] The risk of electrolyte disturbance exceeds that of osmotic demyelination syndrome secondary to rapid correction. Chronic hyponatremia is associated with brain cells adaptively losing organic osmolytes, and thus life-threatening cerebral edema is less likely.[6] This adaptation renders the brain vulnerable to osmotic demyelination syndrome in response to a rapid increase in serum [Na^+].[7-9] Therefore, management of hyponatremia entails balancing the risks of hyponatremia with those of rapid correction. For decades, a total increase of 12 mEq/L per day was considered safe[10,11]; however, osmotic demyelination syndrome has been reported with correction of only 10 mEq/L per day.[12,13] Consequently, even lower limits of correction have been recommended: 10 mEq/L in 24 hours and 18 mEq/L in 48 hours.[1]

Patients with severe hyponatremia and kidney failure with volume expansion pose a unique therapeutic challenge. Hypertonic saline is undesirable in patients with kidney failure and expanded volume status. Similarly, V_2 receptor antagonists are not likely to be effective at reduced glomerular filtration rates because of diminished fluid delivery to the distal nephron[14]; in the absence of published experience at reduced glomerular filtration rates, the use of these agents cannot be recommended.

Successful treatment of patients with kidney failure and hyponatremia using different extracorporeal modalities, including hemodialysis at low blood flow rates,[15] CVVH,[16] and continuous venovenous hemodialysis,[17,18] has been reported. However, all renal replacement modalities could be deleterious when used in severe cases of hyponatremia (Fig 2).

In patients with kidney failure and severe hyponatremia, hemodialysis would induce a rapid increase in serum Na^+ with the potential for osmotic demyelination syndrome.[2,19] The high blood flow rates (Q_b; $>$ 200 mL/min) and inability to reduce the dialysate bath's [Na^+] to $<$130 mEq/L are 2 reasons for the high Na^+ transfer when using conventional hemodialysis to treat hyponatremia. Theoretically, the dialysis machine's alarm system could be manipulated and calibrated to a lower [Na^+], at the expense of a treatment session with nonfunctional conductivity monitoring, posing an unwarranted and significant safety risk.

Complex Na^+ kinetic models were shown to be able to predict end-dialysis serum [Na^+] in previous clinical studies.[20] We present a simpler set of Na^+ kinetic equations that are more easily applicable in clinical practice and can be used to estimate serum [Na^+] at the end of treatment. By applying urea clearance principles to Na^+ dialysance (D), serum [Na^+] at the end of hemodialysis and CVVH treatments is predictable. The final serum [Na^+] is the sum of the initial serum [Na^+]

Box 1. CVVH With Fluid Customization

- Determine target correction for the next 24 hours (not to exceed 10 mEq/L)

$$initial\ serum\ [Na^+] = 98\ mEq/L,\ desired\ \Delta\ serum [Na^+] = 10\ mEq/L$$

- Determine minimum urea clearance (K) in L/h

Urea clearance for a 50-kg female: 25 mL/kg/h × 50 kg = 1.25 L/h

- Determine delivered K for a fixed blood flow rate (Q_b), replacement fluid (Q_{rf}), and ultrafiltration rate (Q_{uf})

$$Urea\ clearance\left(\frac{L}{h}\right) = \left(\frac{Q_b}{Q_b + Q_{rf}}\right) \times (Q_{rf} + Q_{uf})$$

- Adjust replacement fluid rate for a fixed Q_b and Q_{uf} to achieve a desired K

K = 1.3 L/h with Q_b = 300 mL/min, Q_{rf} = 1.2 L/h, and Q_{uf} = 167 mL/h

- Assume Na^+ dialysance (D) = K
- To calculate delivered Dt/V over each 24-hour period, estimate total-body water (TBW) volume (V):

V ≈ TBW = 0.5* × estimated dry weight for females + estimated ECF expansion

V ≈ TBW = 0.6* × estimated dry weight for males + estimated ECF expansion

We estimated about 6 L of edema. Estimated dry weight ≈ 44 kg and 6 L of edema = 44 × 0.5 + 6 = 28 L.

- Determine replacement fluid [Na^+] needed to achieve desired [Na^+] change

$$Replacement\ fluid\ [Na^+] = \frac{desired\ \Delta\ serum\ [Na^+]}{\left(1 - e^{-\frac{D \times 24\ h}{V}}\right)} + initial\ serum\ [Na^+]$$

Declining V with ultrafiltration will have minimal impact on $1 - e^{-\frac{D \times 24\ h}{V}}$. If desired, an average of time = 0 and time = 24-hour estimated V can be used to predict the replacement fluid with better accuracy.
It is ~0.66 with an estimated V = 28 L and 0.71 with an estimated V = 24 L by the end of the first 24 hours. The average of the 2 values can be used when estimating the replacement fluid [Na^+].

- Refer to Table 1 or 2 to determine the volume of water to be added to replacement fluid or to be exchanged to achieve desired replacement fluid [Na^+].
- In summary, in those in whom 24-hour Kt/V = 1.2, we use fluid [Na^+] about 10-12 mEq/L higher than the patient's serum [Na^+] for daily correction of 6-8 mEq/L.

Abbreviations: CVVH, continuous venovenous hemofiltration; ECF, extracellular fluid; [Na^+], sodium concentration.
*Multiply by 0.4 and 0.5 for elderly females and males, respectively.

and the change in serum [Na^+] incurred during dialysis (equation 1).

$$(1)\quad Final\ serum\ [Na^+] = initial\ serum [Na^+] + \Delta\ serum [Na^+]$$

The change in serum [Na^+] (ignoring ultrafiltration) at time t is determined by a number of variables (equation 2), including the initial serum [Na^+], the dialysate [Na^+], total-body water volume (V),[21] and D.

$$(2)\quad \Delta\ serum\ [Na^+] = (dialysate\ [Na^+] - initial\ serum\ [Na^+]) \times \left(1 - e^{-\frac{Dt}{V}}\right)$$

An estimate of V can be calculated by using Watson formula applied to the patient's euvolemic weight and adding any estimated edema volume. Fixed-volume (as opposed to variable-volume) single-pool Na^+ kinetic modeling can be used for simplicity without compromising clinically sufficient accuracy. However, one also could use the average of pre- and posttreatment V to better account for the variable volume. Because Na^+ and urea are both non–protein-bound small solutes and have similar effective blood water flow, their dialyzer solute transfer characteristics would be similar. Therefore, effective urea clearance can be used to estimate D.[22] An estimate for urea clearance could be obtained from nomograms that display the relationship of blood water urea clearance as a function of dialyzer efficiency, Q_b, and dialysate flow rate. Our patient had a predialysis body weight of 50 kg. We estimated that she had an approximate V of approximately 26-27 L. Predialysis serum [Na^+] was 98 mEq/L. Hemodialysis treatment for 3 hours with 130-mEq/L dialysate [Na^+], 1.6-m^2 surface area hemodialyzer, 180-minute treatment time, 500-mL/min dialysate flow rate, and 200-mL/min Q_b would have achieved an approximate single-pool Na^+ Dt/V of 1.2. This should result in change in serum [Na^+] of 22 mEq/L by the end of the 3-hour treatment, or change in serum [Na^+] of ~7 mEq/h, and would have put the patient at risk for osmotic demyelination syndrome.

The change in serum [Na^+] using sustained low-efficiency dialysis (SLED) also can be estimated using equation 2. For example, at Q_b of 200 mL/min, dialysate [Na^+] of 130 mEq/L, and dialysate flow rate of 100 mL/min, D would be at least 80 mL/min, somewhat lower than the dialysate flow due to dialysate shunting and channeling on the dialyzer. Nevertheless, an 8-hour SLED treatment would still result in a 24-mEq/L increase in serum [Na^+] with an adequate urea Kt/V of 1.4. The previous equations ignore the Gibbs-Donnan effect on Na^+ kinetics, the impact of possible access recirculation, and non-isotonic intravenous fluid, Na^+, or potassium administration to the patient, yet demonstrate the limitations and dangers posed by hemodialysis and SLED in severe hyponatremia.

Alternatively, by using CVVH, the serum [Na^+] correction rate can be controlled by making successive dilutions of the replacement fluid bags every 24 hours. Simply, the [Na^+] of the replacement fluid needs to be about 3-4 mEq/L higher than the desired goal serum [Na^+] while delivering a urea Kt/V of 1.2 every 24 hours. Through kinetic modeling of D, we can estimate the concentration of the replacement fluid required every 24 hours to achieve a specific desired change. Importantly, the purely convective Na^+ kinetics in CVVH allows us to predict D accurately, even without online clearance tools. The replacement fluid [Na^+] is determined by the desired change in serum [Na^+] in 24 hours, the D, the duration of treatment, and the V, which has to be adjusted every 24 hours to account for changing total-body weight. To account for the variable volume, the mean value of the estimated initial and final volume could be used as an estimate of V:

$$(3)\ Replacement\,fluid\left[Na^+\right] = \frac{desired\,\Delta\,serum\left[Na^+\right]}{\left(1-e^{-\frac{D\times 24\,h}{v}}\right)} + initial\,serum\left[Na^+\right]$$

D in predilution CVVH mode is determined by replacement fluid flow rate (Q_{rf}); ultrafiltration rate (Q_{uf}); effective blood water flow for Na^+, which is about equal to Q_b; and the Na^+ sieving coefficient (S_{Na^+}), which is almost equal to 1:

$$(4)\ D = \left(\frac{Q_b}{Q_b + Q_{rf}}\right) \times S_{Na^+} \times \left(Q_{rf} + Q_{uf}\right)$$

For our patient, the goal for the first 24 hours was to increase serum [Na^+] by 10-12 mEq/L to 108 mEq/L because we assumed an element of acute hyponatremia in the presence of mental status changes and pulmonary edema, and to perform 4-L Q_{uf}. To estimate the replacement fluid [Na^+] needed, we first had to estimate D using equation 4. We selected flows to deliver ~25 mL/kg per hour or 1.2 Kt/V per day urea clearance for adequacy and perform 4-L ultrafiltration. The estimated D was 1.28 L/h at Q_b of 300 mL/min, Q_{rf} of 1.2 L/h, and Q_{uf} of 167 mL/h. For a desired change of 10 mEq/L and an initial serum [Na^+] of 98 mEq/L, the estimated replacement fluid [Na^+] using equation 3 was 112 mEq/L. The replacement fluid used achieved the desired serum [Na^+] target of 108 mEq/L at the end of 24 hours. Our goal for the second 24 hours was to increase serum [Na^+] to ~116 mEq/L and perform 2-L ultrafiltration. We adjusted the replacement fluid Na^+ to 120 mEq/L to achieve serum [Na^+] of 116 mEq/L after the second 24 hours. Using equations 1 and 2, the predicted serum [Na^+] after 24 hours was 116.8 mEq/L using an estimated clearance of 1.2 Kt/V with V of 23 L. Serum [Na^+] increased to 118 mEq/L by the end of treatment. This was slightly higher than estimated by the equations, which might be explained in part by intravenous medications suspended in normal saline solution (total, 500 mL). The patient's mentation and responsiveness improved, and CVVH was withheld and then reinitiated after 8 hours at a serum [Na^+] of 120 mEq/L with the goal to remain at <126 mEq/L over the next 24 hours. Using

Table 1. Effect of Adding Different Volumes of Water to 5-L Replacement Fluid Bag

Volume Added (mL)	Sodium Final (mEq/L)	Potassium Final (mEq/L)	Bicarbonate Final (mEq/L)	Calcium Final (mEq/L)	Magnesium Final (mEq/L)	Chloride Final (mEq/L)
0	140.00	4.00	34.00	3.00	1.00	113.00
250	133.33	3.81	32.38	2.86	0.95	107.62
429	128.94	3.68	31.31	2.76	0.92	104.07
500	127.27	3.64	30.91	2.73	0.91	102.73
713	122.53	3.50	29.76	2.63	0.88	98.90
750	121.74	3.48	29.57	2.61	0.87	98.26
1,000	116.67	3.33	28.33	2.50	0.83	94.17
1,250	112.00	3.20	27.20	2.40	0.80	90.40

Note: The 5-L replacement fluid bag is NxStage PureFlow dialysate solutions RFP 401.

Table 2. Effect of Exchanging Different Volumes of a 5-L Replacement Fluid Bag With Sterile Water

Volume Replaced (mL)	Sodium Final (mEq/L)	Potassium Final (mEq/L)	Bicarbonate Final (mEq/L)	Calcium Final (mEq/L)	Magnesium Final (mEq/L)	Chloride Final (mEq/L)
0	140.00	4.00	32.00	3.00	1.00	113.00
250	133.00	3.80	30.40	2.85	0.95	107.35
429	127.99	3.66	29.25	2.74	0.91	103.30
500	126.00	3.60	28.80	2.70	0.90	101.70
713	120.04	3.43	27.44	2.57	0.86	96.89
750	119.00	3.40	27.20	2.55	0.85	96.05
1,000	112.00	3.20	25.60	2.40	0.80	90.40
1,250	105.00	3.00	24.00	2.25	0.75	84.75

Note: The 5-L replacement fluid bag is NxStage PureFlow dialysate solution RFP 401.

replacement fluid Na^+ of 128 mEq/L, serum [Na^+] increased to 126 mEq/L. A suggested management outline is summarized in Box 1.

A stepwise correction of the patient's serum [Na^+] should be performed using hypotonic replacement fluid, with successively higher [Na^+] adjusted at least every 24 hours. The replacement fluid's [Na^+] could be reduced by adding sterile water to standard replacement fluid bags. Alternatively, sterile distilled water could be exchanged for a volume of replacement fluid. The effect of sterile water added or exchanged on Na^+ and other electrolyte concentrations is demonstrated in Tables 1 and 2. The volume of sterile water to be added to a replacement fluid (RF) bag to achieve a desired [Na^+] can be given by the equation:

$$\text{Volume to add} = \frac{RF\ volume \times (initial\ RF\ [Na^+] - desired\ RF\ [Na^+])}{desired\ RF\ [Na^+]}$$

The use of the former method was not preferred in this case because the large volume of sterile water (1.25 L) required to dilute the standard 5-L NxStage PureFlow dialysate solution to 112 mEq/L would not fit in the manufacturer's bag. We chose to exchange sterile distilled water for a volume of replacement fluid. The volume to be exchanged was calculated using the following formula:

$$\text{Volume to exchange} = RF\ volume - \frac{desired\ RF\ [Na^+] \times RF\ volume}{initial\ RF\ [Na^+]}$$

The NxStage PureFlow dialysate solution for the hemofiltration 5-L bag has [Na^+] of 140 mEq/L. We needed a replacement fluid [Na^+] of 112 mEq/L in the first 24 hours. The volume to be exchanged with free water to lower [Na^+] to 112 mEq/L therefore would be 1,000 mL:

$$Volume\ to\ exchange = 5\ L - \frac{112\ mEq/L \times 5\ L}{140\ mEq/L} = 1\ L$$

Similarly, the volume exchanged with sterile distilled water to achieve replacement fluid [Na^+] of 120 and 128 mEq/L would be 714 and 429 mL, respectively.

If serum [Na^+] increases by >3 mEq/L in any 6 hours, the CVVH prescription may be adjusted to not exceed daily urea Kt/V of 1.2 or urea clearance of 25 mL/kg per hour, or replacement fluid bags with lower [Na^+] may be used. Finally, in an emergency, 5% dextrose in water may be administered intravenously to lower serum [Na^+].

ACKNOWLEDGEMENTS

The authors thank Stephanie Stebens for assistance with manuscript preparation and Sarah Whitehouse for editorial expertise and handling of the paper.

Support: None.

Financial Disclosure: The authors declare that they have no relevant financial interests.

REFERENCES

1. Sterns RH, Nigwekar SU, Hix JK. The treatment of hyponatremia. *Semin Nephrol*. 2009;29(3):282-299.

2. Huang WY, Weng WC, Peng TI, Ro LS, Yang CW, Chen KH. Central pontine and extrapontine myelinolysis after rapid correction of hyponatremia by hemodialysis in a uremic patient. *Ren Fail*. 2007;29(5):635-638.

3. Sirota JC, Berl T. Is osmotic demyelination a concern dialyzing hyponatremic patients? *Semin Dial*. 2011;24(4):407-409.

4. Verbalis JG, Goldsmith SR, Greenberg A, Schrier RW, Sterns RH. Hyponatremia treatment guidelines 2007: expert panel recommendations. *Am J Med*. 2007;120(11)(suppl 1):S1-S21.

5. Arieff AI. Hyponatremia, convulsions, respiratory arrest, and permanent brain damage after elective surgery in healthy women. *N Engl J Med*. 1986;314(24):1529-1535.

6. Videen JS, Michaelis T, Pinto P, Ross BD. Human cerebral osmolytes during chronic hyponatremia. A proton magnetic resonance spectroscopy study. *J Clin Invest*. 1995;95(2):788-793.

7. Verbalis JG, Martinez AJ. Neurological and neuropathological sequelae of correction of chronic hyponatremia. *Kidney Int*. 1991;39(6):1274-1282.

8. Lien YH, Shapiro JI, Chan L. Study of brain electrolytes and organic osmolytes during correction of chronic hyponatremia. Implications for the pathogenesis of central pontine myelinolysis. *J Clin Invest*. 1991;88(1):303-309.

9. Sterns RH, Silver SM. Brain volume regulation in response to hypo-osmolality and its correction. *Am J Med*. 2006;119(7)(suppl 1):S12-S16.

10. Ayus JC, Krothapalli RK, Arieff AI. Treatment of symptomatic hyponatremia and its relation to brain damage. A prospective study. *N Engl J Med*. 1987;317(19):1190-1195.

11. Hantman D, Rossier B, Zohlman R, Schrier R. Rapid correction of hyponatremia in the syndrome of inappropriate secretion of antidiuretic hormone. An alternative treatment to hypertonic saline. *Ann Intern Med*. 1973;78(6):870-875.

12. Leens C, Mukendi R, Foret F, Hacourt A, Devuyst O, Colin IM. Central and extrapontine myelinolysis in a patient in spite of a careful correction of hyponatremia. *Clin Nephrol*. 2001;55(3):248-253.

13. Dellabarca C, Servilla KS, Hart B, Murata GH, Tzamaloukas AH. Osmotic myelinolysis following chronic hyponatremia corrected at an overall rate consistent with current recommendations. *Int Urol Nephrol*. 2005;37(1):171-173.

14. Jovanovich AJ, Berl T. Where vaptans do and do not fit in the treatment of hyponatremia. *Kidney Int*. 2013;83(4):563-567.

15. Wendland EM, Kaplan AA. A proposed approach to the dialysis prescription in severely hyponatremic patients with end-stage renal disease. *Semin Dial*. 2012;25(1):82-85.

16. Ji DX, Gong DH, Xu B, et al. Continuous veno-venous hemofiltration in the treatment of acute severe hyponatremia: a report of 11 cases. *Int J Artif Organs*. 2007;30(2):176-180.

17. Bender FH. Successful treatment of severe hyponatremia in a patient with renal failure using continuous venovenous hemodialysis. *Am J Kidney Dis*. 1998;32(5):829-831.

18. Vassallo D, Camilleri D, Moxham V, Ostermann M. Successful management of severe hyponatraemia during continuous renal replacement therapy. *Clin Kidney J*. 2012;5(2):155-157.

19. Peces R, Ablanedo P, Alvarez J. Central pontine and extrapontine myelinolysis following correction of severe hyponatremia. *Nephron*. 1988;49(2):160-163.

20. Pozzoni P, Di Filippo S, Pontoriero G, Locatelli F. Effectiveness of sodium and conductivity kinetic models in predicting end-dialysis plasma water sodium concentration: preliminary results of a single-center experience. *Hemodial Int*. 2007;11(2):169-177.

21. Spital A, Sterns RD. The paradox of sodium's volume of distribution. Why an extracellular solute appears to distribute over total body water. *Arch Intern Med*. 1989;149(6):1255-1257.

22. Di Filippo S, Manzoni C, Andrulli S, et al. How to determine ionic dialysance for the online assessment of delivered dialysis dose. *Kidney Int*. 2001;59(2):774-782.