Case Report

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Successful Treatment of Extreme Hyponatremia in an Anuric Patient Using Continuous Venovenous Hemodialysis

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Key Words
Hyponatremia · Acute kidney injury · Hemodialysis · Continuous renal replacement therapies · Osmotic demyelination syndrome

Abstract
Rapid correction of severe hyponatremia can result in osmotic demyelination syndrome. Patients with severe hyponatremia and renal failure requiring dialysis pose a therapeutic challenge since the use of conventional intermittent hemodialysis will result in a rapid correction of the serum sodium level. We report the case of a 52-year-old woman with extreme hyponatremia and severe acute kidney injury, who was successfully treated with continuous venovenous hemodialysis using a modified dialysate solution with a low sodium concentration that was adjusted on a daily basis.

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Introduction

Hyponatremia is the most commonly encountered electrolyte disorder in hospitalized patients and is associated with increased mortality [1, 2]. Acute hyponatremia causes cerebral edema that can lead to irreversible brain damage or death [3]. Depending on the severity of acute hyponatremia, the clinical manifestations can range from headache and nausea to seizures, coma and respiratory arrest. In contrast, when hyponatremia develops slowly, the brain cells adapt by extruding electrolytes and organic solutes, thereby ameliorating water accumulation and brain swelling [4, 5]. This adaptation is responsible for the relative scarcity of symptoms associated with chronic hyponatremia, defined as a reduction in the serum sodium concentration developing in more than 48 h. Rapid correction of chronic hyponatremia can result in osmotic demyelination syndrome, presumably caused by dehydration of the adapted brain cells [6]. Osmotic demyelination injury, which most frequently involves the pons, can be fatal and the clinical features may include tremor, hyperreflexia, pseudobulbar palsy and spastic quadriparesis [7, 8]. The risk of this complication has been shown to be increased when the rate of serum sodium correction exceeds 12 mmol/l in 24 h and 18 mmol/l in 48 h [9]. According to recent recommendations, the rate of correction of hyponatremia should not exceed 10–12 mmol/l in 24 h and 18 mmol/l in 48 h [3].

Patients with severe hyponatremia and renal failure requiring dialysis present a unique therapeutic challenge because conventional hemodialysis treatment results in rapid correction of the serum sodium concentration,

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placing the patients at risk of osmotic demyelination injury. We report a patient with extreme hyponatremia and anuric acute kidney injury who was successfully treated with continuous venovenous hemodialysis (CVVHD) using a modified low-sodium dialysate.

Case Report

A 52-year-old woman with long-standing history of alcohol abuse and depression was brought to the emergency department at our institution because of drowsiness and confusion. According to her relative, she began complaining of general malaise, weakness and nausea 10 days prior to admission. Three days prior to admission, she had checked into a detox clinic, where she gradually became lethargic and on the day of admission, multiple bruises on her torso and face were noted. A head injury caused by a fall was suspected and she was brought to the hospital. She had not consumed alcohol since her illness began. There was no history of kidney disease. The medications she had been taking at home included diclophenac, alprazolam and promethazine in unknown doses and she had been prescribed chlordiazepoxide, hydroxocobalamine and thiamine at the detox clinic.

On arrival, the patient was afebrile, blood pressure was 130/64 and heart rate 58 beats/min. Physical examination revealed marked lethargy and dysarthria. She was able to respond coherently to simple questions but was disoriented to place and time. She moved all four extremities symmetrically, and no obvious focal neurologic abnormalities were noted. Multiple bruises were present on her head and trunk. No sacral or leg edema was noted, and the remainder of the examination was unremarkable. Laboratory tests revealed profound hyponatremia with a serum sodium of 92 mmol/l, hyperkalemia and severe renal failure (table 1). The urinalysis showed findings suggestive of acute tubular injury. A bedside chest X-ray showed shallow inspiration and signs of mild congestion. A non-contrast enhanced computed tomography scan of the brain was unremarkable. An ultrasound study showed slightly enlarged, hyperechogenic kidneys but no signs of hydronephrosis.

An intravenous infusion of 0.9% saline at a rate of 200 ml/h was administered in the emergency department. Several hours later, the patient was transferred to the intensive care unit where she experienced hemodynamic instability and progressive respiratory failure requiring intubation and mechanical ventilation. The patient remained anuric, and dialysis was considered necessary for correction of both the hyponatremia and the uremic state. Intermittent hemodialysis was not considered a safe option as it would have corrected the hyponatremia too rapidly. It was decided to use CVVHD with a modified low-sodium dialysate with the goal of providing slow, controlled correction of the serum sodium concentration. The CVVHD was performed using a Prisma® machine with a blood flow rate of 100–120 ml/min and a dialysate flow rate of 1,000 ml/h. Low-dose heparin (5–10 IU/kg/h) was used for anticoagulation. The dialysate fluid was prepared by diluting a Hemosol® dialysate with 5% dextrose solution, yielding an initial dialysate sodium concentration of 105 mmol/l (fig. 1). On initiation of CVVHD, approximately 24 h after arrival, the serum sodium was 97 mmol/l. The dilution of the dialysate was modified on a daily basis to maintain the sodium concentration at 6–8 mmol/l above the patient's serum sodium level. Figure 2 demonstrates the course of the serum sodium concentration which gradually rose at a daily rate ranging from 2–7 mmol/l and had reached a safe level of 131 mmol/l after 9 days of CVVHD, at which time the treatment was discontinued as the patient's renal function had begun to im-

Table 1. Laboratory values on admission and on days 3 and 9 of CVVHD

	Admission	CVVHD day 3	CVVHD day 9
Complete blood count			
WBC, $\times 10^9$/l	14.5	15.5	22.3
Hemoglobin, g/l	107	89	97
Platelets, $\times 10^9$/l	164	84	198
Coagulation studies			
APTT, s	44	76.6	39.3
PT, s	14.8	15.0	14.1
Blood chemistries			
Sodium, mmol/l	92	106	131
Potassium, mmol/l	5.9	4.6	4.1
Chloride, mmol/l	49	78	–
Ionized calcium, mmol/l	0.89	0.98	1.31
Phosphorous, mmol/l	2.5	1.3	0.51
Creatinine, mg/dl (μmol/l)	15.9 (1,403)	5.1 (453)	3.6 (320)
Blood urea nitrogen, mg/dl (mmol/l)	112.6 (40.2)	38.9 (13.9)	51.0 (18.2)
Glucose, mg/dl (mmol/l)	129.6 (7.2)	–	102.6 (5.7)
Creatinine kinase, U/l	7,582	213	26
ASAT, U/l	218	72	41
ALAT, U/l	709	332	144
Amylase, U/l	163	164	320
Albumin, g/l	28		26
TSH, mU/l	0.25		
Arterial blood gases			
pH	7.39		
PCO_2, mm Hg	41		
PO_2, mm Hg	60		
HCO_3, mmol/l	24		
Urinalysis			
Protein	2+		
Hemoglobin	trace		
WBC, per HPF	2–5		
RBC, per HPF	1–2		
Renal tubular epithelial cells, per HPF	2+		
Granular casts, per HPF	2–5		
Sodium, mmol/l	18		
Osmolality, mosm/kg	270		

APTT = Activated partial thromboplastin time; PT = prothrombin time; ASAT = aspartate aminotransferase; ALAT = alanine aminotransferase; HPF = high power field.

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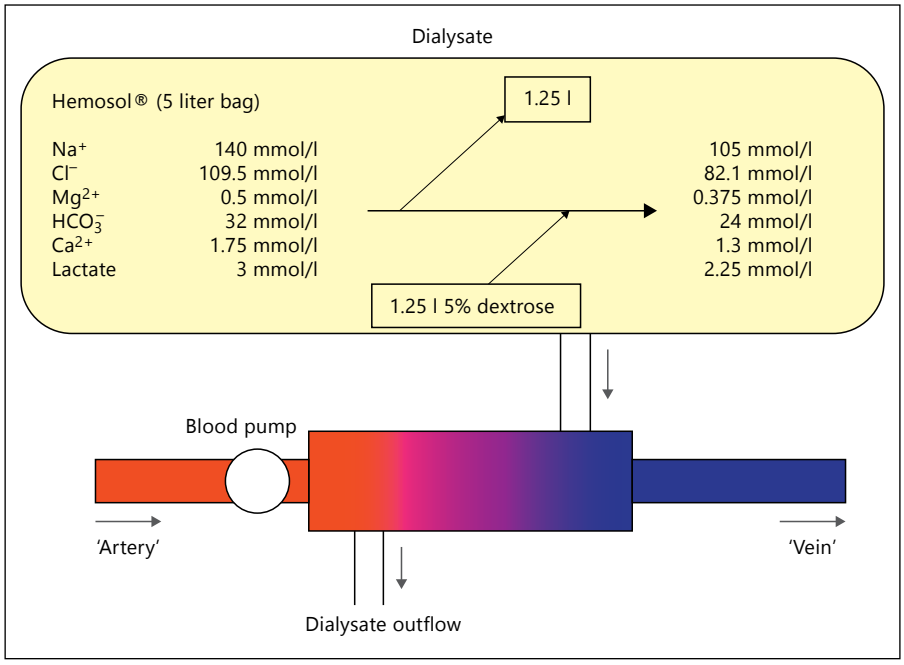

Fig. 1. The CVVHD circuit. The composition of the original Hemosol dialysate and the diluted Hemosol dialysate used at the onset of therapy is displayed; 1.25 l of the original solution were removed from a 5 liter bag and replaced by 1.25 l of 5% dextrose, yielding a sodium concentration of 105 mmol/l.

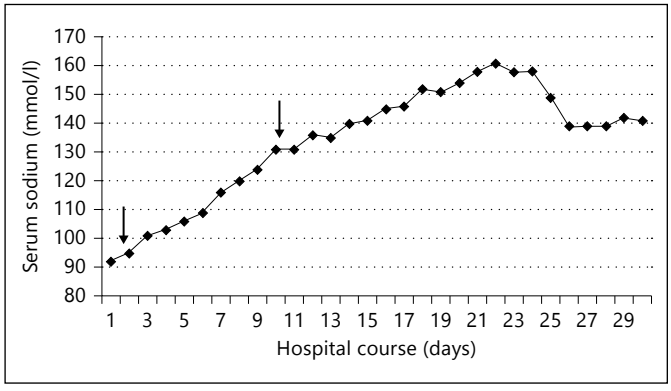

Fig. 2. The time course of the serum sodium concentration. The arrows indicate initiation and cessation of CVVHD.

prove. Over the ensuing 11 days, the urine volume increased to mildly polyuric levels and the serum creatinine normalized. Furosemide was administered by continuous intravenous infusion for 4 days during this period. The patient received enteral nutrition and intravenous fluid, predominantly 0.9% sodium chloride or Ringer's acetate. During the recovery phase of acute kidney injury, the patient developed hypernatremia with the serum sodium concentration peaking at 161 mmol/l on hospital day 22. This occurred in the setting of high-grade fever and was associated with increasing restlessness requiring treatment with large doses of sedative medications. The patient had been extubated 2 days earlier, at which time she was awake and able to communicate but was disoriented. In the preceding 2 weeks, the patient had received antimicrobial therapy for pneumonia and *Clostridium difficile*-associated diarrhea, both of which showed signs of improvement. A *Candida albicans* bloodstream infection was diagnosed and treatment with caspofungin initiated. The hypernatremia was corrected over 2 days with intravenous administration of 5% dextrose. The patient rapidly defervesced, and her mental status returned to the previous level. She was transferred to a general ward 4 weeks after admission to the hospital. The following week, the patient's mental status gradually improved and she became fully oriented. However, she suffered from persistent tremor, minor weakness of the left arm and unsteady gait.

A computed tomography scan of the brain 3 weeks after admission was unremarkable and a magnetic resonance imaging (MRI) study of the brain 6 weeks after admission did not reveal any signs of central pontine or extrapontine myelinolysis or other evidence of brain damage. Nevertheless, a mild osmotic demyelination injury was believed to be a likely explanation for the neurologic findings. Several weeks later, the patient was admitted to a rehabilitation clinic. Over the following several months, she gradually made full recovery.

Discussion

This case demonstrates successful management of extreme hyponatremia in a patient with severe anuric acute kidney injury, using CVVHD. The serum sodium of 92 mmol/l is one of the lowest values reported to date. Despite signs of encephalopathy, the patient's cerebral function was reasonably preserved, reflecting cellular adaptation in response to the hyponatremia. In addition to hyponatremia, the uremic state and alcohol withdrawal

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syndrome may have contributed to the encephalopathy. CVVHD with a modified low-sodium dialysate was chosen as a dialysis modality instead of intermittent hemodialysis in order to avoid a rapid increase in the serum sodium concentration and the associated risk of osmotic demyelination syndrome. This was successfully achieved as the rate of correction of serum sodium averaged 3.8 mmol/l and never exceeded 7 mmol/l in any 24-hour period. Nevertheless, the patient developed minor neurologic dysfunction, reversible over weeks to months, which may have resulted from osmotic demyelination injury, despite a negative MRI study.

The treatment of acute symptomatic hyponatremia is difficult because the rate and magnitude of the correction must be sufficient to reverse the life-threatening brain swelling and simultaneously slow enough to prevent the development of demyelination injury. Available recommendations are based on retrospective studies and expert opinion as no published data from prospective studies or clinical trials are available. A recommended approach is to rapidly raise the serum sodium by 4–6 mmol/l in 4–6 h using 3% saline, followed by a slow controlled correction, not exceeding 6–8 mmol/l in any 24-hour period as a chronic component is frequently present as well [10–12]. The relatively low upper limit of 6–8 mmol/l per day is selected because cases of osmotic demyelination syndrome have been reported when chronic hyponatremia has been corrected at a rate as slow as 9–10 mmol/l in 24 h [7, 9].

Mild to moderate hyponatremia is common in hemodialysis patients and is generally corrected during the dialysis treatment without any adverse effects. In conventional intermittent hemodialysis, patients are usually dialysed against a dialysate with a sodium concentration of 145 mmol/l, and the lowest sodium level that can be achieved with standard hemodialysis machines is 130 mmol/l. Thus, intermittent hemodialysis would be expected to result in a rapid rise in the serum sodium level in cases of severe predialytic hyponatremia. Nonetheless, only two cases of osmotic demyelination syndrome following rapid correction of severe hyponatremia with hemodialysis have been reported [13, 14]. In one of these cases [13], the serum sodium concentration increased by 35 mmol/l over 4 days, and in the other case [14], the serum sodium level rose by 21 mmol/l following a single hemodialysis session. In addition, a singe case of fatal osmotic demyelination syndrome in a patient with chronic renal failure and severe hyponatremia that was rapidly corrected by peritoneal dialysis has been reported [15]. The risk of demyelination injury following correction of hyponatremia with dialysis has not been systematically investigated. The only published study is a retrospective case series of 17 patients with end-stage renal disease who developed severe neurologic manifestations and MRI findings consistent with osmotic demyelination syndrome following hemodialysis treatment [16]. Hyponatremia was observed in 8 of these patients, in one of whom the serum sodium concentration increased by 28 mmol/l in 48 h, during and immediately after the episode. However, the temporal relationship between the correction of the serum sodium concentration by hemodialysis and the development of osmotic demyelination syndrome was not described, and data on the correction of hyponatremia were lacking for the other cases.

While these aforementioned cases demonstrate that osmotic demyelination syndrome can occur following correction of severe hyponatremia by dialysis, this complication is surprisingly rare in hemodialysis patients. One plausible explanation is that severe hyponatremia may be rare in the setting of thrice-weekly hemodialysis treatments and that the short time interval between treatments does not allow for full adaptation of the hypotonic state by the brain cells. It has also been suggested that uremia may protect against demyelination during rapid correction of hyponatremia [17, 18]. The diffusion of urea across the blood-brain barrier is relatively slow and, therefore, the sudden decrease in blood urea levels during hemodialysis may transiently counteract the water movement out of the brain during correction of hyponatremia. Intriguingly, animal experiments have shown that azotemia appears to protect against osmotic demyelination when hyponatremia is rapidly corrected [19, 20]. Furthermore, the reaccumulation of organic osmolytes in the brain cells is much more rapid in azotemic rats than non-azotemic rats after correction of hyponatremia [21].

In spite of the uremic state, our patient was considered to be at great risk of suffering neurologic damage, either from the consequences of the hyponatremia itself or from osmotic demyelination injury caused by overly rapid correction of the hyponatremia. The latter was considered to be more likely due to the apparently compensated nature of the hyponatremia and the increased risk of osmotic demyelination associated with the history of chronic alcoholism [11]. Due to the extreme level of hyponatremia, conventional intermittent hemodialysis was not considered safe as it would have been expected to cause a sudden large increase in the serum sodium level. CVVHD was chosen instead because of its slow and continuous nature. In addition, the dialysate solution was diluted to minimize the gradient between the dialysate and serum sodium concentrations. The dialysate sodium concentration

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was gradually increased to successfully maintain the correction rate of the serum sodium level below 8 mmol/l per 24 h. Despite this very slow correction of the serum sodium concentration, the patient developed minor reversible neurologic abnormalities which may have resulted from osmotic demyelination injury, regardless of the negative MRI findings.

The development of hypernatremia may have contributed to the neurologic abnormalities. While the peak of the hypernatremia was associated with acute mental status alteration, this occurred in the setting of disseminated *Candida* infection which may also have played a major role. Moreover, the improvement of the mental status following correction of the hypernatremia makes the development of significant cerebral damage unlikely. However, the development of hypernatremia in this case illustrates the importance of careful attention to urinary water loss and adequate water replacement during recovery of acute kidney injury. In addition to excessive water excretion by the kidneys, diarrhea and protracted fever may have contributed to the negative water balance.

We believe the correction of severe chronic hyponatremia in patients with renal failure should proceed slowly as in patients with normal renal function. When hemodialysis is performed, the dialysate sodium concentration must be determined based on the severity of the hyponatremia. It is noteworthy that the dialysis dose in the first few days may have been suboptimal for correction of uremia. However, it was decided not to add replacement fluid because of the risk of correcting the hyponatremia too rapidly.

Reports of the use of continuous renal replacement therapy in patients with severe hyponatremia are scarce [22–26]. Ji et al. [25], reported a series of 11 patients with severe, symptomatic hyponatremia and renal failure who received continuous venovenous hemofiltration resulting in rapid correction of the hyponatremia. The average increase in the serum sodium concentration was >21 mmol/l in the first 8 h of treatment. No patient experienced neurologic sequelae. The initial sodium gradient between the replacement fluid and the patient's blood was 16 mmol/l, and the authors concluded by recommending that the sodium concentration of the replacement fluid should be 15–20 mmol/l higher than the serum sodium concentration when continuous venovenous hemofiltration is used to treat patients with severe hyponatremia. It should be noted that all these patients had acute hyponatremia that developed in less than 48 h. In another report of a single case of renal failure and hyponatremia successfully treated with CVVHD [24], the patient's initial serum sodium was 108 mmol/l, and a custom-made low-sodium dialysate with a final sodium concentration of 121 mmol/l was used. CVVHD was discontinued after 28 h, at which time the serum sodium was 119 mmol/l. No neurologic abnormalities developed. Lenk and Kaspar [26] reported 2 cases of long-standing hyponatremia in patients undergoing orthotopic liver transplantation who received intraoperative treatment with continuous venovenous hemodiafiltration. The preoperative serum sodium levels were 121 and 122 mmol/l. The sodium concentration in the replacement fluid and dialysate was adjusted by addition of distilled water, yielding a final sodium level of 128 mmol/l. The serum sodium concentration increased to 127 and 128 mmol/l during surgery which lasted for 5.5 and 7.5 h, respectively.

In conclusion, the use of CVVHD with a modified low-sodium dialysate allowed us to correct extreme hyponatremia in a slow and controlled manner, keeping the increase in serum sodium within the recommended limit of 6–8 mmol/l in 24 h. We propose the use of continuous renal replacement therapy for severe hyponatremia of unknown duration in patients who require dialysis. In the absence of published guidelines, the case presented herein offers some insight into how severe hyponatremia can be managed in the setting of acute kidney injury requiring renal replacement therapy.

Disclosure Statement

The authors declare that they have no relevant financial interests.

References

1 Waikar SS, Mount DB, Curhan GC: Mortality after hospitalization with mild, moderate, and severe hyponatremia. Am J Med 2009;122:857–865.

2 Chawla A, Sterns RH, Nigwekar SU, Cappuccio JD: Mortality and serum sodium: do patients die from or with hyponatremia? Clin J Am Soc Nephrol 2011;6:960–965.

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

4 Melton JE, Patlak CS, Pettigrew KD, Cserr HF: Volume regulatory loss of Na, Cl, and K from rat brain during acute hyponatremia. Am J Physiol 1987;252:F661–F669.

5 Videen JS, Michaelis T, Pinto P, Ross BD: Human cerebral osmolytes during chronic hyponatremia. A proton magnetic resonance spectroscopy study. J Clin Invest 1995;95:788–793.

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6 Kleinschmidt-DeMasters BK, Norenberg MD: Rapid correction of hyponatremia causes demyelination: relation to central pontine myelinolysis. Science 1981;211:1068–1070.
7 Karp BI, Laureno R: Pontine and extrapontine myelinolysis: a neurologic disorder following rapid correction of hyponatremia. Medicine 1993;72:359–373.
8 Martin RJ: Central pontine and extrapontine myelinolysis: the osmotic demyelination syndromes. J Neurol Neurosurg Psychiatry 2004;75(suppl 3):iii22–iii28.
9 Sterns RH, Cappuccio JD, Silver SM, Cohen EP: Neurologic sequelae after treatment of severe hyponatremia: a multicenter perspective. J Am Soc Nephrol 1994;4:1522–1530.
10 Sterns RH, Hix JK, Silver S: Treatment of hyponatremia. Curr Opin Nephrol Hypertens 2010;19:493–498.
11 Adrogue HJ, Madias NE: The challenge of hyponatremia. J Am Soc Nephrol 2012;23:1140–1148.
12 Sterns RH, Nigwekar SU, Hix JK: The treatment of hyponatremia. Semin Nephrol 2009;29:282–299.
13 Peces R, Ablanedo P, Alvarez J: Central pontine and extrapontine myelinolysis following correction of severe hyponatremia. Nephron 1988;49:160–163.
14 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;29:635–638.
15 Loo CS, Lim TO, Fan KS, Murad Z, Suleiman AB: Pontine myelinolysis following correction of hyponatraemia. Med J Malaysia 1995;50:180–182.
16 Tarhan NC, Agildere AM, Benli US, Ozdemir FN, Aytekin C, Can U: Osmotic demyelination syndrome in end-stage renal disease after recent hemodialysis: MRI of the brain. Am J Roentgenol 2004;182:809–816.
17 Sterns R, Silver S: Hemodialysis in hyponatremia: is there a risk? Semin Dialysis 1990;3:3–4.
18 Sirota JC, Berl T: Is osmotic demyelination a concern dialyzing hyponatremic patients? Semin Dialysis 2011;24:407–409.
19 Soupart A, Stenuit A, Perier O, Decaux G: Limits of brain tolerance to daily increments in serum sodium in chronically hyponatraemic rats treated with hypertonic saline or urea: advantages of urea. Clin Sci 1991;80:77–84.
20 Soupart A, Penninckx R, Stenuit A, Decaux G: Azotemia (48 h) decreases the risk of brain damage in rats after correction of chronic hyponatremia. Brain Res 2000;852:167–172.
21 Soupart A, Silver S, Schrooeder B, Sterns R, Decaux G: Rapid (24-hour) reaccumulation of brain organic osmolytes (particularly myo-inositol) in azotemic rats after correction of chronic hyponatremia. J Am Soc Nephrol 2002;13:1433–1441.
22 Sandroni S: Severe post-TURP syndrome in a patient with renal insufficiency: treatment with hemofiltration. J Fla Med Assoc 1986;73:384–385.
23 Larner AJ, Vickers CR, Adu D, Buckels JA, Elias E, Neuberger J: Correction of severe hyponatraemia by continuous arteriovenous haemofiltration before liver transplantation. BMJ 1988;297:1514–1515.
24 Bender FH: Successful treatment of severe hyponatremia in a patient with renal failure using continuous venovenous hemodialysis. Am J Kidney Dis 1998;32:829–831.
25 Ji DX, Gong DH, Xu B, Tao J, Ren B, Zhang YD, et al: Continuous veno-venous hemofiltration in the treatment of acute severe hyponatremia: a report of 11 cases. Int J Artif Organs 2007;30:176–180.
26 Lenk MR, Kaspar M: Sodium-reduced continuous venovenous hemodiafiltration (CVVHDF) for the prevention of central pontine myelinolysis (CPM) in hyponatremic patients scheduled for orthotopic liver transplantation. J Clin Anesth 2012;24:407–411.

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