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A Case of Continuous Venovenous Hemofiltration for Anuric Acute Kidney Injury With Severe Hyponatremia: A Simple Method Involving Flexible Adjustment of Sodium Replacement Solution

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INTRODUCTION

Dialysis therapy for patients with severe hyponatremia is challenging because rapid correction of the serum sodium concentration may lead to osmotic demyelination syndrome (ODS).[1] Gradual correction of hyponatremia is recommended to prevent hazardous sequelae.[2,3] Continuous venovenous hemofiltration (CVVH) with low-sodium replacement solution can be used to prevent rapid correction of the serum sodium concentration;[4] however, preparation of low-sodium replacement solution by dilution is difficult and is not recommended. We developed the "FlexNa" method, which involves flexible adjustment of the sodium concentration of commercially available replacement fluid; it assures provision of CVVH without affecting the patient's serum sodium concentration. We present a case of acute kidney injury concomitant with severe hyponatremia and hyperkalemia, which was treated successfully with CVVH using this FlexNa method.

CASE PRESENTATION

A 46-year-old woman presented to the emergency department with confusion and dysarthria for 12 hours. She had experienced decreased oral intake for 1 week, but had refused to visit a hospital. She had been hospitalized due to symptomatic hyponatremia a few months previously. Her past medical history included anorexia nervosa and chronic tubulointerstitial nephritis. Vital signs were as follows: systolic blood pressure, 70 mm Hg; heart rate, 60 beats per minute; respiration rate, 24 breaths per minute; and pulse oximetry, 100% on room air. Her body weight on admission was 33 kg.

A review of systems showed decreased urinary output. Serum laboratory studies showed the following values: sodium, 99 mEq/l; potassium, 7.7 mEq/l; chloride, 63 mEq/l; bicarbonate, unmeasurable; serum urea nitrogen, 184.5 mg/dl; creatinine, 10.69 mg/dl; phosphorus, 19.6 mg/dl; uric acid, 21.9 mg/dl; albumin, 2.8 g/dl; and serum osmolality, 291 mOsm/kg. Arterial blood gas analysis showed a pH of 7.01, $PaCO_2$ of 7.7 mm Hg, PaO_2 of 165 mm Hg, and bicarbonate level of 1.9 mEq/l. The urine osmolality was 292 mOsm/kg H_2O, the sodium level was 29 mEq/l, the potassium level was 35 mEq/l, the urea nitrogen level was 215 mg/dl, and the creatinine level was 92 mg/dl, with fractional sodium excretion of 3.1%. An electrocardiogram showed peaked T waves and a widened QRS complex.

The patient was diagnosed with acute kidney injury due to acute tubular necrosis, severe hypovolemic hyponatremia, and severe hyperkalemia.

After admission, supportive therapy including fluid resuscitation and insulin therapy with glucose and sodium bicarbonate was initiated. The patient's

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electrocardiogram findings and blood pressure improved, but she remained anuric and her serum potassium level exceeded 5.8 mEq/l for 24 hours. The decision to initiate dialysis therapy was made, but intermittent hemodialysis or CVVH has the risk of rapid correction of hyponatremia. To avoid rapid correction of the serum sodium concentration, we started CVVH using the 5% dextrose solution (D5W) infusion method, which we named the FlexNa method. CVVH using commercially available replacement fluid (Sublood-BSG; FUSO Pharmaceutical Industries Ltd., Tokyo, Japan), which has a sodium concentration of 140 mEq/l, was started with continuous infusion of D5W to the CVVH circuit after hemofiltration. By using the FlexNa method, we were able to effectively administer a replacement solution with a sodium concentration equal to the patient's serum sodium concentration, which was 100 mEq/l at the start of CVVH. This prevented any increase in the serum sodium attributable to the CVVH. The prescription of the CVVH was: blood flow, 100 ml/min; replacement fluid, 500 ml/h; and infusion rate of D5W, 200 ml/h. Correction of hyponatremia and hypovolemia was achieved by i.v. administration of sodium bicarbonate solution, which safely raised the patient's serum sodium level to 108 mEq/l over 24 hours. After 24 hours of CVVH, her serum potassium level decreased to 3.6 mEq/l and urine output was recovered, and CVVH was discontinued (Figure 1). Thereafter, she received supportive therapy and recovered completely from hyponatremia and AKI with no neurologic complication. Her serum sodium concentration at the time of discharge was 143 mEq/l.

This case was presented at the Japan Society for Blood Purification in Critical Care meeting on October 2015 and published in Japanese.[5] The patients provided full informed consent for gathering the data and publishing the case.

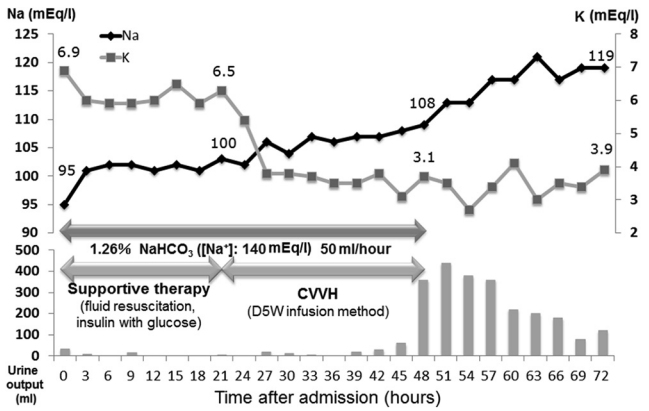

Figure 1. Hospital course of the patient.

DISCUSSION

Patients with symptomatic hyponatremia with severe renal failure pose a therapeutic challenge. Severe hyperkalemia with kidney failure requires dialysis therapy; however, conventional hemodialysis therapy involves the risk of ODS due to rapid correction of the serum sodium concentration ($[Na^+]$). The FlexNa method can provide safe, effective, and effortless renal replacement therapy.

Hyponatremia is associated with increased mortality and morbidity.[6] In patients with chronic hyponatremia, brain cells lose organic solutes, which decreases the risk of life-threatening cerebral edema.[1] However, this adaptation makes the brain more vulnerable to ODS in response to rapid correction of hyponatremia.[7,8] Furthermore, risk factors for the development of ODS, such as severe hyponatremia (serum $[Na^+]$ $\leq$105 mmol/l), hypokalemia, alcoholism, malnutrition, and adverse liver disease, must be considered. Guidelines recommend that a 5-mEq/l increase in serum $[Na^+]$ is sufficient to improve symptoms, and the therapeutic "limits" of the increase in serum $[Na^+]$ are 10 mEq/l in 24 hours and 18 mEq/l in 48 hours.[2,3]

In contrast, severe hyperkalemia associated with electrocardiogram changes is a life-threatening condition. Although severe hypokalemia with kidney failure requires dialysis therapy, the treatment of hyponatremia must be performed in parallel when the patient presents concomitant severe symptomatic hyponatremia. This condition renders the treatment more complicated in severe cases of hyponatremia because renal replacement therapy (intermittent hemodialysis or CVVH) can be hazardous due to rapid correction. In patients with severe hyponatremia, intermittent hemodialysis especially provokes rapid correction of serum sodium concentration and puts the patient at risk of ODS.[9]

The conventional strategy to prevent rapid correction of serum $[Na^+]$ is to provide CVVH using low-sodium replacement fluid. Yessayan *et al.*[4] proposed a sophisticated method to correct hyponatremia gradually using CVVH with low-sodium replacement fluid. They introduced an equation to modify replacement fluid $[Na^+]$ according to the desired "target" serum $[Na^+]$ for the first 24 hours. However, Yessayan *et al.*'s direct hyponatremia correction method was not used in our case because the patient seemed to be more susceptible to ODS due to several risk factors, such as chronic severe hyponatremia and malnutrition. In Yessayan *et al.*'s method, the replacement fluid must be adjusted to the estimated "target" $[Na^+]$, that is the "limit" $[Na^+]$ for the correction of hyponatremia, which is likely to increase the risk of ODS development due to the increase in sodium concentration,

regardless of symptom improvement. Furthermore, frequent changes of replacement fluid may be required if the increase in serum [Na^+] far exceeds or fails to reach the predicted value. Moreover, preparation of commercially available replacement fluid by dilution is not recommended by manufacturers for safety reasons.

The goal of hyponatremia treatment is improvement of symptoms, not correction of serum [Na^+] *per se*. Dialysis therapy, which does not alter serum [Na^+] but removes uremic toxins, such as potassium and urea, is desired. Therefore, providing CVVH using low-sodium replacement solution while slowly correcting hyponatremia by continuous infusion of 3% NaCl or normal saline is a simple, safe, and effective method (Figure 2). Addition of D5W to the commercially available replacement solution enables adjustment of the replacement fluid [Na^+]; however, when CVVH is required for several days, repeated preparation of the modified replacement fluid is labor intensive. Instead, we developed the easier and novel FlexNa method, which uses CVVH with standard replacement fluid and i.v. D5W infusion to the post-hemofilter CVVH circuit (Figure 2). By diluting the blood exiting the dialyzer using D5W, the serum [Na^+] can be easily maintained at the desired level, which prevents overcorrection of hyponatremia; this FlexNa method would result in no change in the patient serum [Na^+], and correction of hyponatremia is achieved not by CVVH but by i.v. administration of sodium. The amount of sodium required for correction of hyponatremia can be estimated using the equation of Edelman *et al.*, Na deficit = (desired Na concentration − serum Na concentration) × total body water.[10] From this equation, we can estimate that administration of 1 ml/kg of 3% sodium chloride solution would raise serum Na concentration by approximately 1 mEq/l.

The main advantage of the FlexNa method is that replacement fluid [Na^+] can be adjusted to any desired concentration at any time by increasing or decreasing the D5W infusion rate. We fixed replacement fluid [Na^+] to the patient's serum Na concentration and corrected hyponatremia by i.v. administration of sodium bicarbonate solution; theoretically, the FlexNa method *per se* can correct hyponatremia by adjusting replacement fluid [Na^+] to target serum sodium concentration.

The rate of ultrafiltration (Q_{uf}) is determined to be equal to the D5W infusion rate if fluid removal by CVVH is not necessary. Because commercially available replacement fluid bags contain physiological sodium concentrations of 140 mmol/l, the D5W volume to be infused to any given Q_{uf} is calculated using the following equation:

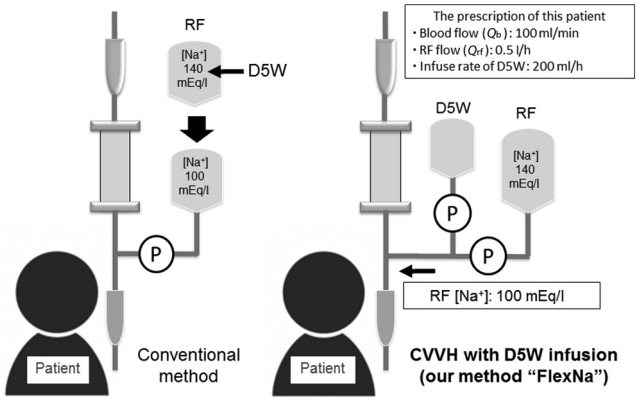

Figure 2. Differences between the conventional and FlexNa methods. Conventional: Prepare low-[Na^+] replacement fluid (RF) by diluting standard-[Na^+] bags with 5% dextrose in water (D5W) in the first continuous venovenous hemofiltration (CVVH). FlexNa: Mix the D5W and standard-[Na^+] RF bags immediately before infusion of RF into the V-line chamber. P, pump.

$$\text{volume to infuse (ml/h)} = Q_{uf} = (140\ (\text{mEq/l}) - \text{serum } [Na^+]) \times \text{replacement fluid flow rate } (Q_{rf}: \text{ml/h}) \,/\, \text{serum } [Na^+]$$

For our patient, an adequate renal replacement dose of 25 ml/kg per hour filtration was provided. Her serum [Na^+] level was about 100 mEq/l; therefore, the estimated infusion rate and Q_{uf} were 400 ml/h and 1000 ml/h, respectively.

Alternatively, D5W can be infused i.v. using CVVH with standard replacement fluid, which is theoretically identical to the FlexNa method because the infused replacement fluid is diluted in the body and the serum [Na^+] does not change.

The FlexNa method has several limitations. Treatment risks include hyperglycemia induced by infusion of D5W, which requires insulin injection. Our patient required insulin therapy because of hyperglycemia during CVVH, which fortunately improved the hyperkalemia. Infusion pump precision is a critical factor, and serial monitoring of the concentrations of serum [Na^+] and other electrolytes is mandatory.

CONCLUSION

The FlexNa method is a safe, controllable, and effortless treatment modality for patients with severe hyponatremia requiring CVVH therapy. However, infusion of D5W for diluting replacement solution leads to hyperglycemia. Continuous monitoring of glucose and serum potassium is needed for this therapy.

DISCLOSURES

All the authors declared no competing interests.

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