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Correction of Hyper- and Hyponatraemia during Continuous Renal Replacement Therapy

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Key Words
Continuous renal replacement therapy · Hypernatraemia · Hyponatraemia · Sodium disorder

Abstract
Background: Severe hyper- and hyponatraemia is associated with significant risks, yet its correction can also have serious consequences when implemented too fast or inadequately. The safe correction of serum sodium levels is particularly challenging when renal replacement therapy (RRT) is required. ***Methods:*** Using 2 case scenarios, we aim to illustrate a simple method of correcting hyper- and hyponatraemia safely by step-wise manipulation of the dialysate/replacement fluid. ***Results:*** During continuous RRT, hypernatraemia can be corrected effectively and safely by adding small pre-calculated amounts of 30% NaCl to the dialysate/replacement fluid bags aiming for a [Na^+] in the fluid that allows safe equilibration and correction of the serum [Na^+]. To correct hyponatraemia safely, pre-calculated amounts of sterile water can be added in a step-wise manner to achieve a fluid [Na^+] that equals the desired target serum [Na^+]. ***Conclusion:*** During continuous RRT, the step-wise adjustment of [Na^+] of dialysate/replacement fluids offers a safe and reliable method to correct sodium disorders.

Introduction

Sodium disorders are frequent in hospitalized patients, especially in the intensive care unit (ICU) [1] and often co-exist with acute kidney injury (AKI). Controlled normalization of serum [Na^+] is crucial as rapid correction can lead to cerebral oedema and osmotic demyelination syndrome (ODS) [2–4]. This is particularly challenging if renal replacement therapy (RRT) is needed, as the [Na^+] of commercially available dialysate or replacement fluids is fixed at 136–140 mmol/l. In this report, we discuss methods of correcting serum [Na^+] during RRT, with focus on our locally developed protocol of adjusting the [Na^+] in the dialysate/replacement fluid [5].

Cases and Methods

Case 1: Hypernatremia

A 45-year-old male patient (169 kg, body mass index 59) with no medical history was admitted after an out-of-hospital cardiac arrest. On arrival in hospital, his blood pressure was 230/120 mm Hg, and he had uncontrolled fast atrial fibrillation (ventricular rate 195/min). An urgent angiogram did not show any signs of coronary artery disease. The mechanism of cardiac arrest was thought to be an arrhythmia combined with hypoxia from untreated obstructive sleep apnoea.

The patient was treated with inotropes and an intra-aortic balloon pump. He stabilized but gradually developed progressive AKI related to sepsis, diarrhoea and statin-induced rhabdomyolysis.

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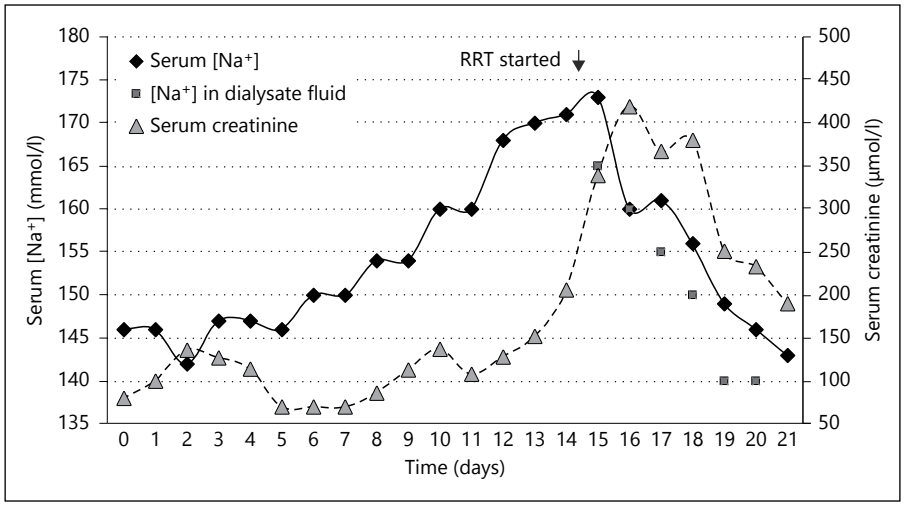

Fig. 1. Management of hypernatraemia in patient 1. The green squares represent the [Na^+] in the dialysate fluid, changed 3 times in total (colour refers to the online version only).

Table 1. For treatment of hypernatraemia: effect of adding different volumes of 30% NaCl to 5-litre bags of pre-prepared dialysis/replacement fluid containing [Na^+] = 140 mmol/l

Volume of 30% NaCl added to 5-litre bag	nil	5 ml (=25 mmol [Na^+])	10 ml (=50 mmol [Na^+])	15 ml (=75 mmol [Na^+])	20 ml (=100 mmol [Na^+])
Final [Na^+] in CRRT fluid, mmol/l	140	145	150	155	160

Added volumes are small and therefore do not significantly alter the bicarbonate and potassium concentrations. CRRT = Continuous RRT.

Despite administration of hypotonic crystalloid fluids, his serum [Na^+] gradually rose. On day 18, he was uraemic and fluid overloaded with a serum [Na^+] of 175 mmol/l. Continuous veno-venous haemodialysis was started using a dialysate solution with [Na^+] adjusted as per tables 1 and 2. Over the following 6 days, the patient's serum [Na^+] gradually decreased at an average rate of 4.7 mmol/day (fig. 1). He needed RRT until day 38 and remained in ICU until day 62 due to marked critical illness and statin-induced myopathy. He was discharged from hospital with a nighttime continuous positive airway pressure device and remained in relatively good health 8 months later.

Case 2 – Hyponatraemia

A 44-year-old female with type 2 diabetes mellitus and chronic kidney disease (CKD) was admitted with septic shock due to *Escherichia coli* pyelonephritis complicated by oligo-anuric AKI, thrombocytopenia and diabetic ketoacidosis. Treatment with fluids, vasopressors and broad-spectrum antibiotics was promptly started in the Emergency Department.

On admission to the ICU, her serum [Na^+] was 112 mmol/l. The exact cause was unclear but most likely related to CKD and diuretic use. Maintenance fluids were switched from Hartman's solution ([Na^+] 131 mmol/l) to saline 0.9% ([Na^+] 154 mmol/l). Serum [Na^+] rose to 122 mmol/l over the next 24 h but subsequently fell again. She remained oliguric and developed fluid overload.

Table 2. Guide for correction of hypernatraemia during CRRT

Serum [Na^+] concentration, mmol/l	Suggested [Na^+] in dialysate/replacement fluid, mmol/l
140–150	140
151–155	145
156–160	150
161–165	155
166–170	160

Example of correction of serum [Na^+]: in patients with serum [Na^+] 163 mmol/l, it is advised to alter the [Na^+] concentration of the replacement fluid to achieve a [Na^+] of 155 (by adding 15 ml of 30% NaCl as per table 1). When the patient's serum [Na^+] has been equilibrated to 155 mmol/l, the [Na^+] in the replacement fluid can be changed to 150 mmol/l. CRRT = Continuous RRT.

A decision was made to start continuous veno-venous haemodialysis with adjustment of the [Na^+] in the dialysate fluid as per tables 3 and 4. Over the following 6 days, her serum [Na^+] gradually rose to 130 mmol/l (fig. 2). Her condition improved without any neurological complications, and she was discharged home.

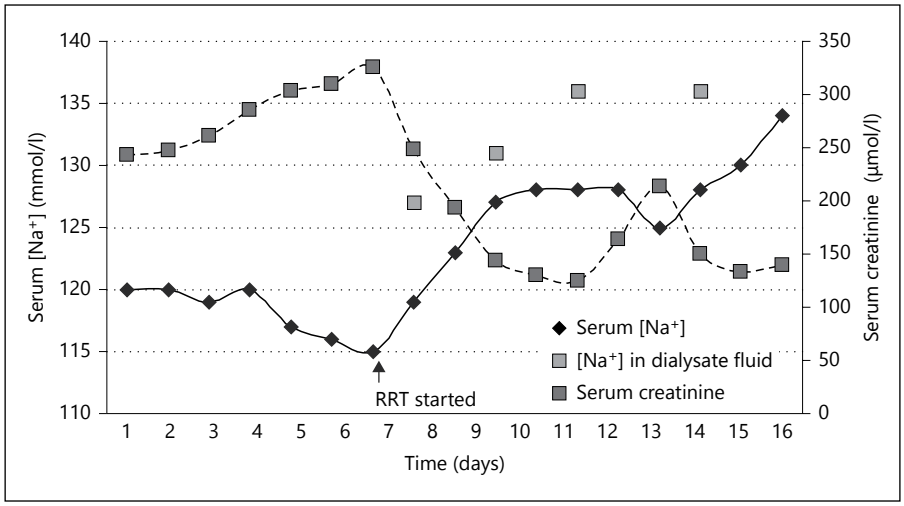

Fig. 2. Management of hyponatraemia in patient 2. The green squares represent the [Na^+] in the dialysate fluid, changed 4 times in total (colour refers to the online version only).

Table 3. For treatment of hyponatraemia: effect of adding different volumes of sterile water to 5-litre bags of pre-prepared replacement/dialysis fluid containing [Na^+] = 140 mmol/l [5]

Volume of water added, ml	Final volume of diluted replacement fluid/dialysate, l	[Electrolyte] in diluted replacement fluid/dialysate, mmol/l		
		[Na^+]	[HCO_3^-]	[K^+]
Nil	5.00	140	35	4.0
150	5.15	136	34	3.9
250	5.25	133	33	3.8
350	5.35	131	33	3.7
500	5.50	127	32	3.6
750	5.75	122	30	3.5
1,000	6.00	117	29	3.3
1,250	6.25	112	28	3.2

Table 4. Guide for correction of hyponatraemia during CRRT

Serum [Na^+] concentration, mmol/l	Suggested [Na^+] in dialysate/ replacement fluid, mmol/l
132–140	140
128–131	136
125–129	133
123–127	131
119–122	127
114–118	122
109–113	117
102–108	112

Example of correction of serum [Na^+]: in patients with serum [Na^+] 110 mmol/l, it is advised to alter the [Na^+] concentration of the replacement fluid to reach an [Na^+] of 117 (by adding 1,000 ml of sterile water as per table 3). When the patient's serum [Na^+] has equilibrated to 117 mmol/l, the [Na^+] in the replacement fluid can be changed to 122 mmol/l. CRRT = Continuous RRT.

Discussion

The correction of sodium and water disorders can be challenging, especially in patients with impaired renal function and fluid overload. Both cases illustrate that step-wise manipulation of [Na^+] in the dialysate/replacement fluid can safely normalize serum [Na^+].

Hypernatraemia

Hypernatraemia is defined as serum [Na^+] >145 mmol/l and develops in 1% of hospitalized patients and up to 9% of patients admitted to ICUs [1]. It is independently associated with increased mortality [6].

The main causes involve pure water loss, attributable to decreased water intake and/or high losses of hypotonic fluids. Rarely, hypernatraemia is caused by sodium excess in relation to body water, for instance following hypertonic saline administration [7].

Risk factors include older age, brain injury, altered mental status, diabetes mellitus, surgery and certain drugs [1, 3]. The clinical manifestations, typically nausea, anorexia, restlessness and lethargy, are related to cerebral dysfunction secondary to water shift out of brain cells [1]. Decreased consciousness, irritability, hyperreflexia and seizures may develop as hypernatraemia worsens. The most dramatic symptoms are witnessed when the increase in serum [Na^+] has been either too large or too brisk. Chronic hypernatraemia is less symptomatic because organic osmolytes (glutamine, glutamate, taurine and myo-inositol) enter brain cells and help restore normal brain volume [3].

Treatment of hypernatraemia should target the cause in the first instance. Water deficit, if present, should be

replaced, taking into account ongoing losses (water deficit = total body water × [([Na^+]$_{corrected}$/[Na^+]$_{target}$) − 1]), where [Na^+]$_{corrected}$ = [Na^+]$_{measured}$ + 0.4 mmol/l × [glucose] − 5.6 mmol/l [5]. Total body water is estimated as being 60% of the body weight in men and 50% in women, and 50 and 45%, respectively, in elderly patients [3]. Excess sodium stores, when involved, can only be excreted if renal function is adequate [3]. The rate of correction should not exceed 10–12 mmol/day (0.5 mmol/l/h) [1, 7]. A rapid decrease in serum [Na^+], especially in chronic situations when compensation has occurred, can lead to significant water shifts into brain cells and cerebral oedema.

Hyponatraemia

Hyponatraemia is the most common electrolyte disturbance. In the majority of cases (75–80%), it is chronic, and patients are asymptomatic [1]. The prevalence is around 15% in hospitalized patients [7] but higher amongst ICU patients, rising up to 30% [1]. Risk factors include advanced age, CKD, diabetes mellitus and drugs (diuretics and hypotonic fluid) [1]. Severe hyponatraemia is associated with increased mortality, prolonged hospitalization and an increased risk of falls and fractures [1, 4, 8], although it may simply be a surrogate for the underlying severity of disease [9].

Symptoms of hyponatraemia depend on the severity and rapidity of occurrence. Acute hyponatraemia results in water shift into brain cells, leading to cerebral oedema [10]. Brain protection mechanisms including shifts of electrolytes and organic osmolytes out of cells reduce intracellular oedema but take >24 h to develop [1]. Mild-to-moderate hyponatraemia (Na^+ >120 mmol/l) causes nonspecific symptoms such as headaches, nausea and general malaise [1, 4]. Acute severe hyponatraemia can lead to seizures, coma, brainstem herniation and permanent neurological insult. Chronic disorders often manifest more subtly with falls and cognitive deficits, progressing towards confusion and delirium [2].

Causes of hyponatraemia can be subdivided into either excess body water relative to sodium or loss of sodium in excess of water deficiency [1]. The kidney's ability to excrete electrolyte-free water may be decreased as a result of CKD and medications. Free water can also accumulate due to non-osmotic stimulation of vasopressin, i.e. in situations of reduced effective circulating volume, accompanied by sodium retention (chronic heart failure, cirrhosis or nephrotic syndrome) or sodium loss (diuretics, cerebral salt-wasting syndrome or adrenal or thyroid insufficiency), and in conditions associated with the syndrome of inappropriate secretion of anti-diuretic hormone [7, 10].

Rapid overcorrection of hyponatraemia (>8–10 mmol/24 h) can lead to ODS [9]. For this reason, the correction target was recently lowered to 4–6 mmol/24 h in patients at high risk of ODS [4]. However, if hyponatraemia is severe, acute and accompanied by neurological symptoms, correction should be initiated promptly with boluses of hypertonic saline (recommended 2 ml/kg of 3% saline) [6, 11]. If using other fluids, the expected change in serum [Na^+] with 1 litre of specified solution can be calculated as Δ [Na^+]$_{serum}$ = ([Na^+]$_{intravenous\ solution}$ − [Na^+]$_{serum}$)/(total body water + 1) [2]. Once neurological symptoms resolve, serum [Na^+] should be corrected at slower rates as described above.

ODS typically occurs in two phases. Initially, the patient displays encephalopathic symptoms consistent with hyponatraemia. As serum [Na^+] is corrected, the patient usually improves, but 2–3 days later, new symptoms develop, ranging from mutism and dysarthria to spastic quadriparesis and pseudobulbar palsy depending on which cerebral regions are affected [12]. Neurological sequelae often persist, although the condition is reversible in one third of the cases [8]. Risk factors for ODS include severe hyponatraemia, hypokalaemia, alcoholism, malnutrition and liver disease [8]. The only treatment is prevention of rapid changes in serum [Na^+] [13].

Treatment of Sodium Disorders during Continuous RRT

In patients with oligo-anuric AKI, intravenous fluids, diuretics or fluid restriction may be less effective than in patients with normal renal function. Vaptans (vasopressin receptor antagonists) have recently emerged as a therapy of euvolemic and hypervolemic hyponatraemia but are ineffective when serum creatinine is higher than 2.5 mg/dl [4]. If RRT is necessary, it is vital to remember that standard bags of dialysate/replacement fluid have a [Na^+] of 136–140 mmol/l and that electrolyte concentrations of these fluids will equilibrate with concentrations in the serum. Therefore, conventional RRT using standard bags could result in rapid overcorrection of hypo- and hypernatraemia.

There are several methods of correcting sodium disorders safely in this setting. One approach consists in using standard dialysate/replacement fluid in combination with the administration of intravenous dextrose 5% to 'redilute' the patient's serum [Na^+] in hypernatraemia or saline infusion to 'concentrate' the patient's serum [Na^+] in hyponatraemia. This method is effective but requires

close monitoring and carries a high risk of either overcorrection or inefficiency [14]. A second approach consists in modifying the rate of RRT. In hyponatraemia, the dialysate flow or total effluent rate can be reduced so that serum [Na^+] is corrected more slowly. In intermittent haemodialysis for instance, lowering the blood flow rate to 50–100 ml/min during a 3-hour session slows the transfer of sodium from the dialysate to serum [15]. The same principle can be applied to continuous RRT. As a result, the blood flow rate may be approximately 500–1,000 ml/h compared to standard rates of 6,000–12,000 ml/h [15]. This method is effective but will obviously have an impact on solute clearance and metabolic control [14].

Our protocol involves step-wise adjustment of the [Na^+] of dialysate/replacement fluid as guided by the serum [Na^+]. The method is effective and allows safe and predictable correction of hypo- and hypernatraemia. It is routinely applied in our department and administered and monitored by the nursing staff. To correct hypernatraemia, pre-calculated amounts of 30% NaCl are added to the fluid bags to raise their [Na^+] (table 1). A switch to fluid with lower [Na^+] can be considered every 12–24 h to achieve the recommended rate of correction (table 2). It is a relatively simple procedure, especially since the volumes added to the bags are small. To avoid contamination of the fluid, an aseptic non-touch technique is used. The protocol to correct hyponatraemia is more labour-intensive. Pre-calculated amounts of sterile water up to 1.25 litres are added to the dialysate/replacement fluid to reduce the fluid [Na^+] (table 3). To avoid contamination of the fluid, the procedure of adding water can be undertaken in the pharmacy aseptic unit or at the bedside with the operator (usually a nurse) fully gowned, masked and gloved using a sterile technique. In our practice, an assistant helps with the opening of the bags. The sterile water is inserted into the fluid bags using a syringe and a 3-way tap.

In case of hyponatraemia, the fluid [Na^+] should be increased every 12–24 h to normalize the serum [Na^+] at the desired rate (table 4). If serum [Na^+] still rises too quickly, the rate of RRT can be reduced. Our protocol is based on using 5-litre bags of dialysate/replacement fluid (tables 1, 3). Obviously, depending on whether smaller or larger bags are being used, the added volumes of sterile water or 30% NaCl have to be adjusted accordingly to achieve the desired final [Na^+] in the dialysate/replacement fluid.

It is also important to point out that the hyponatraemia protocol involves the addition of large volumes of water to the dialysate/replacement fluid that will alter the concentration of other electrolytes such as potassium and bicarbonate, and supplementation may be necessary [5].

Conclusion

The main objective during treatment of sodium disorders is a controlled rate of normalization of serum [Na^+]. In the context of continuous RRT, the step-wise adjustment of [Na^+] of dialysate/replacement fluids offers a safe and reliable method to achieve this.

References

1 Bagshaw SM, Townsend DR, McDermid RC: Disorders of sodium and water balance in hospitalized patients. Can J Anesth 2009;56:151–167.
2 Adrogué HJ, Madias NE: The challenge of hyponatremia. J Am Soc Nephrol 2012;23:1140–1148.
3 Adrogué HJ, Madias NE: Hypernatremia. N Engl J Med 2000;342:1493–1499.
4 Verbalis JG, Goldsmith SR, Greenberg A, Korzelius C, Schrier RW, Sterns RH, Thompson CJ: Diagnosis, evaluation, and treatment of hyponatremia: expert panel recommendations. Am J Med 2013;126(suppl 1):S1–S42.
5 Ostermann M, Dickie H, Tovey L, Treacher D: Management of sodium disorders during continuous haemofiltration. Crit Care 2010; 14:418–419.
6 Hoorn EJ, Betjes MGH, Weigel J, Zietse R: Hypernatraemia in critically ill patients: too little water and too much salt. Nephrol Dial Transplant 2008;23:1562–1568.
7 Overgaard-Steensen C, Ring T: Clinical review: practical approach to hyponatraemia and hypernatraemia in critically ill patients. Crit Care 2013;17:206–219.
8 Sterns RH, Hix JK, Silver SM: Management of hyponatremia in the ICU. Chest 2013;144: 672–679.
9 Asadollahi K, Beeching N, Gill G: Hyponatraemia as a risk factor for hospital mortality. Q J Med 2006;99:877–880.
10 Adrogué HJ, Madias NE: Hyponatraemia. N Engl J Med 2000;342:1581–1589.
11 Spasovski G, Vanholder R, Allolio B, Annane D, Ball S, Bichet D, Decaux G, Fenske W, Hoorn E, Ichai C, Joannidis M, Soupart A, Zietse R, Haller M, van der Veer S, Van Biesen W, Nagler E: Clinical practice guideline on diagnosis and treatment of hyponatraemia. Intensive Care Med 2014;40:320–331.
12 Laureno R, Karp BI: Myelinolysis after correction of hyponatremia. Ann Intern Med 1997;126:57–62.
13 Morard I, Gasche Y, Kneteman M, Toso C, Mentha A, Meeberg G, Mentha G, Kneteman N, Giostra E: Identifying risk factors for central pontine and extrapontine myelinolysis after liver transplantation: a case-control study. Neurocrit Care 2014;20:287–295.
14 Vassallo D, Camilleri D, Moxham V, Ostermann M: Successful management of severe hyponatraemia during continuous renal replacement therapy. Clin Kidney J 2012;5:155–157.
15 Wendland EM, Kaplan AA: A proposed approach to the dialysis prescription in severely hyponatremic patients with end-stage renal disease. Semin Dial 2012;25:82–85.