Hyponatremia : Management Errors

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Rapid correction of hyponatremia is frequently associated with increased morbidity and mortality. Therefore, it is important to estimate the proper volume and type of infusate required to increase the serum sodium concentration predictably. The major common management errors during the treatment of hyponatremia are inadequate investigation, treatment with fluid restriction for diuretic-induced hyponatremia and treatment with fluid restriction plus intravenous isotonic saline simultaneously. We present two cases of management errors. One is about the problem of rapid correction of hyponatremia in a patient with sepsis and acute renal failure during continuous renal replacement therapy in the intensive care unit. The other is the case of hypothyroidism in which hyponatremia was aggravated by intravenous infusion of dextrose water and isotonic saline infusion was erroneously used to increase serum sodium concentration.

Key Words : Hyponatremia, Management errors, Fluid restriction, Hypothyroidism

Introduction

Hyponatremia is the most common electrolyte disturbance encountered in clinical practice, with a prevalence up to 15% in a general hospital population[1]. Hyponatremia in critically ill patients can cause significant morbidity and mortality. Inappropriate treatment of hyponatremia can make the matters worse. The diagnosis and management of salt and water abnormalities in critically ill patients is often challenging. A systematic approach by clinicians, using a detailed history, physical examination, and relevant diagnostic tests, will assist in efficient management of salt and water problems[2]. The management of hyponatremia is not a simple theme because of the difficulty of the assessment of each patient's volume status evaluation. Clinical judgment and laboratory investigations are important to help elucidate a diagnosis.

The major common management errors during the treatment of hyponatremia are as follows[3]:

1) Inadequate investigation, which could have changed management

2) Treatment with fluid restriction for diuretic-induced hyponatremia

3) Treatment with fluid restriction plus intravenous saline simultaneously

4) Continuing the use of thiazide despite of the probable cause of hyponatremia is thiazide-induced hyponatremia

5) "Blind" intravenous saline for modest (>125 mmol/L) hyponatremia in a non-critical situation

6) Iatrogenic causes secondary to intravenous dextrose

In this report, we present two cases of management errors that occur commonly in our clinical practice. One is about the rapid correction of severe hyponatremia in a patient admitted to the intensive care unit. The other case is about the unreasonable use of isotonic saline and hypertonic saline infusion in a hypothyroid patient who needs fluid restriction and thyroid hormone replacement.

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Case

Case 1

A 87-year-old woman presented to the emergency department complaining of progressive weakness, fever, and myalgia over the past 5 days. Her mental status was alert but sometimes confused. She had moderate tenderness in her both costovertebral angles. Vital signs on admission revealed : blood pressure 100/70 mmHg, body temperature 36.9℃, pulse 72 bpm, and respiratory rate 20/min. Laboratory findings were as follows : blood urea nitrogen 60 mg/dL, creatinine 3.5 mg/dL, serum sodium 117 mmol/L, serum potassium 3.8 mmol/L, serum total CO_2 14.6 mmol/L, and ionized calcium 1.02 mmol/L. The patient was presumed to have acute renal failure associated with urosepsis and managed with continuous renal replacement therapy. After admission to the intensive care unit, her serum sodium increased to 130 mmol/L after 7 hours later with normal saline infusion of 1,600 mL. Even though there were no immediate complications associated with rapid correction of hyponatremia in this patient, the total increment of serum sodium was 21 mmol/L (from 117 mmol/L to 138 mmol/L) during the duration of 22 hr 30 min. The results of thyroid and adrenal function test were within normal limits. Two days later, the continuous renal replacement therapy was stopped because of the increase in urine output. Thereafter, she was recovered from acute renal failure associated with urosepsis and her serum sodium levels were stable without any further deterioration. Until now, for about 6 weeks after rapid correction of her hyponatremia, no neurologic changes were present suggestive of the development of the osmotic demyelination syndrome (ODS).

Case 2

A 55-year-old man consulted with the nephrology division about the evaluation and management of persistent hyponatremia over the past 7 days. He was admitted to the neurosurgery department due to the second lumbar vertebra burst fracture caused by fall down injury. When he was admitted to the hospital, laboratory findings were as follows: blood urea nitrogen 19 mg/dL, creatinine 0.8 mg/dL, serum sodium 137 mmol/L, serum potassium 4.0 mmol/L, and serum total CO_2 22 mmol/L. The serum sodium decreased to 129 mmol/L 12 days after his admission. His serum sodium concentrations were in the range of 122-132 mmol/L for 12 days, and the final serum sodium level was 129 mmol/L when the consultation was done. Physical examination revealed no evidence of volume depletion. His mental status was alert and well oriented. Vital signs on the consultation day showed: blood pressure 120-140/70-80 mmHg, body temperature 36.9℃, pulse 72 bpm, and respiratory rate 20/min. Daily intake/output were 3,250/1,800 mL, 3,100/1,850 mL and 2,260/2,200 mL during the consecutive 3 days before the consultation. He was taking soft diet and fluids ad lib. The main fluids infused during the last 12 days were intravenous dextrose water and isotonic saline. On the consultation day, hypertonic saline (3% saline) was infused without notifying the nephrologist. The hypertonic saline was stopped immediately. Thereafter, oral fluid restriction (<urine output+estimated insensible loss) was done and the saline infusion was held simultaneously. The thyroid function test revealed that he had hypothyroidism: T3 47.4 ng/dL (reference values : 60-181), TSH 58.1 uIU/mL (0.35-5.5), and free T4 0.30 ng/dL (0.89-1.76). The results of adrenal function test were within normal limits. His serum sodium levels slowly returned to normal after oral fluid restriction and thyroxine administration without any further infusion of intravenous fluids.

Discussion

The first case was about the problem of rapid correction of hyponatremia with continuous renal replacement therapy in a patient with urosepsis-

associated acute renal failure. In this case, the mental status of the 87-year-old woman was not altered. If sepsis is combined in a patient with severe hyponatremia, we usually have a difficulty in assessing the mental status. Thus, it is tempted for us to use hypertonic saline for correction of hyponatremia. It should be more complex when we apply the continuous renal replacement therapy for the management of acute renal failure accompanying hyponatremia in the intensive care unit. In the first case, we should have checked the plasma Na^+ concentration more frequently but, plasma Na^+ concentration was checked after 1600 mL of isotonic saline was infused over 7 hours. Meanwhile, the plasma Na^+ concentration increased by 13 mmol/L (from 117 mmol/L to 130 mmol/L) during the first 7 hours. It is a kind of very common management error that frequently occurs in our clinical practice. In this case, even though we did not use hypertonic saline, we had to consider the effect of continuous renal replacement therapy (CRRT) on the level of plasma Na^+ concentration and had to check the plasma Na^+ concentration at least every two hours or so. In the report by Ji et al.[4], continuous veno-venous hemofiltration (CVVH) was effective in the treatment of acute severe hyponatremia. They suggested that CVVH could be considered as a treatment option because of its slow and continuous nature. For the adequate rate of correction of hyponatremia when we use CRRT, they recommended that the serum sodium concentration be corrected at an average rate of 2.5±0.14 mmol/L/h at 6 h, 1.2±0.1 mmol/L/h at 24 h and 0.82±0.1 mmol/L/h at 48 h.

The rate of correction of hyponatremia depends on whether neurologic dysfunction is present. In asymptomatic patients, the plasma Na^+ concentration should be raised by no more than 0.5 to 1.0 mmol/L per h and by less than 10 to 12 mmol/L over the first 24 h. Acute or severe hyponatremia (plasma Na^+ concentration <110 to 115 mmol/L) tends to present with altered mental status and/or seizures and requires more rapid correction[5]. Park et al. reported that hyponatremic neurologic symptoms included lethargy (33.3%), confusion with drowsy mentality (33.3%), dizziness (18.6%), and semicoma (7.4%). At a single medical center they retrospectively analyzed the clinical course of 27 consecutive patients who presented with neurologic hyponatremic symptoms and with plasma Na^+ concentrations less than 125 mmol/L[6]. Severe symptomatic hyponatremia should be treated with hypertonic saline, and the plasma Na^+ concentration should be raised by 1 to 2 mmol/L per hour for the first 3 to 4 h or until the seizures subside. In other words, the plasma Na^+ concentration should probably be raised by no more than 12 mmol/L during the first 24 h. In volume-contracted states, the treatment of choice is to increase the serum Na^+ concentration by 10 mmol/L or to levels of 120 to 125 mmol/L over 6 hours by administering hypertonic 3 to 5% saline[5].

Hyponatremia in critically ill patients can cause significant morbidity and mortality. Inappropriate treatment of hyponatremia can make the matters worse. As in the study by Huda et al.[3], the main treatments given for hyponatremic patients were fluid restriction, intravenous saline, simultaneous fluid restriction and intravenous saline, and diuretic stopped/reduced. In their analysis, overall 34 cases (33%) were considered to have significant management errors. Out of these, 14 patients died (41%). The cohort that was felt to be managed appropriately, however had a mortality of 14 of 70 (20%).

Rapid correction of hyponatremia is frequently associated with increased morbidity and mortality. Therefore, it is important to estimate the proper volume and type of infusate required to change the serum sodium concentration predictably. Recently, Adrogue and Madias proposed a new formula for the management of both hyponatremia and hypernatraemia. According to this formula, the anticipated change in the patient's serum sodium concentration as a result of administration of 1 L of any infusate can be calculated by equation (1):

$\triangle[Na^+] = ([Na^+]inf - [Na^+]s)/(TBW+1)$ (1)

where $[Na^+]$, $[Na^+]inf$ and $[Na^+]s$ represent the expected change in the patient's serum sodium concentration, the sodium concentration of the infusate and the sodium concentration of the patient's serum, respectively, expressed in mEq/L, and TBW represents the patient's estimated total body water, expressed in liters. When the administered solution contains potassium chloride also, the equation (1) is converted as follows:

$\triangle[Na^+]=\{([Na^+]inf+[K^+]inf)-[Na^+]s\}/(TBW+1)$ (2)

where $[K^+]inf$ represents the potassium concentration of the infusate.

This formula that has been proposed by Adrogue and Madias predicted with relatively accuracy the changes in serum sodium concentration in almost all patients. Thus, it should be considered as a very useful tool for the management of dysnatremias. However, special attention should be paid when this equation is used in patients with hyponatremia due to extracellular volume depletion after euvolemia's restoration and primary polydipsia in order to avoid rapid correction of hyponatremia[7].

Under normal conditions, total body water is 50 or 60% of lean body weight in women or men, respectively. Therefore, to raise the plasma Na^+ concentration from 105 to 115 mmol/L in a 65-kg man requires 390 mmol $[(115-105)\times65\times0.6]$ of Na^+. It is suggested that if one cannot remember this formula, a useful practice is to administer 250 mL of either 3 or 5% saline over 4 to 6 hours[8].

The risk of correcting hyponatremia too rapidly is the development of the osmotic demyelination syndrome (ODS). This is a neurologic disorder characterized by flaccid paralysis, dysarthria, and dysphagia. The diagnosis is suspected clinically and can be confirmed by appropriate neuroimaging studies. There is no specific treatment for the disorder, which is associated with significant morbidity and mortality. Patients with chronic hyponatremia are most susceptible to the development of ODS, since their brain cell volume has returned to near normal as a result of the osmotic adaptive mechanisms. Therefore, administration of hypertonic saline to these individuals can cause sudden osmotic shrinkage of brain cells[5]. The review of the reported cases in which initial transient neurologic recovery by the initial rapid correction of hyponatremia, then was followed by delayed deterioration of ODS (biphasic course) suggests that clinicians treating the patients with severe symptomatic hyponatremia should be aware of the possibility of delayed neurologic sequelae despite the initial recovery of neurologic status[9].

The second case was about the erroneous management with isotonic saline and dextrose water infusion instead of fluid restriction and thyroxin administration in a patient with hypothyroidism-induced hyponatremia. For the long term correction of asymptomatic, non-volume-depleted hyponatremia, the general rule is to restrict electrolyte-free water intake. Fluid intake should be coupled with high dietary salt intake. Isotonic saline infusion with a loop diuretics are sometimes prescribed. In this case, diuretic induces urinary salt loss and reduces the risk of ECF volume expansion. For the patient with hyponatremia which is iatrogenically induced by intravenous dextrose and isotonic saline infusions, fluid restriction is the mainstay of treatment. Water restriction is also a component of the therapeutic approach to hyponatremia associated with primary polydipsia, renal failure and syndrome of inappropriate antidiuretic hormone secretion (SIADH). Water restriction is not usually used for the diuretic-induced hyponatremia or hypovolemic hyponatremia. If hypothyroidism is a possible cause of hyponatremia such as in our case, giving thyroxine is the most important step for the management of hyponatremia associated with hypothyroidism. In our patient, the hyponatremia was resolved by oral fluid restriction and thyroxine replacement therapy. Further intravenous fluid infusion was not required any more.

Disorders of sodium and water balance can be

approached by following a few basic steps: Thorough history taking and physical examination that focuses on volume assessment and laboratory evaluation that includes serum electrolytes, osmolality, urine osmolality, and urine sodium concentration are usually all that are required for diagnosis. Results of these findings are helpful in guiding therapy. Monitoring serum sodium concentration often to ensure adequate treatment and to avoid potential complications is required in management of both hyponatremia and hypernatremia[10].

The development of severe hyponatraemia in hospitalized patients was associated with treatment-related factors and inadequate management. Early recognition of risk factors and expedited therapy may make hospital-acquired severe hyponatraemia more preventable[11].

In summary, the most important therapeutic guidelines for the restoration of acute and severe hyponatremia should aim for gradual correction, i.e., by 10 to 12 mmol/L within 24 h and 20 mmol/L within 48 h. Water restriction is also an important component of the therapeutic approach to hyponatremia associated with primary polydipsia, renal failure and SIADH. Water restriction should not usually be indicated for the diuretic-induced hyponatremia or for the hypovolemic hyponatremia.

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