Hyponatremia: Review Questions

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QUESTIONS

Choose the single best answer to each question.

Questions 1 and 2 refer to the following case.

An 80-year-old woman with a history of depression presents to the emergency department (ED) with weakness and dizziness. She takes furosemide 20 mg daily for lower extremity edema. She reports that her primary care physician prescribed hydrochlorothiazide for elevated blood pressure 1 week ago. The patient denies fevers, chills, nausea, or vomiting. She claims to be more thirsty than usual and has been drinking apple juice in response. Her blood pressure is 100/60 mm Hg lying down and 84/40 mm Hg sitting, and her weight is 60 kg. Lungs are clear with no lower extremity edema. Laboratory studies reveal a serum osmolality of 260 mOsm/kg, serum sodium of 125 mEq/L (normal, 135–154 mEq/L), serum potassium of 3.4 mEq/L (normal, 3.5–5.0 mEq/L), and serum creatinine level of 0.8 mg/dL (normal, 0.6–1.2 mg/dL). Urinalysis reveals a sodium level of 50 mEq/L (normal, 0–300 mEq/L) and urine osmolality of 200 mOsm/kg.

1. **Which of the following is this patient's most likely diagnosis?**
   (A) Adrenal insufficiency
   (B) Furosemide-induced hyponatremia
   (C) Hydrochlorothiazide-induced hyponatremia
   (D) Syndrome of inappropriate antidiuretic hormone (SIADH)
   (E) Thyroid disease

2. **How should this patient be managed?**
   (A) Give intravenous (IV) normal saline (0.9%) at 125 mL/hr
   (B) Give IV 5% dextrose in half-strength normal saline at 50 mL/hr
   (C) Restrict free water intake orally
   (D) Provide salt tablets orally

Questions 3 and 4 refer to the following case.

A 25-year-old woman with a history of frequent hospitalizations for alcohol intoxication is brought to the ED after a week of binge drinking. On physical examination, her blood pressure is 120/75 mm Hg, heart rate is 85 bpm, and weight is 70 kg. She is lethargic and mumbling incoherently. In the ED, the patient has a generalized tonic-clonic seizure, which resolves with IV diazepam. Laboratory results are significant for a serum sodium level of 110 mEq/L, serum potassium level of 3.8 mEq/L, alcohol level of 250 mg/dL, serum osmolality of 230 mOsm/kg, and serum glucose concentration of 92 mg/dL (normal, 70–115 mg/dL). Renal function is normal.

3. **How should this patient be managed at this time?**
   (A) IV hypertonic saline (3%) at 130 mL/hr
   (B) IV hypertonic saline (3%) at 200 mL/hr
   (C) IV normal saline (0.9%) at 100 mL/hr
   (D) IV normal saline (0.9%) at 1000 mL/hr

4. **Eight hours after therapy is started, a serum chemistry profile reveals a sodium level of 120 mEq/L. The patient is now euvolemic and more responsive. What is the next step in this patient's management?**
   (A) Continue current therapy, recheck sodium every 6 hours
   (B) Start meningitic doses of IV ceftriaxone
   (C) Stop IV fluids and administer a 1-time dose of IV furosemide 80 mg
   (D) Stop IV fluids, restrict free water intake, and monitor serum sodium closely

5. **Serum chemistry results for a 50-year-old man admitted to the cardiac care unit with a myocardial infarction reveal a sodium level of 124 mEq/L. There are no other laboratory abnormalities; however, the sample is lipemic. The patient is resting comfortably and denies any symptoms. Which of the following is most likely to establish the diagnosis?**

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(A) Serum osmolality
(B) Serum uric acid
(C) Urine osmolality
(D) Urine sodium

6. **A 40-year-old man with a history of type 2 diabetes and end-stage renal disease on hemodialysis presents to the ED with weakness. He reports that he missed his regularly scheduled outpatient dialysis that day and ran out of his long-acting insulin 2 days ago. The patient has no other complaints. Physical examination is unremarkable, including a normal neurologic examination. Laboratory results reveal a serum sodium level of 125 mEq/L, serum potassium level of 5.2 mEq/L, serum chloride level of 104 mEq/L (normal, 96–106 mEq/L), and serum bicarbonate level of 19 mEq/L (normal, 21–27 mEq/L). Serum glucose is 700 mg/dL and serum osmolality is 310 mOsm/kg. A chest radiograph reveals clear lungs, and an electrocardiogram shows normal sinus rhythm with no acute T-wave changes. Which of the following is the most appropriate next step in this patient's management?**
(A) Immediate hemodialysis
(B) Initiate IV short-acting insulin therapy
(C) Restart subcutaneous insulin therapy for dosing at home
(D) Restrict free water to correct hyponatremia

ANSWERS AND EXPLANATIONS

1. **(C) Hydrochlorothiazide-induced hyponatremia.** In the elderly, diuretic use has been associated with hyponatremia and usually occurs within 1 to 2 weeks of starting the drug. Diuretics can induce volume depletion and stimulate the release of antidiuretic hormone (ADH), which acts on the collecting duct to cause water reabsorption. However, this movement of water depends on a medullary concentration gradient. Loop diuretics (eg, furosemide) impair this gradient, and therefore water reabsorption is diminished even with adequate ADH levels. Thiazide diuretics have no effect on the medullary gradient and water reabsorption is sustained. Diuretics often cause a heightened thirst response leading to increased fluid intake and further elevations of plasma free water. Older women in particular have been found to be most susceptible to thiazide-related hyponatremia.[1] Although thyroid disease and adrenal insufficiency can be associated with hyponatremia, there is nothing in the patient's history to support these conditions as the reason for an acute presentation. A high urine sodium level may be caused by SIADH, but in this case, the elevated urinary sodium level is due to diuretic use. SIADH is characterized by an inappropriately concentrated urine (urine osmolality > serum osmolality), which is not the case here.

2. **(A) Give IV normal saline (0.9%) at 125 mL/hr.** This woman has chronic hypovolemic hyponatremia as a result of diuretic use, and the hyponatremia must be corrected slowly. In cases in which hyponatremia is not life-threatening (sodium > 120 mEq/L), the goal is to replace one third of the sodium deficit over the first 12 to 24 hours and the remainder over the next 2 to 3 days. IV normal saline corrects hyponatremia because the stimulus for ADH release in this case (volume depletion) is inhibited. This patient's total sodium deficit is 450 mEq/L (total body water [TBW] × [desired serum sodium – current serum sodium]), which equals approximately 3 L of normal saline (154 mEq/L). One liter of normal saline should be given over the first 8 to 12 hours (125 mL/hr) with a subsequent infusion rate reduction. Using hypotonic saline at a slow rate is not indicated in severe hypovolemic hyponatremia. Although restriction of free water may have initially prevented the development of hyponatremia, it will not play a role in its correction or in raising blood pressure. Salt tablets, which can play a role in treatment of SIADH, would not be used for immediate treatment in this case.

3. **(A) IV hypertonic saline (3%) at 130 mL/hr.** This patient is exhibiting severe neurologic manifestations of hyponatremia, and the appropriate treatment is to raise serum tonicity. The goal rate of correction in such serious cases is generally 1.5 to 2 mEq/L/hr for the first 3 to 4 hours or until symptoms have resolved.[2] TBW is a fraction of body weight (0.5 L/kg for younger women and older men, 0.6 L/kg for younger men, and 0.45 L/kg for older women), and infusate sodium varies with the type of fluid chosen (513 mEq/L for 3% saline; 154 mEq/L for 0.9% saline). When neurologic symptoms continue, 3% saline can be used to provide more rapid correction. Given that this patient is symptomatic, serum sodium should be raised by 6 mEq/L rapidly over 3 hours or until neurologic symptoms resolve. To increase the serum sodium from 110 mEq/L to 116 mEq/L in a 70-kg woman (35 L TBW), 210 mEq/L of sodium or approximately 400 mL of 3% saline is required. This should be given over 3 hours or at a rate of 130 mL/hr to raise the serum sodium concentration by no more than 2 mEq/L/hr.

4. **(D) Stop IV fluids, restrict free water intake, and monitor serum sodium closely.** Therapy for hyponatremia must be closely monitored because rapid correction can cause fluid shifts in the brain and result in irreversible and often fatal osmotic demyelination (central pontine myelinolysis). Clinical observations suggest that the degree of correction over the first 24 hours correlates with the development of demyelination, with the safest rate of correction being limited to 10 to 12 mEq/L over 24 hours.[3] As treatment has already corrected this patient's sodium level from 110 to 120 mEq/L over 8 hours and her neurologic condition has improved, therapy should be targeted to slow the rise of serum sodium. At this point, stopping hypertonic saline and restricting free water should slow the rise of sodium. If the sodium level continues to rise despite these measures, hypotonic solution must be administered. This will ensure that the target level of correction is not exceeded. Continuing current therapy would certainly cause an overcorrection. Furosemide will not slow the rate of correction. IV ceftriaxone does not play a role in this case.

5. **(A) Serum osmolality.** This is a case of pseudohyponatremia related to laboratory technique. If the nonaqueous phase of plasma is expanded, such as with high triglyceride levels, assays that employ plasma dilution while measuring serum sodium levels may report an abnormally low value. However, these lipids and proteins do not contribute to serum osmolality, which remains in large part a function of serum sodium (2 × plasma Na + [glucose/18] + [blood urea nitrogen/2.8]). Therefore, pseudohyponatremia is diagnosed when serum osmolality is normal. Ion-selective electrodes for sodium will also reveal a normal sodium level. Pseudohyponatremia can also be seen with multiple myeloma and the production of paraproteins. Urine osmolality, urine sodium, and serum uric acid can vary and have no role in diagnosing pseudohyponatremia.

6. **(B) Initiate IV short-acting insulin therapy.** Because glucose is an effective osmole, hyperglycemia leads to hyponatremia by causing an osmotically driven shift of water from cells into the extracellular compartment, resulting in dilution of serum sodium. This osmotic shift can be estimated by a correction factor that predicts a 1.6 mEq/L decrease in sodium for every 100 mg/dL rise in glucose. However, validation studies of this correction factor have suggested that the decrease in sodium may be even greater, from 2.4 to 4.0 mEq/L, depending on the plasma glucose level.[4] Thus, in this patient, the corrected sodium would be 135 mEq/L or greater based on which correction factor is used. In patients with intact renal function, the osmotic shift in water to the extracellular compartment caused by glucose is somewhat balanced by an osmotic diuresis also driven by glucose. The result is usually a mild decrease in serum sodium. A patient on dialysis cannot respond with diuresis, and therefore hyponatremia tends to be more pronounced. In this case, the treatment is to remove the osmotic driving force, which will require immediate IV insulin. Subcutaneous insulin is not recommended for managing critical hyperglycemia. Free water intake will likely worsen underlying hyponatremia. Although the patient missed his hemodialysis session, hyponatremia is not a primary indication for urgent dialysis; correction of hyperglycemia is the first line of treatment. In addition, this patient has no other indications for activating immediate hemodialysis, such as critical hyperkalemia or volume overload.

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