Hyponatremia: practical considerations in the acute geriatric setting

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Abstract

In older adults, hyponatremia often represents a medical emergency and is frequently associated with neurological manifestations or symptomatic pictures that the clinician mistakes for other pathologies. This paper deals with some practical considerations in the assessment and management of hyponatremia in older adults in the acute care setting, following the clinical discussion that took place at the Soave (Italy) meeting convened by the scientific committee of the Italian Society of Geriatrics Hospital and Territory.

Introduction

Hyponatremia is a common electrolyte disorder caused by an excess of total body water when compared to total body sodium (Na) content, defined as a serum Na concentration of less than 135 mmol/L.1 Hyponatremia is the most frequent electrolyte disturbance in older people, caused by the presence of comorbidities, polypharmacy, and poor food accessibility. It is particularly common in frail hospitalized patients. About 40% of the older adults admitted to an acute setting suffer from acute hyponatremia during hospitalization.1-4 Hospital-associated hyponatremia is a common occurrence. All forms of hyponatremia are independently associated with in-hospital mortality and heightened resource consumption. Community-acquired hyponatremia occurred in 37.9% of hospitalizations, and it was associated with in-hospital mortality, discharge to a short- or long-term care facility, and an increase in hospital length of stay. Hospital-acquired hyponatremia developed in 38.2% of hospitalizations and was associated with in-hospital mortality, discharge to a facility, and an increase in hospital length of stay.3 In 51% of cases, hyponatremia in older persons is multifactorial.1,4 There are many risk factors associated with the development of hyponatremia in hospitalized patients:1 i) physiologic changes of aging that induce water and Na homeostasis abnormalities (altered sense of thirst, reduced number of functioning nephrons, reduction in renal blood flow); ii) diseases/drugs accompanied by the syndrome of inappropriate antidiuretic hormone (SIADH) secretion (subdural hematoma or intracranial hemorrhage, malignancies like lung small cell carcinoma, pulmonary diseases, and endocrine diseases such as hypothyroidism, adrenal insufficiency, and diabetes mellitus); iii) increased hypo-osmotic fluid intake or decreased Na intake (low Na diet, tube feeding); iv) increased Na loss (renal diseases, gastrointestinal vomiting/diarrhea).

Pathogenesis

Na concentration is tightly controlled by water homeostasis, which is mediated by the mechanisms of thirst, vasopressin secretion, and renal compensation.1,3 An altered sense of thirst in older adults can be caused by a possible age-related alteration of the system that mediates thirst stimuli or other factors that can reduce the sense of thirst (psychological factors, food ingestion, food, and liquid temperature). Therefore, water must be prescribed to older adults. Besides, due to renal aging, the kidney is characterized by a reduced number of working nephrons (by age 80, 30-40% fewer glomeruli and 600 mL of renal blood flow), altered capacity urine concentration with impaired renal response to vasopressin, and...
increased permeability of the glomerulus in older adults. This determines a variation in effective blood volume due to less reabsorption and more Na elimination. Aldosterone deficiency is closely linked to renin deficiency (not secondary to adrenal deficiency), with the actual risk of developing dyselectrolytemia.1

Classification and diagnosis

Hyponatremia can be divided into hypertonic, isotonic, and hypotonic based on serum osmolality.24 Effective osmolality may be calculated with Equations 1 and 2:

\[
\text{Effective osmolality (mmol/kg H}_2\text{O)} = 2 \times (\text{serum Na (mmol/L)} + \text{serum K (mmol/L)} + \text{serum glycemia (mg/dL)})/18\]  
\[
\text{Effective osmolality (mmol/kg H}_2\text{O)} = 2 \times (\text{serum Na (mmol/L)} + \text{serum K (mmol/L)} + \text{serum glycemia (mmol/L)})\]  

Effective osmolality is important because, for example, in hyperglycemia-induced hyponatremia, hyponatremia is caused by dilution due to hyperosmolality, adding 2.4 mmol/L to the measured serum Na concentration for every 5.5 mmol/L (100 mg/dL) incremental rise in serum glucose concentration above a standard serum glucose concentration of 5.5 mmol/L (100 mg/dL) or using a calculated value using an equation in a table. Urea is not an effective osmole because it readily passes across the cellular membrane. This form is defined as hypertonic hyponatremia (serum osmolality greater than 290 mOsm/kg) and can be caused not only by hyperglycemia but also by the infusion of mannitol.5810

Isotonic hyponatremia or pseudohyponatremia (serum osmolality between 275 mOsm/kg and 290 mOsm/kg) is mostly caused by an exaggerated increase in lipids and/or plasma proteins or by solutions containing mannitol, glycine, or sorbitol. Hypotonic hyponatremia (serum osmolality less than 275 mOsm/kg) represents an excess of free water that can be caused by increased free water intake (psychogenic polydipsia) or decreased free water excretion caused by the inability of the kidneys. It is the most common form in older people, and its etiology can be classified based on the volume status of the extracellular fluid: hypovolemic (vomiting or diarrhea, use of diuretics, adrenal insufficiency), euvoletic, including SIADH, or hypervolemic (decreased cardiac output, cirrhosis, or chronic kidney disease).2381113 Figure 1 illustrates the types of hypotonic hyponatremia.

If the older patient has hypotonic hyponatremia after plasma osmolality, it is necessary to measure the urine osmolality. If the urine osmolality is greater than 100 mOsm/kg, then the volume status must be assessed. If the patient is hypovolemic, urine Na less than 10 mmol/L indicates extrarenal loss of fluid (remote diuretic use and remote vomiting); levels greater than 20 mmol/L are indicative of renal loss of urine (diuretics, vomiting, cortisol deficiency, and salt-wasting nephropathies).14

In hypervolemic/hypovolemic states, anamnestic collection (e.g., chronic heart failure) or objective examination may be important; just the measurement of blood tests may be useful in differential diagnosis (serum thyroid-stimulating hormone, serum adrenocorticotropic hormone, serum urea, liver function tests).

Figure 1. Types of hyponatremias based on extracellular volume.

Syndrome of inappropriate antidiuretic hormone

SIADH is an inappropriate vasopressin secretion that occurs independently from effective serum osmolality or circulating volume. It may result from increased release by the pituitary gland or ectopic production.6 It may also result from increased vasopressin
Diagnostic criteria for the syndrome of inappropriate antidiuresis are shown in Table 1.5,15

General anesthesia, nausea, pain, stress, carcinoma (lung, pancreas, bladder, lymphomas, leukemias, sarcomas, mesotheliomas, thymomas), neurological disorders (head trauma, subarachnoid hemorrhage), lung diseases (pneumonia, severe chronic obstructive pulmonary disease, ventilation), and drugs are frequent causes of SIADH in hospitalized patients.4 Some drugs such as thiazides cause SIADH with multifactorial mechanisms (excessive introduction of free water with polydipsia, reduced clearance of free water, and reduced ability to produce free water in advanced age for inhibition of tubular electrolyte transport renal, stimulation of the release of vasopressin, renal loss of Na and potassium).5,11,15 Cerebral salt-wasting syndrome is a rare condition observed in individuals with subarachnoid bleeding. There may be a reduction in extracellular fluid volume due to natriuresis. A very high urinary Na concentration, elevated serum urea, orthostatic hypotension, and low venous central pressure are consistent with the diagnosis.16 If a neoplastic or infectious disease is suspected, it may be useful to perform an X-ray or computed tomography scan of the chest or the head.14

Clinical features

Hyponatremia between 130 and 134 mmol/L is usually defined as mild, moderate between 125 and 129 mmol/L, or severe <125 mmol/L, as measured by ion-specific electrodes. Nevertheless, symptoms depend on the severity and time of development of hyponatremia, for which moderate hyponatremia, if chronic, is not entirely asymptomatic.4,5 Patients with mild-to-moderate hyponatremia (greater than 120 mmol/L) or a gradual decrease in Na (greater than 48 hours) have minimal symptoms like anorexia, fatigue, walking disorders, attention deficit, increased risk of falls and fractures, and osteoporosis.20-22 Patients with severe hyponatremia (less than 120 mmol/L) or a rapid decrease in Na levels have multiple severe and varied symptoms that can range from nausea and vomiting to headaches, muscle cramps, altered mental status, agitation, seizures, and even coma due to brain edema and increased intracranial pressure. If hyponatremia cannot be classified, it must be considered chronic.4

Table 1. Diagnostic criteria for the syndrome of inappropriate antidiuresis.

<table>
<thead>
<tr>
<th>Essential criteria</th>
<th>Supplemental criteria</th>
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<tbody>
<tr>
<td>Effective serum osmolality &lt;275 mOsm/kg</td>
<td>Serum uric acid &lt;0.24 mmol/L (&lt;4 mg/dL)</td>
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<tr>
<td>Urine osmolality &gt;100 mOsm/kg at some level of decreased effective osmolality</td>
<td>Serum urea &lt;3.6 mmol/L (&lt;21.6 mg/dL)</td>
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<tr>
<td>Clinical euvolemia</td>
<td>Failure to correct hyponatremia after 0.9% saline infusion</td>
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<tr>
<td>Urine sodium concentration &gt;30 mmol/L with normal dietary salt and water intake</td>
<td>Correction of hyponatremia through fluid restriction</td>
</tr>
<tr>
<td>Absence of adrenal, thyroid, pituitary or renal insufficiency</td>
<td>Fractional sodium excretion &gt;0.5%</td>
</tr>
<tr>
<td>No recent use of diuretic agents</td>
<td>Fractional urea excretion &gt;55% Fractional uric acid excretion &gt;12%</td>
</tr>
</tbody>
</table>

NaCl 0.9%: 154 mEq/L  NaCl 3%: 513 mEq/L  Mixed solution: 77 mEq/L  Glucose solution: 5%: 0 mEq/L  Lactate ringer: 130 mEq/L  NaCl 2 fl 2 mEq/L : 20 mEq/L

Figure 2. Amount of sodium in main parenteral infusion. NaCl, sodium chloride.

Treatment

The fundamental assessments that must be made for treatment are characterization of the type of hyponatremia; identification of the etiology; if possible, removal of the cause; and assessment of the presence or absence of symptoms (depending both on the extent of the Na deficit and on the speed with which the deficit arose). Treatment of hyponatremia depends upon the severity, duration of hyponatremia, and volume status.5,23 In asymptomatic or less symptomatic forms, the therapy is based on the correction of the cause, but during hospitalization, care must be taken with the administration of intravenous fluids. Figure 2 highlights the Na content for solution.

The acute and severe symptomatic forms must be promptly treated with hypertonic solutions. Rapid correction of chronic hyponatremia (greater than 10 mmol/L to 12 mmol/L of Na in 24 hours) can lead to osmotic demyelination syndrome, known as central pontine myelinolysis, a severe complication with death risk.5,24 Hyponatremia with severe symptoms, regardless of whether it is acute or chronic, requires an intravenous infusion of 150 mL of 3% hypertonic over 20 minutes, checking the serum Na concentration after 20 minutes, while simultaneously supplementing with potassium if deficient.5 General recommendations are: correction of Na can be satisfactory, reaching a value of safety Na (125 mmol/L); correction speed should not exceed 8-10 mmol/L within 24 hours; 18 mmol/L within 48 hours (0.4 mmol/hour); and 1-2 mmol/hour in the first hours in patients with severe symptoms.[5] To increase Na, Equation 3 should be considered [also, taking into account that older patients’ total body water is body weight × 0.5 (men) or × 0.45 (women)].5,25

Na (after 1 L)=(Na infused infused-Serum Na)/(total body water+1) [Eq. 3]

NaCl 0.9%: 154 mEq/L  NaCl 3%: 513 mEq/L  Mixed solution: 77 mEq/L  Glucose solution: 5%: 0 mEq/L  Lactate ringer: 130 mEq/L  NaCl 2 fl 2 mEq/L : 20 mEq/L

Figure 2. Amount of sodium in main parenteral infusion. NaCl, sodium chloride.
In hypovolemic hyponatremia, it is necessary to reach adequate extracellular volume, while in hypervolemic hyponatremia, water restriction is recommended. Water restriction in patients with SIADH corrects hyponatremia by only <2 mmol/L in the first 24–48 hours, even when drastic (<500 ml/d), and it is poorly tolerated due to the poor compliance given by the sense of thirst.4,26,27 Thus, selective vasopressin 2 receptor antagonists (vaptans), medications that increase the excretion of water in the kidneys without affecting Na, can be used in patients with euvolemic conditions.

Vaptans block the action of arginine vasopressin on water retention, thus acting with an “aquaretic” effect (elimination of pure water and not electrolytes). Oral administration (15 and 30 mg tablets) must be once a day (peak after 2 hours, half-life about 8 hours), preferably in the morning regardless of meals. Patients on tolvaptan therapy can and should drink in response to thirst. The dose may be increased gradually (at intervals >24 hours to a maximum of 60 mg/day) to achieve the desired serum correction. The co-administration of other treatments for hyponatremia is not recommended. In the dose titration phase, due to the need for close monitoring of blood and volume levels, tolvaptan should be administered in the hospital. The duration of therapy with vaptans depends on the etiology.28

Conclusions

Approximately a quarter of older patients in the emergency department may present with a Na disorder. In a battery of biochemical tests to be performed on the older patient in the emergency room and upon entry to a geriatric ward, the dosage of Na cannot be missed, associated with the calculation of the plasmatic osmolality and the state of hydration of the patient. The etiological diagnosis constitutes a clinical challenge due to the many causative factors of hyponatremia, especially in older patients with a greater predisposition to physiological deterioration.4 It must be considered that even mild chronic hyponatremia, often asymptomatic, could be clinically significant because it could be a marker of frailty and be related to greater mortality and morbidity.29,30 Particular attention must be paid to the severity of the symptoms and the appropriate modalities of correction. Upon discharge, a reconciliation of the home medical therapy must be carried out.

References