Sodium Disorders in the Elderly

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Disorders of sodium imbalance are commonly encountered in clinical practice and can have a substantial impact on the prognosis of the patient. These disorders are more common in the elderly. Sodium disorders can cause serious neurologic symptoms and even death, particularly among hospitalized patients. The identification of sodium abnormalities and appropriate clinical intervention are critical for improving patient outcomes. Early recognition of hyponatremia and hypernatremia can provide a clue to an underlying disorder. In this update, we have summarized age-related homeostatic changes that impair sodium balance, medications that alter salt and water handling, and the recognition and management of sodium disorders in elderly patients.

Key words: sodium ■ elderly ■ hyponatremia ■ hypernatremia

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OBJECTIVES

After reading the article, "Sodium Disorders in the Elderly," the learner should be able to recognize sodium abnormalities and do the appropriate clinical intervention to improve the patient outcome, and should also be able to complete the quiz (that appears on page 221) and evaluation questions.

EXPIRATION

The quiz must be completed, postmarked and mailed by Feb. 25, 2005 for eligibility to receive continuing medical education credit for this CME activity.

INTRODUCTION

With advancing age, the kidney undergoes several anatomical and physiological changes that limit the adaptive mechanisms responsible for maintaining the composition and volume of the extracellular fluid. These include a decline in glomerular filtration rate (GFR) and an impaired ability to maintain water and sodium homeostasis in response to dietary and environmental changes. Consequently, elderly patients become more susceptible to clinical complications involving salt and water abnormalities.

Hypernatremia was reported in approximately 1% of hospitalized patients over the age of 60 years and up to 60% of febrile nursing home residents.[1,2] Among those with impaired oral intake, the incidence of hypernatremia was even higher.[3] Importantly, the presence of hypernatremia is associated with a mortality rate of more than 40%.[4] Likewise, hyponatremia is more common in older individuals, occurring in 11% of the ambulatory geriatric population in one series.[5] The occurrence of hyponatremia among hospitalized patients confers twice the risk of death compared to those without.[6] Thus, both hypernatremia and hyponatremia can cause serious neurologic symptoms and even death.

As we care for an increasing number of older individuals, particularly in a hospital setting with acute medical problems, the recognition of sodium abnormalities and appropriate clinical intervention is criti-

cal for improving patient outcomes. In this update, we have summarized age-related homeostatic changes that impair sodium balance, medications that alter salt and water handling, and the recognition and management of sodium disorders in elderly patients.

Water Metabolism

Water, comprising 55–65% of healthy adults, is the predominant constituent of the human body. This percentage diminishes proportionally with age, as the ratio of muscle to water-poor tissues, such as fat and bone, falls.[7] Between 55% and 75% of water is contained within the intracellular compartment. Serum constitutes approximately one-fourth of the extracellular space, and antidiuretic hormone (ADH)—a nonapeptide produced by the neurohypophysis[8]—closely regulates the water content within this compartment. Although multiple variables influence the secretion of ADH under normal physiologic conditions, the most important modulator of ADH secretion is the serum osmolality.[9]

Derangements in water metabolism are largely reflected as changes in serum osmolality and sodium concentration. By adjusting water content, the body maintains serum osmolality and its principal determinant, serum sodium concentration, within an extremely narrow range of 285–295 mosm/l and 135–145 mmol/l, respectively. Two additional key factors that regulate water homeostasis in combination with ADH are: 1) renal handling of water and solute and 2) an intact thirst mechanism. With aging, urinary concentration and diluting abnormalities occur which reflect diminished tubular function.[10] These changes are integral in the predisposition of the elderly to water and sodium imbalances. While a healthy young adult can attain a maximum urinary concentration of 1,200 mosm/kg, a healthy elderly person can often only achieve a urine osmolality of 700–800 mosm/kg, thus, increasing the risk of developing hypernatremia.[11]

Additionally, elderly individuals cannot dilute urine to less than 100 mosm/kg compared to 50 mosm/kg in young adults,[12] possibly due to a decline in GFR or reduced tubular responsiveness to ADH.[13] This dilutional defect predisposes them to hyponatremia. These alterations limit the ability of the elderly to handle water excesses or deficits that may occur. Although the sensitivity of the osmoregulatory system appears to increase with age,[13] the sensitivity of thirst—like the renal concentrating capacity—is also diminished, further predisposing older patients to the development of water deficiency and hypernatremia.[14-16] Elderly patients are also more likely to consume prescribed and/or over-the-counter medications for a variety of conditions, and many of these medications can influence ADH secretion and affect water metabolism (Table 1). Less commonly, conditions, such as the destruction of the neurohypophysis by tumors, granulomatous disease, vascular insults, trauma, metabolic or other disturbances, can lead to ADH deficiency and

Table 1. Common Drugs Used by Elderly that can Influence Antidiuretic Hormone (ADH) Secretion and Effect on Water Metabolism

Nicotine[1]	Alcohol[3]	Lithium[4]
Morphine (high dose)[1]	Morphine (low dose)[3]	Colchicine[4]
Epinephrine[1]	Clonidine[3]	Demclocycline[4]
Cyclophospahmide[1]	Glucocorticoids[3]	Glyburide[4]
Tolbutamide[2]	Haloperidol[3]	Loop Diuretics[4]
Chlorpropamide[2]	Cisplatinum[3]	Vinblastine[4]
NSAIDs[2]	Cabamazepine[3]	Methoxyflurane[4]

1: enhances ADH secretion, 2: increases renal tubular responsiveness, 3: reduces ADH secretion, 4: diminishes renal tubular responsiveness; NSAIDs: Nonsteroidal anti-inflammatory drugs

Table 2. Common Causes of Hyponatremia in Elderly

Decreased Total Body Sodium	Normal Total Body Sodium (Excess Water)	Increased Total Body Sodium
Thiazide diuretics (up to 50% of cases), renal salt wasting, Addison's disease	SIADH; drugs affecting vasopressin hypothyroidism, glucocorticoid deficiency	Congestive heart failure, cirrhosis of liver, nephrotic syndrome, renal failure
Vomiting, Diarrhea, low solute intake: tea-toast diet, Low osmolar tube feeding	Psychogenic polydipsia, hypotonic intravenous fluids,	

SIADH: Syndrome of Inappropriate Antidiuretic Hormone Secretion

reduced thirst. This is especially important in elderly persons, when even a partial deficiency of ADH may be superimposed on an impaired thirst response and lead to negative free water balance and hypernatremia.

Sodium Metabolism

With aging, the ability of the kidney to both conserve sodium in response to sodium deprivation and to excrete sodium in response to sodium loading are impaired. Epstein and Hollenberg noted the half-time for reduction of urinary sodium after salt restriction was 17.6 hours in young and 31 hours in old subjects.[17] The salt-losing tendency of the senescent kidney is due to: 1) nephron loss that leads to increased osmotic load per nephron and resultant mild osmotic diuresis and 2) age-related reductions in renin and aldosterone levels.[18-21] By contrast, the impaired ability to excrete a sodium load may reflect an age-related reduction in end-organ responsiveness to atrial natriuretic peptide (ANP), a 28-amino-acid peptide that has both a natriuretic effect as well as a vasodilatory effect.[22-24]

Hyponatremia

Serum sodium is usually maintained within the normal range of 135–145 mmol/l. Hyponatremia is defined as a reduction in the concentration of sodium in the aqueous portion of the serum. A reduction in serum sodium below 130 mmol/l should be considered clinically significant. Hyponatremia is one of the most common electrolyte disorders in the elderly,[5] and female gender is an important risk factor for the development of severe complications.[25]

The first step in evaluating a patient with a reduced serum sodium concentration is to evaluate the serum osmolality. If the serum osmolality is low, the patient is classified as being in a true hypo-osmotic state. Serum vasopressin levels are not routinely measured in clinical practice. A useful working classification of patients with hypo-osmolar hyponatremia is to then place the patient into one of three categories based on the clinical assessment: 1) hyponatremia with ECF volume depletion, 2) hyponatremia with normal ECF volume, or 3) hyponatremia with ECF volume excess. A detailed approach to the patient with hyponatremia has been described elsewhere.[26]

In the elderly patient with hyponatremia and ECF volume depletion, it is particularly important to consider diuretic use and/or poor oral low-solute intake with a predominant liquid diet, such as tea or juices (Table 2), as important etiologic factors. Elderly patients with hyponatremia and normal ECF volume and a nondilute urine should be screened for hypothyroidism, which is more prevalent in the elderly, as well as glucocorticoid deficiency. In addition, medications that lead to an excess secretion of vasopressin and/or enhance renal tubular responsiveness to circulating vasopressin should be considered (Table 1). If these possibilities have been excluded, the diagnosis of the syndrome of inappropriate ADH secretion (SIADH) is likely, and although an etiology may not be found in all cases, evaluation for a central nervous system disorder, malignancy or abnormal pulmonary process should be

Table 3. Calculating Free Water Excess and Deficit

Free Water Excess = TBW – {(actual serum Na/ desired serum Na) x TBW}

Free Water Deficit = [(serum Na – 140)/140] x 0.6 Body Weight (kilograms)

TBW: Total body water or body weight in kilograms x 0.6

[Calculating the Effect of 1 liter of an Intravenous Solution on Serum Sodium
Change in serum Na = {[Na] infused – [Na] serum}/(total body water +1)]

Table 4. Etiology of Hypernatremia in Elderly

Decreased Water Intake	Increased Water Loss	Increased Sodium Intake
Febrile illness	Diarrhea, fever	Prolonged saline infusion
Altered mental status	Osmotic diuresis (glycosuria, high protein tube feeding), lithium	Sodium bicarbonate therapy
Physical impairment	Diabetes insipidus, hypercalcemia, hypokalemia	
	Chronic kidney disease	

initiated. Indeed, in an ambulatory geriatric population, Miller and colleagues reported that 46/405 subjects (11%) had hyponatremia, with SIADH the apparent cause in 27/46 (59%); one-quarter of these subjects had no apparent underlying etiology and were considered to have idiopathic SIADH. This SIADH-like hyponatremia occurred more commonly among the old elderly (individuals 75 years of age or older), suggesting that aging might be a risk factor for the development of SIADH-like hyponatremia.[5]

Symptoms and Signs of Hyponatremia

Depending on the magnitude and rate of development of hyponatremia, the clinical presentation may range from asymptomatic to overt central nervous system symptoms, such as lethargy, confusion, seizures, coma and death. Subtle findings, such as loss of attention, may be one of the earliest signs of altered sensorium, and this should be specifically evaluated in the older patients with hyponatremia or other metabolic abnormalities.

Therapy for Hyponatremia

Treatment is dependent upon the pathogenesis of the hyponatremia and the severity of symptoms. Patients with hypotension should initially be treated with normal saline to replenish the intravascular volume. Patients should then be reassessed and if symptoms of hyponatremia persist following normalization of blood pressure, hypertonic saline should be given. Furthermore, the change in serum sodium concentration in response to treatment needs to be followed closely. The rate of rise of serum sodium should not exceed 0.3–0.4 mmol/hr (7–10 meq/24 hours), since correction at a rate greater than 0.5 mmol/hr has been associated with severe neurologic complications, including osmotic demyelination syndrome.[27] Care must also be taken not to induce fluid overload and pulmonary vascular congestion. The administration of normal saline at 75 ml/hr should raise serum sodium by approximately 0.3–0.4 mmol/hr. If there is any concern of heart disease, a lesser rate of about 50 ml/hr is advisable. The serum sodium level should be repeated as necessary, regulated as dictated by the clinical situation with adjustment of the fluid rate as required. In sodium depletion, the quantity of sodium required to increase the serum sodium concentration by a given amount can be estimated more precisely by multiplying the desired change in serum sodium by the total body water (e.g., 8 mmol/liter change in a 60-kg person over 24 hours is 8 mmol/liter x 36 liters = 288 mmol = approximately 1.9 liter normal saline or 560 ml 3% NaCl). It should be noted that symptoms related to hyponatremia occur disproportionately throughout the population. Both aging and male gender appear to confer protection against the development of hyponatremia-associated seizures, permanent brain damage and/or mortality, although the reason(s) for this is unclear.[28,29] In asymptomatic patients with no evidence of volume depletion, as in SIADH, correction of the underlying problem and restriction of free water intake to 1 liter per day is usually sufficient to normalize the serum sodium.

Chronic hyponatremia in postmenopausal women is not uncommon and is often viewed as a benign condition. Recommended therapy for asymptomatic patients is usually fluid restriction. A nonrandomized prospective multicenter study found that chronic symptomatic hyponatremia in postmenopausal women can be associated with major morbidity and mortality, and therapy with IV sodium chloride was associated with better outcomes than fluid restriction.[25] In patients with clinical evidence of excess extracellular fluid volume, the free water excess can be estimated using the formula shown in Table 3. Bed rest, water restriction and/or increasing water excretion with furosemide (20–40 mg intravenously twice a day), which induces hypotonic urine that results in a negative free water balance, are effective in most patients. In cases of SIADH refractory to free water restriction (i.e., malignancies, other), demeclocycline 300 mg orally four times a day for up to 10 days can be used to blunt the renal tubular response to circulating ADH and stimulate water diuresis. Although lithium was used as a treatment in the

Table 5. Simplified Initial Approach to Treating Hyponatremia and Hypernatremia in the Elderly

Hyponatremia

A) Correct underlying cause if feasible.
B) Normal saline at 75 ml/hr should raise serum sodium by approximately 0.3–0.4 mmol/hr. (this should raise serum sodium by about 8 meq/day*; use 50 ml/hr if high risk of heart disease)

* if symptomatic consider 3% normal saline at 25 ml/hr

Hypernatremia

A) Correct underlying cause if feasible.
B) 5% dextrose in water at a rate of 25ml/hr over 2-3 days for each 5 meq/L increase in serum sodium above 150 meq/L

Continuing Medical Education (CME) Quiz and Evaluation—Sodium Disorders in The Elderly—Quiz

A CME activity sponsored by the National Medical Association (NMA)

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Instructions: Select the correct answer to each question and mark in the corresponding boxes provided. Mail, scan and e-mail, or fax the completed test and evaluation questions by Feb. 25, 2005 to *JNMA*, 1012 Tenth St, NW, Washington, DC 20001; (202) 371-1162 ; ktaylor@nmanet.org. You will receive notification of your test results with in one month. If you have successfully completed the test (seven or more correct answers), you will receive via fax, a certificate for one credit hour in category 1 of the Physician's Recognition Award or one Prescribed AAFP credit hour. There is no fee for participating in this CME activity.

1. Antidiuretic hormone assists in the regulation of water content within the extracellular space.
A. True B. False

2. Common causes of hyponatremia in elderly with decreased total body sodium are:
A. Thiazide diuretics
B. Low solute intake
C. SIADH
D. Psychogenic polydipsia
E. B, C and D
F. A and B

3. Correction of the underlying problem and restriction of free water intake to 1 liter per day is usually sufficient to normalize the serum sodium level in asymptomatic elderly patients with no evidence of volume depletion (e.g. SIADH).
A. True B. False

4. Rapid sodium correction has been reported to induce severe neurologic complications including cerebral edema progressing to permanent brain damage.
A. True B. False

5. An important step in evaluation of hyponatremia is the measurement of:
A. Urine anion gap
B. Serum osmolality
C. Serum vasopressin levels
D. None of the above

6. Common causes of hyponatremia with normal total body sodium in elderly include:
A. SIADH
B. Hypothyroidism
C. Glucocorticoid deficiency
D. Psychogenic polydipsia
E. All of the above

7. Chronic hyponatremia secondary to SIADH and refractory to free water restriction can best be treated with:
A. Identification and correction of underlying problem
B. Oral demeclocycline
C. Lithium
D. Subcutaneous Vasopressin
E. A and B
F. A and D

8. A common cause of hypernatremia in hospitalized elderly and nursing home residents is decreased access to free water:
A. True B. False

9. In elderly patients with hypernatremia the serum sodium level should not be lowered more rapidly than 0.5mEq/l/hr.
A. True B. False

10. Excessively rapid correction of hypernatremia may lead to osmotic demyelination syndrome.
A. True B. False

Look for answers to this quiz in the next issue of *JNMA*.

past, as it also induces a renal tubular resistance to ADH, the risk of clinical side effects is too great to recommend it as a standard therapeutic option.

Hypernatremia

Hypernatremia is not uncommon at the extremes of age and is particularly prevalent among the elderly. A serum sodium level of 150 meq/l or greater should be considered clinically significant. The prevalence of hypernatremia in the elderly has been reported to be about 1% in both hospitalized patients and in residents of long-term care facilities.[1,2] Since the percentage of body water falls with age, equal volumes of fluid loss in older individuals may represent more severe dehydration than in younger individuals.[30] In healthy older men compared to younger controls, there are deficits in both the intensity and threshold of the thirst response,[14-16] compared to younger controls. As mentioned earlier, the ability of the elderly to conserve water is also impaired. In the elderly, hypernatremia carries a high risk of morbidity and mortality ranging from 40–60%.[30] Although mortality rate was highest in those with a rapid onset and those with serum sodium level >160 meq/L, a slow correction of serum sodium over a 72-hour period was reported to improve recovery of mental functions.[29,30] Several common causes of hypernatremia in the elderly are shown (Table 4).

In many studies, dehydration is defined as a deficit in water (manifested as hypernatremia) and is commonly confused with hypovolemia, which is defined as a reduction in intravascular volume, independent of a change in the serum sodium.[7] Dehydration associated with hypernatremia or hyponatremia is common in older individuals. In one study, dehy-

Evaluation

The program evaluation below must be completed to process your exam. Your responses to the following questions will have no effect on the grading or results of the CME quiz.

1. Rate the accuracy and timeliness of the article's content.
A. Excellent B. Good C. Satisfactory D. Poor

Rate the relevance of the topic to your daily practice.
A. Excellent B. Good C. Satisfactory D. Poor

Rate the relevance of the content to the learning objectives.
A. Excellent B. Good C. Satisfactory D. Poor

4. Rate the effectiveness of the teaching method.
A. Excellent B. Good C. Satisfactory D. Poor

Rate the objectivity and lack of commercial bias found in this article.
A. Excellent B. Good C. Satisfactory D. Poor

Rate the impact this CME activity had on your professional knowledge or attitude about this topic.
A. Excellent B. Good C. Satisfactory D. Poor

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dration occurred in approximately 7% of hospitalizations among patients older than 65 years of age and was associated with significant morbidity.[31]

Symptoms and Signs of Hypernatremia

Nonspecific lethargy and weakness are common. Obtundation, stupor, coma and seizures may accompany more severe hypernatremia. Clinical signs include decreased skin turgor, dry mouth, orthostatic hypotension, absent sweating and hemoconcentration. In rare cases, hyperosmolality may lead to shrinkage of brain volume, capillary hemorrhage or spontaneous subtotal hematoma, resulting in permanent neurological deficits.

Therapy for Hypernatremia

The treatment is based on the etiology of the hypernatremia and the estimated rapidity of development. Hypernatremic patients may have low, high or normal total body sodium. Hypovolemic hypernatremia is a much more common entity. These patients may have evidence of ECF volume depletion and have sustained water losses that are greater than the sodium losses. On the other hand, hypernatremic patients may have evidence of ECF expansion. These are invariably patients who have received excessive amounts of hypertonic NaCl or sodium bicarbonate. This variety of hypervolemic hypernatremia is rather infrequent. Most patients with hypernatremia secondary to water loss appear clinically euvolemic with near-normal total-body sodium status on physical examination. Hypernatremia usually occurs only in those who have no access to water. The renal losses of water that lead to euvolemic hypernatremia are a consequence of a defect in vasopressin production or release, or a failure of the collecting duct to respond to vasopressin.

When hypernatremia is associated with ECF depletion, the primary therapeutic goal is to administer isotonic saline or volume expanders to improve blood pressure and end-organ perfusion. Including projected insensible loss, the estimated water deficit should be replaced over 48–72 hours. The calculation of the water deficit is described in Table 3. Hypotonic (0.45%) NaCl or 5% glucose solutions can be used to correct serum osmolality, once intravascular volume is replete.

By contrast, if hypernatremia is secondary to ECF volume expansion, diuretics (furosemide) can be used—but in the presence of advanced renal failure and fluid overload the patient may need to be dialyzed to treat hypernatremia. For euvolemic hypernatremic patients, oral water replacement is preferred if the patient is alert and cooperative. If oral fluids cannot be given, an intravenous infusion of dextrose in water is appropriate. An older person who does not have ongoing renal water losses can usually be treated with an infusion of 5% dextrose in water at a rate of 25 ml/hr over two-to-three days for each 5 meq/L increase in serum sodium. Serum electrolytes should be monitored at least daily and more frequently if the patient is severely ill, so adjustments in therapy can be made accordingly. Serum sodium level should be lowered no more rapidly than 0.5 mEq/L/hr. Excessively rapid correction may lead to cerebral edema that can progress to permanent brain injury. Vasopressin replacement is required for the treatment of central diabetes insipidus.

CONCLUSION

In summary, hypo- and hypernatremia are common in older individuals and are usually successfully treated if approached correctly. Acutely ill elderly are at greater risk for the development of marked derangements in sodium and water balance that delay recovery, prolong hospitalizations and adversely affect outcomes. A greater understanding of the changes in renal physiology and the related neurohormonal responses that occur with aging can help guide the clinician toward a more timely and appropriate response to sodium disorders in the elderly.

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