Emergency Management of Salt and Water Disturbances in the Elderly

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Fluid and electrolyte disturbances are prevalent in the elderly. In a retrospective review of discharge diagnoses from the California hospital database, there is a progressive increase in the prevalence of acid-base and electrolyte disturbances with advancing age. Hyponatremia and hypokalemia were the most common disturbances, followed by hyperkalemia and hypernatremia.[1] The kidneys modulate and maintain the volume and composition of the extracellular fluid (ECF). Several anatomic and physiologic changes in the aging kidneys impair their ability to respond promptly and appropriately to changes in the volume and composition of the ECF and predispose the elderly to fluid and electrolyte disturbances with a significant impact on clinical outcomes in this population. This article highlights some of the age-related structural and functional changes in the kidneys and their probable roles in the pathophysiology of salt and water disturbances in the elderly.

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Structural and Functional Changes in the Aging Kidneys

The kidneys are a paired organ composed of about a million nephrons each, and together they receive about 25% of the total resting cardiac output. There is a progressive decrease in the number of nephrons and renal blood flow with an increase in age,[2-6] which culminates in an average decline of about 1% per year (10% per decade) in glomerular filtration rate (GFR) after age 40.[4,7]

This fall in GFR is not usually reflected in the serum creatinine due to a proportional reduction in muscle mass and endogenous creatinine production,[8] but it can be estimated using the Cockcroft and Gault formula (Table I).[9] The formula adjusts for weight, age, and gender, and is commonly used in clinical practice. For example, a serum creatinine of 1.2 mg/dL in a 20-year-old 80-kg man reflects a GFR of 111 mL/min, whereas a serum creatinine of 1.2 mg/dL in a 70-year-old 60-kg woman reflects a GFR of 41 mL/min, a nearly threefold difference. Adequate renal function is crucial for the maintenance of the volume and composition of the ECF. Age-related changes in both renal function and the renal response to neurohormonal homeostatic mechanisms (discussed in more detail herein) responsible for maintenance of the volume and composition of the ECF predispose the elderly to abnormalities of sodium and water.

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Water Metabolism

Water is the most abundant constituent of the human body, accounting for about 60% of the body weight. Two-thirds of the body water exists in the intracellular fluid (ICF), where-

as one-third exists in the ECF.[10] Antidiuretic hormone (ADH), a polypeptide produced by the neurohypophysis, maintains the osmolality of the ECF by modulating the water content in this compartment. Although multiple variables influence the secretion of ADH, under normal physiologic conditions, the most important modulator of ADH secretion is the plasma osmolality.[11] ADH stimulates thirst and acts on the renal collecting duct to increase water permeability, promotes water reabsorption, and produces urine with low volume and high osmolality. Poor perception of thirst,[12] as well as impaired ability of the renal tubules to concentrate and dilute urine,[13] predisposes the elderly to abnormalities of water homeostasis. Whereas healthy young adults can attain a maximum urinary concentration of 1,200 mOsm/kg and dilute urine to about 50 mOsm/kg, comparable healthy but elderly persons rarely achieve urine osmolality in excess of 700 to 800 mOsm/kg and cannot dilute urine to less than 100 mOsm/kg.[14,15] These disturbances in renal free-water clearance affect water content in the ECF and are reflected as abnormalities of sodium concentration in the ECF.

TABLE I

Cockcroft and Gault Formula for Estimating Glomerular Filtration Rate (GFR)

$$\text{Estimated GFR (mL/min)}^{*} = \frac{(140 - \text{age in years}) \times \text{lean body mass in kg}}{72 \times \text{serum creatinine (mg/dL)}}$$

*(x 0.85 for women)

Sodium Metabolism

Sodium is the most abundant cation in the ECF. Its content to a large extent determines the ECF volume. Appropriate renal response to volume and hormonal changes associated with abnormalities of sodium and water homeostasis is essential for the maintenance of the ECF volume. Aldosterone, an adrenal mineralocorticoid stimulated by the renin angiotensin system (RAS) in response to ECF volume depletion, acts on the kidneys to enhance sodium reabsorption, whereas atrial natriuretic peptide (ANP), a polypeptide released primarily from the atria in response to ECF volume expansion, acts on the kidneys to enhance sodium excretion. The aging kidneys exhibit an impaired ability to conserve sodium in response to sodium deprivation and to excrete sodium in response to sodium loading. Indeed, a doubling of the half-time for reduction of urinary sodium after salt restriction has been reported in older subjects.[16] The progressive nephron loss with aging, coupled with age-related reductions in renin and aldosterone levels[17] and diminished renal response to ANP,[18] impairs the ability of the kidneys to respond promptly and appropriately to large changes in sodium intake and output.

Hyponatremia

Normal serum sodium ranges between 135 and 145 mEq/L. Whereas a serum sodium below 135 mEq/L establishes the diagnosis of hyponatremia, values below 130 mEq/L are clinically significant. Hyponatremia is one of the most common electrolyte disorders in the elderly, resulting in part from the attenuated response of the aging kidney to sodium deficiency, a diminished diluting capacity, and an impaired ability to excrete free water. Hyponatremia is associated with hypo-osmolarity and can be categorized on the basis of clinical assessment into one of three groups: hyponatremia with ECF volume depletion, hyponatremia with normal ECF volume, and hyponatremia with ECF volume excess. Hyponatremia with ECF volume depletion in the elderly is most commonly due to diuretic therapy, poor oral intake, or both. Other less common causes in the elderly are listed in Table II. Hyponatremia with normal ECF volume is often related to the syndrome of inappropriate ADH secretion (SIADH). Medications that lead to an excess secretion of vasopressin or enhance renal tubular responsiveness to circulating vasopressin should be sought (Table III), and the diagnoses of hypothyroidism and glucocorticoid deficiency should be excluded before the diagnosis of SIADH is entertained in the elderly. SIADH in the elderly should prompt an investigation for a central nervous system (CNS) disorder, malignancy, or abnormal pulmonary processes. No apparent underlying disease may be found in up to a quarter of elderly with SIADH, suggesting that aging itself is a possible risk factor for the development of an idiopathic SIADH-like hyponatremia.[19] Finally, hyponatremia with ECF volume excess is seen in edematous states with low renal perfusion and secondary increases in ADH such as in cirrhosis, nephrosis, and congestive heart failure (CHF).

Clinical manifestations

The signs and symptoms of hyponatremia depend on the magnitude and rate of development and may range from asymptomatic to overt CNS manifestations such as lethargy, confusion, seizures, coma, and death. Some of these signs and symptoms may be subtle and atypical in the elderly. For reasons yet unclear, aging and male gender may confer protection against the development of hyponatremia-associated seizures and permanent brain damage.[20]

TABLE II

Common Causes of Hyponatremia in the Elderly

Thiazide diuretics (up to 50% of cases)
Hypotonic intravenous fluids
SIADH: pulmonary disorders, central nervous system disorders, idiopathic
Edematous states: congestive heart failure, cirrhosis of liver, nephrotic syndrome
Low solute intake: tea-toast diet, low osmolar tube feeding
Miscellaneous: Addison's disease, hypothyroidism, glucocorticoid deficiency, psychogenic polydipsia, drugs affecting vasopressin

SIADH = syndrome of inappropriate antidiuretic hormone secretion.

Emergency treatment

The treatment and urgency of therapy of hyponatremia depend on the pathogenesis of the hyponatremia and the severity of symptoms. A low serum sodium level in a symptomatic volume-depleted patient requires emergent therapy and should be corrected with normal saline infusion. A rough guide for treatment would include the initiation of normal saline at 75 to 100 cc/hr (should raise sodium by 0.3 to 0.4 mEq/hr), with monitoring of serum sodium one to two times daily in cases with mild hyponatremia and every four to six hours in more severe cases. Correction of serum sodium at a rate greater than 0.5 mEq/hr has been associated with severe neurologic complications including central pontine myelinolysis.[21] Saline infusion in the elderly must be cautious so as not to induce volume overload and precipitate pulmonary edema. In cases of severe volume depletion, however, more rapid rates of infusion are indicated. In asymptomatic volume-repleted patients, the correction of the underlying problem and restriction of free water intake to 1 L daily is usually sufficient to normalize the serum sodium. In cases of SIADH refractory to free water restriction, 300 mg of demeclocycline 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. Edematous patients with clinical evidence of ECF volume excess can be managed on bed rest with water restriction and diuretic therapy, preferably with furosemide (20 to 40 mg twice daily), which induces hypotonic urine generating a negative free water balance.

TABLE III

Medications That Can Influence ADH Secretion and Affect Water Metabolism in Elderly

Nicotine*
Morphine (high dose)*
Epinephrine*
Cyclophosphamide*
Tolbutamide**
Chlorpropamide**
NSAIDs**
Alcohol#
Morphine (low dose)#
Clonidine#
Glucocorticoids#
Haloperidol#
Cisplatin#
Carbamazepine#
Lithium+
Colchicine+
Demeclocycline+
Glyburide+
Loop diuretics+
Vinblastine+
Methoxyflurane+

**Enhances ADH secretion.*
***Increases tubular responsiveness.*
#Reduces ADH secretion.
+Diminishes renal tubular responsiveness.
ADH = antidiuretic hormone; NSAIDs = nonsteroidal anti-inflammatory drugs.

HYPERNATREMIA

Hypernatremia is common at the extremes of age and is particularly prevalent among the elderly. A serum sodium above 145 mEq/L establishes the diagnosis of hypernatremia, but the disturbance assumes clinical significance when serum sodium exceeds 150 mEq/L. Some of the more common causes of hypernatremia in the elderly are shown in Table IV. With the exception of the rare patient with increased sodium intake,

TABLE IV

Etiology of Hypernatremia in the 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)	Sodium bicarbonate therapy
Physical impairment (limited water access)	Diabetes insipidus, hypercalcemia, hypokalemia	
	Chronic renal disease	

hypernatremia signals a free-water deficit. Because the percentage of body water falls with advancing age, equal volumes of fluid loss in older individuals represent relatively greater free-water deficit and place the elderly with hypernatremia at a higher risk for morbidity and mortality.[22]

Clinical manifestations

Nonspecific lethargy and weakness are common symptoms in patients with hypernatremia. Obtundation, stupor, coma, and seizures may accompany more severe hypernatremia. Clinical/laboratory signs commonly include decreased skin turgor, dry mouth, orthostatic hypotension, flat neck veins, absent sweating, and hemoconcentration. In severe cases, hyperosmolality may lead to shrinkage of brain volume, capillary hemorrhage, and spontaneous subdural hematoma resulting in permanent neurologic deficits.

Emergency treatment

The treatment of hypernatremia usually involves the replacement of free-water deficits with hypotonic fluid. Oral water replacement is preferred in asymptomatic patients who are alert and cooperative, but the route and rate are dependent on severity of the deficit. Urgent intravenous infusion (IV) of dextrose in water is indicated for symptomatic patients and those with poor oral intake. An older person 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 increase in serum sodium. Emergency therapy is indicated for hypernatremic patients with hypotension, and they should receive normal saline infusion to restore blood pressure and end-organ perfusion before the replacement of free-water deficits. The calculation of the water deficit is described in Table V. 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 insult. Potential underlying disorders should be diligently sought and corrected in all patients with hypernatremia.

TABLE V

Calculating Free-Water Excess and Deficit

Free-water excess = TBW - ([actual pNa/desired pNa] x TBW)

Free-water deficit = ([pNa -140]/140) x 0.6 body weight (kg)

TBW = total body water or body weight in kg x 0.6; pNa = plasma sodium in mEq/L.

POTASSIUM DISORDERS

Potassium is the main intracellular cation maintained within the cells by the Na-K ATPase pump. The ratio of the intracellular potassium concentration to the extracellular potassium concentration determines the resting membrane potential and plays a critical role in the generation of action potential that is essential for normal neuromuscular function. Normal serum potassium ranges between 3.5 and 5.0 mEq/L. Abnormalities of potassium homeostasis are not uncommon in the elderly. There is evidence to suggest that the age-related reduction in muscle mass is associated with a decrease in the total body potassium store.[23] The inability to maintain an adequate dietary potassium intake in a subset of the aging population and the use of diuretics for prevalent disorders like hypertension may further contribute to potassium reductions in the elderly. By contrast, the reductions in renal plasma flow and glomerular filtration rate associated with aging along with the impairment in beta-adrenergic modulation of transcellular

potassium fluxes[24] and the reduced activity of the renin-aldosterone system[25] predispose the elderly patient to hyperkalemia.

Clinical manifestations

Significant abnormalities in serum potassium levels affect the resting membrane potential and interfere with neuromuscular function. Nonspecific lethargy and weakness are common in patients with both hyperkalemia and hypokalemia. The electrocardiographic (ECG) changes associated with abnormalities of serum potassium are more specific and reliable. Prolonged PR interval, flattening or absence of P waves, tall and peaked T waves, widening of the QRS complex, and the presence of sine waves can be seen in patients with hyperkalemia. Prolonged QRS duration usually signals an impending life-threatening cardiac complication and should prompt emergent treatment. Cardiac complications in the elderly person may be associated with increased arrhythmias or sudden death, particularly in the presence of underlying or overt coronary artery disease.[26] By contrast, the ECG changes of hypokalemia include flattening of the T waves and the presence of U waves that may give a false impression of prolonged QT interval.

Emergency treatment

The ECG findings associated with abnormalities of serum potassium determine the treatment approach. Cation exchange resin therapy with sodium polystyrene sulfonate, a potassium-sodium exchange resin, or kaliuresis with a loop diuretic such as furosemide will remove potassium from the body and may suffice for patients with hyperkalemia and non-life-threatening ECG changes. With peaked T waves on the ECG, more vigorous therapy is indicated, that is, insulin and glucose infusion with or without beta$_2$-adrenergic agonist therapy to shift serum potassium into the cells while potassium-depleting therapies are instituted. Bicarbonate treatment is rarely indicated in elderly patients unless severe acidemia exists, as it is less effective than insulin therapy and the rapid sodium infusion may precipitate CHF. Emergency treatment is required in the presence of widened QRS complexes or sine wave pattern on the ECG and constitutes an indication for IV calcium therapy for cardiac membrane stabilization followed by vigorous efforts to increase both transcellular potassium shift and potassium removal from the body. Dialytic therapy may be necessary if renal insufficiency complicates efforts to achieve effective kaliuresis and timely potassium removal. The treatment for hypokalemia is potassium replacement (primarily potassium chloride), but the rate and route of replacement depend on the level of serum potassium. Oral potassium supplements (100 to 150 mEq in four divided daily doses for each 1 mEq fall in plasma potassium) will suffice for serum potassium levels between 2.5 and 3.5 mEq/L. IV replacement should be considered for serum potassium levels below 2.5 mEq/L. The rate of IV potassium should not exceed 10 mEq/hr (10 mEq potassium chloride in 100 cc dextrose [5%] in water at 100 cc/hr) without telemetry monitoring.

Conclusion

The subtlety of the early manifestations of sodium and water disturbances can predispose the elderly to the more severe and life-threatening complications. Undiagnosed and untreated disturbances in sodium and water homeostasis can also have serious implications for drug pharmacokinetics and further jeopardize disease outcome in the elderly. Early detection and treatment can prevent some of the serious complications of sodium and water disturbances. Although laboratory tests are required for specific diagnosis, they must often be ordered in anticipation of these disturbances, particularly in high-risk patients, for early diagnosis and treatment. Dietary counsel (primary care provider/dietitian) to patient and caregiver on fluid and electrolyte requirements can minimize the risk of salt and water disturbances in the elderly in an outpatient setting. Recommended daily allowances are difficult to define for the ambulatory elderly because of enormous differences in body size, activity, medication use, and disease profiling among the elderly. The counsel should provide information on the fluid and electrolyte properties of a wide range of beverages and tailor their use to the specific needs of individual patients. This can help prevent hospitalizations or reduce the severity of associated fluid and electrolyte disorders when an intercurrent illness requires acute hospital care.

References

1. Adetola A, Pan D, Martins D, Norris KC. Magnitude of acid-base and electrolyte disorders in the elderly. *Ethnicity Disease* 1999;9:479.
2. Moore RA. The total number of glomeruli in the normal human kidney. *Anat Rec* 1958;48:153-168.
3. Feinstein EI. Renal disease in the elderly. In: Rossman I, ed. *Clinical Geriatrics*, 3rd ed. Philadelphia, PA: Lippincott; 1986:215-220.
4. Davies D, Shock N. Age changes in glomerular filtration rate, effective renal plasma flow, and tubular excretory capacity in adult males. *J Clin Invest* 1950;29:496-507.
5. Brandfonbrener M, Landsdowne M, Shock NW. Changes in cardiac output with age. *Circulation* 1955;12:557-565.
6. Hollenberg NK, Adams DF, Solaman HS, et al. Senescence and the renal vasculature in normal man. *Circ Res* 1974;34:309-316.
7. Rowe JW, Andres R, Tobin JD, et al. The effect of age on creatinine clearance in men: A cross-sectional and longitudinal study. *J Gerontol* 1976;31(2):155-163.
8. Wolser M. Creatinine excretion as a measure of protein nutrition in adults of varying age. *JPEN* 1987;11:73S-78S.
9. Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. *Nephron* 1976;16:31-41.
10. Edelman IS, Leibman J. Anatomy of body water and electrolytes. *Am J Med* 1959;27:256-277.
11. Robertson GL. Thirst and vasopressin function in normal and disordered states of water balance. *J Lab Clin Med* 1983;101(3):351-371.
12. Phillips PA, Rolls BJ, Ledingham JG, et al. Reduced thirst after water deprivation in healthy elderly men. *N Engl J Med* 1984;311(12):753-759.
13. Lewis W, Alving A. Changes with age in the renal function in adult men. *Am J Physiol* 1938;123:500-515.
14. Rowe J, Shock N, DeFronzo R. The influence of age on the renal response to water deprivation in man. *Nephron* 1976;17:270-278.
15. Crowe MJ, Forsling ML, Rolls BJ, et al. Altered water excretion in healthy elderly man. *Age Ageing* 1987;16(5):285-293.
16. Epstein M, Hollenberg N. Age as a determinant of renal sodium conservation in normal man. *J Lab Clin Med* 1976;87:411-417.
17. Holl JE, Coleman TG, Guyton AC. The renin-angiotensin system: Normal physiology and changes in older hypertensives. *J Am Geriatr Soc* 1989;37:801-813.
18. Clark BA, Elahi D, Shannon RP, et al. Influence of age and dose on the end-organ responses to atrial natriuretic peptide in humans. *Am J Hypertens* 1991;4(6):500-507.
19. Miller M, Carter JM, Friedlander DA, Hecker MS. Apparent idiopathic hyponatremia in an ambulatory geriatric population. *J Am Geriatr Soc* 1996;44:404-408.
20. Arieff AI, Kazniewska E, Roberts TP, et al. Age, gender, and vasopressin affect survival and brain adaptation in rats with metabolic encephalopathy. *Am J Physiol* 1995;268(5 pt 2):R1143-R1152.
21. Sterns RH. Severe symptomatic hyponatremia: Treatment and outcome. *Ann Intern Med* 1987;107:656-664.
22. Borra SI, Kleinfeld M, Bereda R. Hypernatremia in the aging: Causes, manifestations, and outcome. *J Natl Med Assoc* 1995;87(3):220-224.
23. Allen TH, Anderson EC, Langham WH. Total body potassium and gross body composition in relation to age. *J Gerontol* 1960;15:348-357.
24. Ford GA, Blaschke T, Wiswell R, Hoffman B. Effect of aging on changes in plasma potassium during exercise. *J Gerontol* 1993;48:M140-M145.
25. Mulkerrin E, Clark BA, Epstein FH. Aldosterone responses to hyperkalemia in healthy elderly humans. *J Am Soc Nephrol* 1995;6(5):1459-1462.
26. Cohen JD. Abnormal electrocardiograms and cardiovascular risk: Role of silent myocardial ischemia: Evidence from MRFIT. *Am J Cardiol* 1992;70(16):14F-18F.