Hyponatremia

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Hyponatremia

Classification and external resources

Sodium

ICD-10	E87.1
ICD-9	276.1
DiseasesDB	6483
MedlinePlus	000394
eMedicine	emerg/275 med/1130ped/1124
MeSH	D007010

Hyponatremia (American English) or **hyponatraemia** (British English) is an electrolyte disturbance in which the sodium concentration in the serumis lower than normal. (Hypo = low; natraemia = sodium in blood) Sodium is the dominant extracellular cation and cannot freely cross the cell membrane. Its homeostasis is vital to the normal physiologic function of cells. Normal serum sodium levels are between 135 and 145 mEq/L. Hyponatremia is defined as a serum level of less than 135 mEq/L and is considered severe when the serum level is below 125 mEq/L.[1]

In the vast majority of cases, hyponatremia occurs as a result of excess body water diluting the serum sodium.

Hyponatremia is most often a complication of other medical illnesses in which excess water accumulates in the body at a higher rate than can be excreted (for example in congestive heart failure, syndrome of inappropriate antidiuretic hormone, SIADH, or polydipsia). Sometimes it may be a result of overhydration.

Lack of sodium is virtually never the cause of hyponatremia, although it can promote hyponatremia indirectly. In particular, sodium loss can lead to a state of volume depletion, with volume depletion serving as signal for the release of ADH (anti-diuretic hormone). As a result of ADH-stimulated water retention, blood sodium becomes diluted and hyponatremia results.

Exercise-associated hyponatremia (EAH), however, is not uncommon. Researchers found, for instance, that 13% of the athletes who finished the 2002 Boston Marathon were in a clinically hyponatremic condition.

Contents

[hide]

[edit]Signs and symptoms

Symptoms of hyponatremia include nausea and vomiting, headache, confusion, lethargy, fatigue, appetite loss, restlessness and irritability, muscle weakness, spasms, or cramps, seizures, and decreased consciousness or coma. The presence and severity of symptoms are associated with the level of serum sodium, with the lowest levels of serum sodium associated with the more prominent and serious symptoms. However, emerging data suggest that mild hyponatremia (serum sodium levels at 131 mEq/L or above) is associated with numerous complications and undiagnosed symptoms.[2]

Many medical illnesses, such as congestive heart failure, liver failure, renal failure, or pneumonia may be associated with hyponatremia. These patients frequently present because of primary disease symptomatology and are diagnosed after presenting due to manifestations of other medical issues.

Neurological symptoms often show for extremely low levels of sodium. When sodium levels in blood become too low, excess water enters cells and causes the cells to swell. Swelling in the brain is especially dangerous because the brain is confined by the skull and is unable to expand. The disorder in the brain caused by hyponatremia is called *hyponatremic encephalopathy*, and accounts for symptoms such as headache, nausea, vomiting and confusion, but can also present with seizures, respiratory arrest and non-cardiogenic pulmonary edema.[3] Neurological symptoms most often are due to very low serum sodium levels (usually <115 mEq/L), resulting in intracerebral osmotic fluid shifts and brain edema. This neurological symptom complex can lead to tentorial herniation with subsequent brain stem compression and respiratory arrest, resulting in death in the most severe cases. The severity of neurological symptoms correlates with the rapidity and severity of the drop in serum sodium. A gradual drop, even to very low levels, may be tolerated well if it occurs over several days or weeks, because of neuronal adaptation. The presence of underlying neurological disease, like a seizure disorder, or non-neurological metabolic abnormalities, also affects the severity of neurologic symptoms.

[edit]Causes

Based on the above classification, some of the many specific causes of hyponatremia can be listed as follows:

Hypervolemic hyponatremia - both sodium & water content increase, but the water gain is greater

- cirrhosis
- congestive heart failure
- nephrotic syndrome
- massive edema of any cause

Euvolemic hyponatremia - total body water increases, but the body's sodium content stays the same

- states of severe pain or nausea
- in the setting of trauma or other damage to the brain
- SIADH (and its many causes)
- Hypothyroidism
- Glucocorticoid deficiency

Hypovolemic hyponatremia - water & sodium are both lost from body, but the sodium loss is greater

- any cause of hypovolemia such as prolonged vomiting, decreased oral intake, severe diarrhea
- diuretic use (due to the diuretic causing a volume depleted state and thence ADH release, and not a direct result of diuretic-induced urine sodium loss)

Miscellaneous causes of hyponatremia that are not included under the above classification scheme include:

- factitious hyponatremia (due to massive increases in blood triglyceride levels, extreme elevation of immunoglobulins as may occur in multiple myeloma, and extreme hyperglycemia)
- hypothyroidism and adrenal insufficiency (both thyroid hormone and cortisol are required to excrete free water)
- beer potomania and other malnourished states where poor dietary protein intake leads to inadequate urine solute formation thereby impeding the kidney's ability to excrete free water
- primary polydipsia (where the amount of urine solute required to excrete huge quantities of ingested water exceeds the body's ability to produce it; this typically occurs when 12 or more litres of water are ingested per day)
- Addison's disease in which the adrenal glands do not produce sufficient steroid hormones (glucocorticoids and often mineralocorticoids)

[edit]Diagnosis

Examination should include orthostatic vital signs and an accurate assessment of volume status. This determination (i.e. hypervolemic, euvolemic, hypovolemic) often guides treatment decisions. A full assessment of medical comorbidity also is essential, with particular attention paid to cardiopulmonary and neurological components of the examination.

[edit]Pathophysiology

The etiology of hyponatremia can be categorized pathophysiologically in three primary ways, based on the patient's plasma osmolality.

Hypertonic hyponatremia, caused by resorption of water drawn by osmols such as glucose (hyperglycemia or diabetes) or mannitol (hypertonic infusion).

Isotonic hyponatremia, more commonly called "pseudohyponatremia," is caused by lab error due to hypertriglyceridemia (most common) or hyperparaproteinemia.

Hypotonic hyponatremia is by far the most common type, and is often used interchangeably with "hyponatremia." Hypotonic hyponatremia is categorized in 3 ways based on the patient's blood volume status. Each category represents a different underlying reason for the increase in ADH that led to the water retention and thence hyponatremia:

- ***Hypervolemic hyponatremia***, wherein there is decreased effective circulating volume even though total body volume is increased (by the presence of edema). The decreased effective circulating volume stimulates the release of ADH, which in turn leads to water retention. Hypervolemic hyponatremia is most commonly the result of congestive heart failure, liver failure (cirrhosis), or kidney disease (nephrotic syndrome).

- ***Euvolemic hyponatremia***, wherein the increase in ADH is secondary to either physiologic but excessive ADH release (as occurs with nausea or severe pain) or inappropriate and non-physiologic secretion of ADH, i.e. syndrome of inappropriate antidiuretic hormone hypersecretion (SIADH). Often categorized under euvolemic is hyponatremia due to inadequate urine solute as occurs in beer potomania or "tea and toast" hyponatremia, hyponatremia due

to hypothyroidism or adrenal insufficiency, and those rare instances of hyponatremia that are truly secondary to excess water intake (i.e., extreme psychogenic polydipsia)

- ***Hypovolemic hyponatremia***, wherein ADH secretion is stimulated by volume depletion.

The volemic classification fails to include spurious and/or artifactual hyponatremia, which is addressed in the osmolar classification. This includes hyponatremia that occurs in the presence of massive hypertriglyceridemia, severe hyperglycemia, and extreme elevation of immunoglobulin levels.

In ***chronic hyponatremia***, sodium levels drop gradually over several days or weeks and symptoms and complications are typically moderate. Chronic hyponatremia is often called asymptomatic hyponatremia in clinical settings because it is thought to have no symptoms; however, emerging data suggests that "asymptomatic" hyponatremia is not actually asymptomatic.[2]

In ***acute hyponatremia*** sodium levels drop rapidly, resulting in potentially dangerous effects, such as rapid brain swelling, which can result in coma and death.

[edit]Treatment

The treatment of hyponatremia will depend on the underlying cause and whether the patient's volume status is hypervolemic, euvolemic, or hypovolemic. In the setting of hypovolemia, intravenous administration of normal saline may be effective, but caution must be exercised not to raise the serum sodium level too quickly (see below). Euvolemic hyponatremia is usually managed by fluid restriction and treatment to abolish any stimuli for ADH secretion such as nausea. Likewise, drugs causing SIADH should be discontinued if possible. Patients with euvolemic hyponatremia that persists despite those measures may be candidates for a so-called vaptan drug as discussed below. Hypervolemic hyponatremia should be treated by treating the underlying cause (e.g. heart failure, cirrhosis). In practice, it may not be possible to do so, in which case the treatment of the hyponatremia becomes the same as that for euvolemic hyponatremia (i.e. fluid restriction and/or use of a vaptan drug).

Hyponatremia must be corrected slowly in order to lessen the chance of the development of central pontine myelinolysis (CPM), a severe neurological disease. In fact, overly rapid correction of hyponatremia is the most common cause of that potentially devastating disorder.[4] During treatment of hyponatremia, the serum sodium should not be allowed to rise by more than 8 mmol/l over 24 hours (i.e. 0.33 mmol/l/h rate of rise). In practice, too rapid correction of hyponatremia and thence CPM is most likely to occur during the treatment of hypovolemic hyponatremia. In particular, once the hypovolemic state has been corrected, the signal for ADH release disappears. At that point, there will be an abrupt water diuresis (since there is no longer any ADH acting to retain the water). A rapid and profound rise in serum sodium can then occur. Should the rate of rise of serum sodium exceed 0.33 mmol/l/h over several hours, vasopressin may be administered to prevent ongoing rapid water diuresis.[5]

Pharmaceutically, vasopressin receptor antagonists can be used in the treatment of hyponatremia, especially in patients with SIADH, congestive heart failure or liver cirrhosis. A vasopressin receptor antagonist is an agent that interferes with the action at the vasopressin receptors. A new class of medication, the "vaptan" drugs has been specifically developed to inhibit the action of vasopressin on its receptors (V1A, V1B, and V2). These receptors have a variety of functions, with the V1A and V2 receptors are expressed peripherally and involved in the modulation of blood pressure and kidney function respectively, while the V1A and V1B receptors are expressed in the central nervous system. V1A is expressed in many regions of the brain, and has been linked to a variety of social behaviors in humans and animals.

[edit]Vaptan drugs

The “vaptan” class of drugs contains a number of compounds with varying selectivity, several of which are either already in clinical use or in clinical trials as of 2010.

Unselective (mixed V1A, V2)

- Conivaptan

V1A selective

- Relcovaptan

V1B selective

- Nelivaptan

V2 selective

- Lixivaptan
- Mozavaptan
- Satavaptan
- Tolvaptan

The V2-receptor antagonists tolvaptan and conivaptan allow excretion of electrolyte free water and are effective in increasing serum sodium in euvolemic and hypervolemic hyponatremia.[6]

[edit]Complications

Chronic hyponatremia can lead to such complications as neurological impairments. These neurological impairments most often affect gait and attention and can lead to falls, osteoporosis, and decreased reaction time.

Complications for chronic hyponatremia are most dangerous for geriatric patients. Falls are the leading cause of deaths related to injury among people 65 years or older. In a recent study[7] the incidence of hyponatremia in elderly patients with large-bone fractures was more than double that of non-fracture patients. Recent work by Verbalis *et al.*[8] suggests that hyponatremia induces osteoporosis and found the adjusted odds ratio for developing osteoporosis to be 2.87 times higher among adults with mild hyponatremia compared to those without.

Acute hyponatremia can lead to much more serious complications including brain disease, brain herniation, cardiopulmonary arrest, cerebral edema, seizures, coma, and death.

[edit]Epidemiology

Hyponatremia is the most common electrolyte disorder. Its frequency is higher in females, the elderly, and in patients who are hospitalized. The incidence of hyponatremia depends largely on the patient population. A hospital incidence of 15–20% is common, while only 3–5% of patients who are hospitalized have a serum sodium level of less than 130 mEq/L. Hyponatremia has been reported in up to 30% of elderly patients in nursing homes and is also present in approximately 30% of depressed patients on selective serotonin reuptake inhibitors.[2]

[edit]In other animals

Sodium deficiency exists in grazing animals where soil sodium levels have been depleted by leaching. This is more common in mountainous regions. Agricultural science research conducted in the northern Thai highlands in the 1970s found that an endemic sodium deficiency masked all other nutrient deficiencies across all seasons and reduced productivity. Sodium supplementation increased liveweight gain by around 30% and also reproductive rates by around 30%. Simple salt supplementation is now recommended in this region and neighboring mountains, as both a herd management tool and for increased productivity.[9]

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