Introduction to Clinical Medicine - Sodium Disorders

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Disorders of sodium concentration in body fluids are another common clinical electrolyte disturbance.

In most cases, hyponatremia and hypernatremia are silent and are not detected until serum electrolytes are measured. However, hyponatremia can be cause seizures, decreased mental status and death. Hypernatremia can be associated with diffuse or localized CNS disease.

Determining the appropriate treatment requires an accurate diagnosis. Both the failure to treat rapidly enough and treating too rapidly can result in irreversible CNS damage or death.

Hyponatremia

Hyponatremia causes clinical effects because of changes in cell volume. Sodium is the major solute in extracellular fluids. As a result, changes in extracellular sodium concentration cause changes in extracellular osmolality, which is equivalent to a change in the extracellular [H_2O]. Because water is permeable across cell membranes, cells are unable to maintain differences between extracellular and intracellular osmolality.

> Decreasing extracellular sodium concentration (hyponatremia) decreases extracellular osmolality, equivalent to increasing extracellular [H_2O]. Extracellular [H_2O] is then greater than intracellular [H_2O], resulting in H_2O entry into cells. H_2O entry continues until the cell has swollen sufficiently that intracellular osmolytes are sufficiently diluted that intracellular osmolality is now the same as extracellular osmolality.
>
> This is the acute, short-term effect of hyponatremia.
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> With longer term hyponatremia, the cells recognize that they are swollen, and that they wish to return to their normal size. They will activate transporters that extrude intracellular ions, decreasing intracellular osmolality, and causing a reversal of the movement of water. With time (days) cell volume will return to normal.
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> Short-term hyponatremia is associated with cell swelling, whereas longer-term hyponatremia is not. Cell swelling causes its most important effects in the brain, because of the lack of room available for swelling inside the fixed cranium.
>
> Hypernatremia has the opposite effects. Most important, acute hypernatremia causes cell shrinkage.

Critical point: Extracellular sodium concentration is not the same as total body sodium content. Plasma sodium concentration is the amount of extracellular sodium divided by the amount of extracellular water.

Hyponatremia occurs either because of:

a. Decreased amounts of extracellular sodium and water, but extracellular water content is less decreased (hypovolemic),

b. Normal amounts of extracellular sodium with a slightly increased amount of extracellular water (euvolemic),

c. Increased amounts of extracellular sodium and water, but extracellular water content is increased even more (hypervolemic).

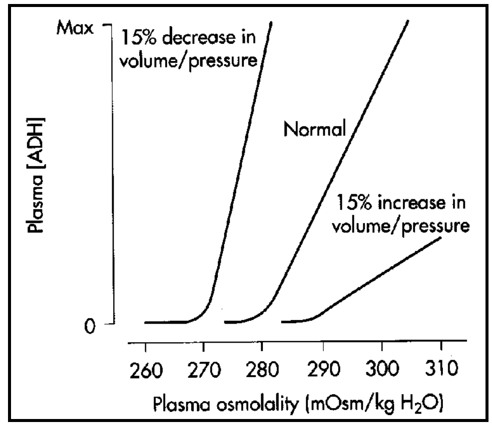

Figure 1. Interaction between osmotic and hemodynamic stimuli for ADH release.

Because the amount of extracellular water is the same as extracellular fluid volume, assessment of extracellular fluid volume identifies whether the patient is hypovolemic, euvolemic or hypervolemic.

Figure 2 shows how this can be used to identify the cause of hyponatremia.

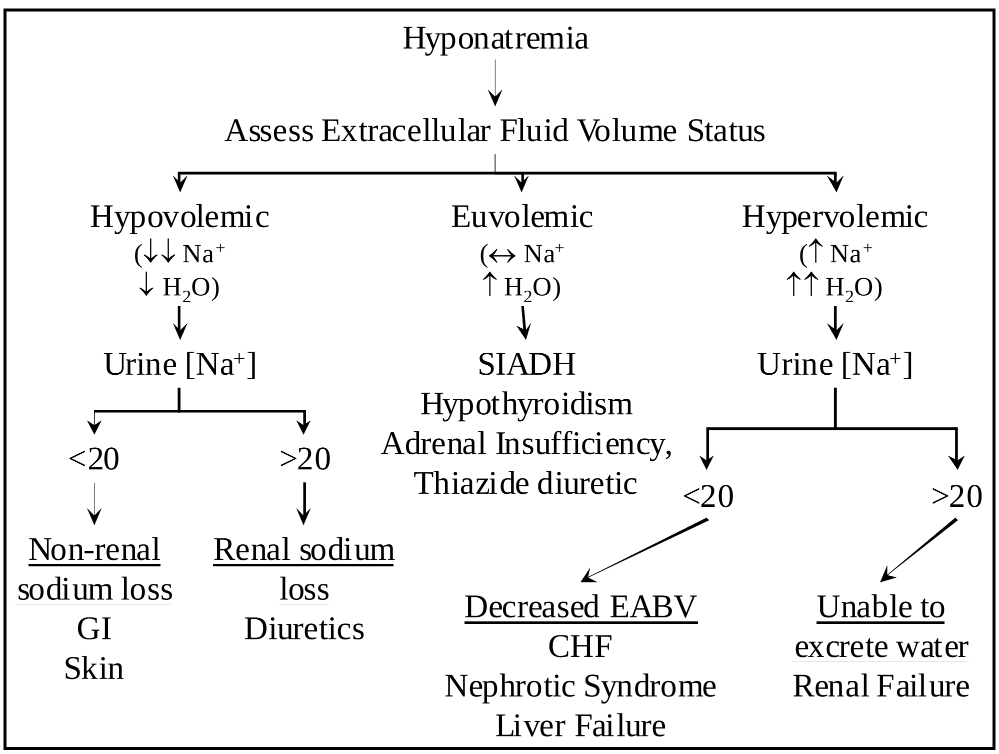

Figure 2. Evaluation of hyponatremia. Abbreviations: EABV, effective arterial blood volume; SIADH, Syndrome of Inappropriate ADH secretion; CHF, Congestive Heart Failure.

Treatment of these three conditions is based on treating their underlying causes.

Hypovolemic hyponatremia occurs when volume depletion is so severe that ADH release is stimulated due to baroreceptor stimulation. The treatment is replacement of the salt and water losses, generally with IV normal saline.

Euvolemic hyponatremia occurs when there is inappropriate ADH release (SIADH) or when the kidneys are unable to generate a dilute urine, most commonly due to hypothyroidism or adrenal insufficiency. These endocrine causes are treated by hormone replacement. SIADH is commonly related to either lung cancer, pain, surgery or vomiting. Until ADH antagonists become clinically available, the only treatment for SIADH is to restrict water intake to the point that water intake is less than renal water excretion, which then results in a decrease in extracellular water content and a slow increase in sodium concentration.

Hypervolemic (volume overloaded) hyponatremia most commonly occurs when the body senses a decreased effective arterial blood volume (EABV), despite total body fluid overload, that may be massive. Because a decreased blood volume is sensed, the kidneys attempt to increase blood volume by increasing sodium and water reabsorption, thereby decreasing urinary sodium and water excretion. Cardiac failure (CHF), nephrotic syndrome and liver failure are the most common causes. Treatment is treatment of the underlying condition. Water restriction, as described for SIADH, is also helpful.

The rapidity of treatment should depend on the rapidity of onset.

Acute hyponatremia causes cell swelling that may cause irreversible CNS damage. Rapidly increasing serum sodium to increase osmolality and thereby reverse swelling is necessary. Infusion of hypertonic saline is critical in this condition.

Chronic hyponatremia does not cause cell swelling. Rapidly increasing serum sodium would cause cell shrinkage, tearing of bridging veins in the CNS and development of an irreversible, debilitating neurologic condition known as central pontine myelinolysis (CPM). Chronic hyponatremia should be treated over days and, in general, should not be treated with hypertonic saline.

Hypernatremia

Hypernatremia occurs when there is a deficit of total body water in excess of any deficit in sodium. Because hypernatremia stimulates thirst through direct CNS effects, hypernatremia almost never occurs in the absence of either CNS disease or restrictions on the patient's access to water.

In almost all cases of hypernatremia, there is some cause of water loss in excess of sodium loss. Causes include:

2. Excess skin water loss (sweat, burns)
3. Hypotonic urine formation (osmotic diuresis, post-obstructive diuresis, non-oliguric ATN)
4. Water uptake into damaged cells (rhabdomyolysis)

5. **Failure of ADH production (central diabetes insipidus [cDI])**
6. **Failure of ADH to increase renal water reabsorption (nephrogenic DI [nDI]).**

Central DI will respond to ADH replacement. DDAVP is an ADH-like molecule that only activates the V2 (vasopressin type 2) receptor that is present in the kidney and platelets, and does not activate V1 receptors present in the vasculature.

If total body volume depletion is present, then this should be corrected first.

If severe, $[Na^+] > 150$, and total body volume depletion has been corrected, then provision of additional water may be needed. The water volume necessary to completely correct the hypernatremia ("free water deficit") is given in Formula 1.

$$\text{FWD (L)} = (0.6 \cdot \text{LBW}) \cdot \frac{([\text{Na}^+] - 140)}{140}$$

This formula is based on:

$$[\text{Na}^+]_1 \cdot V_1 = [\text{Na}^+]_2 \cdot V_2$$

Formula 1. Determination of free water deficit (FWD) in liters in hypernatremia. LBW - lean body weight in kg.

In general, ~25% of the free water deficit should be given in the first 8 hours, followed by an additional 25% over the next 16 hours, aiming for a 50% correction over 24 hours. The response should be assessed at that time and water replacement requirements redetermined.

Obviously, the fluid replacement should be given as "pure" water, without addition of sodium to the IV fluids.