hyponatraemia [created by Paul Young 16/12/07]

general

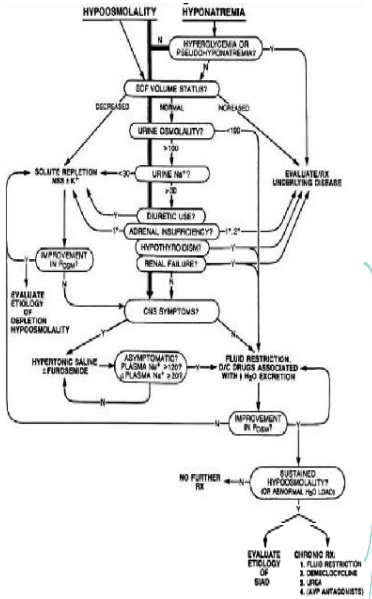
- Hyponatremia is a common electrolyte abnormality that varies greatly in its clinical presentation. It has been estimated that approximately 1% of hospitalised patients have acute symptomatic hyponatremia.
- The incidence of hyponatremia (<134 mmol/L) in the intensive care unit was prospectively found to be approximately 30%. The in-hospital mortality ratefor critical care patients with hyponatremia approaches 40%, and hyponatremia has been shown to be an independent predictor of mortality in the intensive care unit.
- Hyponatremia is generally categorized based on serum tonicity as isotonic, hypotonic, or hypertonic. Although most instances of hyponatremia in critical illness are associated with hypotonicity, isotonic and hypertonic hyponatremia are also well documented

hypertonic hyponatremia

- Hypertonic hyponatremia has also been termed translocational hyponatremia because the presence of osmotically active particles in the plasma induces an osmotic movement of water from the ICF to the ECF, decreasing serum sodium even though serum osmolality remains elevated. Solutes such as glucose, mannitol, sorbitol, or radiocontrast agents all exert this effect.

Corrected Na+ for glucose = [glucose 3] + apparent sodium

evaluation



sodium deficit = 0.6 x weight in kg x [Na desired - Na measured]

hypoosmolar hyponatraemia

general
- Hypotonic hyponatremia can occur as a result of solute depletion, a primary decrease in total body solute (often with secondary water retention), or solute dilution, a primary increase in total body water (often with secondary solute depletion)
- Hypotonic or hypoosmolar hyponatremia is generally subdivided according to the clinical ECF volume status. A recent retrospective analysis found the relative distributions of the types of hypotonic hyponatremia in the intensive care setting to be 24% hypervolemic, 26% hypovolemic, and 50% euvolemic.

*Solute depletion (primary decreases in total body solute plus secondary water retention)**
1. Renal solute loss
   - Diuretic use
   - Solute diuresis (glucose, mannitol)
   - Salt-wasting nephropathy
   - Mineralocorticoid deficiency
2. Nonrenal solute loss
   - Gastrointestinal (diarrhea, vomiting, pancreatitis, bowel obstruction)
   - Cutaneous (sweating, burns)
   - Blood loss

*Solute dilution (primary increases in total body water plus secondary solute depletion)**
1. Impaired renal free water excretion
   A. Increased proximal nephron reabsorption
      - Congestive heart failure
      - Cirrhosis
      - Nephrotic syndrome
      - Hypothyroidism
   B. Impaired distal nephron dilution
      - Syndrome of inappropriate antidiuretic hormone secretion (SIADH)
      - Glucocorticoid deficiency
2. Excess water intake
   - Primary polydipsia

* Virtually all disorders of solute depletion are accompanied by some degree of secondary retention of water by the kidneys in response to the resulting intravascular hypovolemia. This mechanism can lead to hypoosmolality even when the solute depletion occurs via hypotonic or isotonic body fluid losses. Disorders of water retention can cause hypoosmolality in the absence of any solute losses, but, often, some secondary solute losses occur in response to the resulting intravascular hypervolemia, which can further aggravate the dilutional hypoosmolality.

MEDICATIONS ASSOCIATED WITH THE SYNDROME OF INAPPROPRIATE ANTIDIURETIC HORMONE

Barbiturates	Haloperidol
Carbamazepine	Chlorpromazine
Oxcarbazepine	Thioridazine
Thiazides	Imipramine
Vincristine	Monoamine oxidase inhibitors
Cyclophosphamide	Bromocriptine
General anesthetics	Oxytocin
Nicotine	Acetamides
Clofibrate	Tolbutamide
Nonsteroidal anti-inflammatory drugs	

Hypovolemic hypoosmolar hyponatremia
- Simultaneous water and sodium loss results in ECF volume depletion, with secondary AVP secretion and decreased free water excretion. Retention of water from ingested or infused fluids can then lead to the development of hyponatremia. Primary solute depletion can occur via renal or extrarenal sodium losses, each of which can have multiple etiologies.
- Virtually all disorders of solute depletion are accompanied by some degree of secondary retention of water by the kidneys in response to the resulting intravascular hypovolemia. This mechanism can lead to hypoosmolality even when the solute depletion occurs via hypotonic or isotonic body fluid losses. Disorders of water retention can cause hypoosmolality in the absence of any solute losses, but, often, some secondary solute losses occur in response to the resulting intravascular hypervolemia, which can further aggravate the dilutional hypoosmolality.

1. Extrarenal solute losses
- Vomiting, diarrhea, hemorrhage, and excessive sweating all cause extrarenal losses of sodium and potassium, and the fluid loss that accompanies the solute losses is a potent stimulus to AVP secretion.
- Hyponatremia in hypovolemic shock secondary to volume loss (from hemorrhage or gastrointestinal free water losses) or distributive shock (secondary to sepsis in which there is a relative hypovolemia from vasodilatation) is characterized by a urine sodium concentration (UNa) generally less than 10 mmol/L, reflecting appropriate nephron function to maximize sodium reabsorption and to conserve body solute and ECF volume.

2. Renal solute losses
- Diuretics, mineralocorticoid deficiency, and nephropathies are all important etiologies of renal sodium loss that can lead to the development of hypovolemic hyponatremia.
- In patients on diuretics, hypokalemia from kaliuresis can worsen hyponatremia by causing a net movement of sodium intracellularly.
- Thiazides are more commonly associated with severe hyponatremia than are loop diuretics such as furosemide.
- Renal solute loss is characterized by high urine sodium excretion, typically UNa >20 mmol/L, despite the existence of degrees of volume depletion that would normally activate mechanisms causing renal sodium conservation.

Euvolemic hypoosmolar hyponatremia
- Virtually any disease state causing hypoosmolality can present with what appears to be a normal hydration status based on the usual methods of ECF volume assessment.
- Clinical evaluation of volume status is not sensitive, whereas laboratory measures such as normal or low urea and uric acid concentrations and an elevated UNa are useful correlates of normal ECF volume.
- SIADH is the most common cause of euvolemic hyponatremia in critical illness.

Hypervolemic hypoosmolar hyponatremia
- In hypervolemic hyponatremia, there is an excess in total body water and total body sodium, resulting in clinically evident edema or ascites; however, in many cases, the increase in total body water is out of proportion to that of total body sodium, causing hyponatremia.
- Congestive heart failure, cirrhosis, and nephrotic syndrome all share this common pathophysiology, although the specific mechanisms vary among these different disease states.

isotonic hyponatremia

- Isotonic hyponatremia is usually synonymous with so-called "pseudohyponatremia"
- Plasma osmolality can be measured directly in the laboratory by osmometry or osmolarity can be calculated based on the following formula:
Calculated osmolarity = (2 x [Na+]) + [glucose] + [urea]
- Normal serum is typically comprised of 93% water and 7% nonaqueous factors, including lipids and proteins. Although the nonaqueous components do not affect serum tonicity, in states of marked hyperproteinemia or hyperlipidemia (typically, elevated chylomicrons or triglycerides), the nonaqueous proportion of serum is relatively increased with respect to the aqueous portion, artifactually decreasing the concentration of Na/L of serum although the concentration of Na/L of serum water is unchanged.

treatment

General
- The symptom severity of hyponatremia depends in large part upon the rapidity of the decrease in serum sodium. Most patients are not symptomatic until the serum sodium decreases to less than 125 mmol/L.
- Symptoms are predominantly neurologic, including nausea, vomiting, headache, fatigue, irritability, and disorientation. Severe hyponatremia can progress to seizures, brainstem herniation, and death.
- The initial evaluation of patients in the critical care setting with hyponatremia includes a thorough history and physical examination, with particularly careful evaluation of ECF volume status.
- Initial laboratory evaluation should include serum electrolytes, glucose, an evaluation of renal function with urea, creatinine, serum osmolality, and urine osmolality and sodium.
- Treatment of hyponatremia must strike a balance between the risks of the hyponatremia and the risks of correction.
- The magnitude of these risks depends on the degree of brain volume regulation that has transpired as a result of intracranial fluid and solute shifts
- The treatment of some hyponatremia-associated disease states involves treating the underlying etiology, such as steroids for adrenal insufficiency and thyroid hormone for hypothyroidism.
- In most cases, the appropriate treatment of hyponatremia relies on the identification of the underlying ECF volume status, the acuity with which the hyponatremia developed, and the severity of neurologic symptoms present.

Severe acute symptomatic hyponatremia
- Acute hyponatremia (defined as <48 hours duration) with very low sodium values (<110-115 mmol/L) with seizures or coma is a medical emergency.
- The risk for neurologic complications is high, because cerebral edema can evolve quickly as a result of osmotic movement of water into the brain.
- In patients with severe acute hyponatremia, NaCl should be infused at a rate to increase serum [Na] approximately 1 to 2 mmol/L/h until a less hyponatremic serum [Na] (ie, 125-130 mmol/L) has been achieved.
- In comatose or seizing patients, a faster rate of sodium correction of 3-5 mmol/L/h for a short period of time (ie, 1-2 hours) may be warranted to avoid imminent brainstem herniation

- In hypovolemic states, including the majority of patients with a UNa less than 30 mmol/L, fluid resuscitation with isotonic NaCl is appropriate with a goal serum sodium increase of 0.5 mmol/L/h. Accumulated evidence in experimental animals and humans confirms that a slower rate of serum serum correction minimizes the risk for central pontine myelinolysis
- The serum sodium should be measured every 2 to 4 hours during acute corrections of hyponatremia to ensure that the increase in serum is proceeding at the desired rate.
- Young premenopausal women appear to be at greater risk for neurologic sequelae from hyponatremia, with 75% of cases of brain damage occurring in this subpopulation in some studies.

- In SIADH, fluid restriction is the mainstay of serum sodium correction, with the goal of maintaining fluid intake 500 mL/d below urine output; however, this degree of fluid restriction is difficult to maintain in an intensive care setting where obligate fluid intakes for various therapies often exceed this level.
- Other therapies for chronic hyponatremia include demeclocycline (600-1200 mg/d), furosemide (20-40 mg/d), NaCl tablets (3-18 g/d), and urea (30 g/d). Current clinical trials are underway investigating the use of AVP V2 receptor antagonists