Disorder of Sodium and Water Homeostasis

Thitinat D.

Take Home Messages

- Blood volume and serum osmolality are essential for normal cellular function and are tightly regulated in the human body.
- Total Body Water (TBW) ranges from 45-60% of body weight depending on sex and age and is distributed primarily into 2 compartments:
  - Intracellular compartment or intracellular fluid (ICF; 67% of TBW)
  - Extracellular compartment or extracellular fluid (ECF; 33% of TBW)

Take Home Messages

- Arginine vasopressin (AVP) (antidiuretic hormone, ADH) is synthesized in the hypothalamus and secreted by the posterior pituitary in response to both osmotic and non-osmotic regulators.
- Hyponatremia ([Na] < 135 mEq/L) is the most common electrolyte abnormality in both adults and children.
- Hyponatremia is predominantly the result of an excess of extracellular water because of impaired water excretion.

Take Home Messages

- Hypovolemic hypotonic hyponatremia l common in patients taking thiazide diuretics.
- Euvolemic (isovolemic) hypotonic hyponatremia is associated with a normal or slightly decreased ECF sodium content and increased TBW and ECF volume.
- Euvolemic hyponatremia is most often caused by the syndrome of inappropriate ADH secretion (SIADH).

Take Home Messages

- Hyponatremia with ECF hypervolemia occurs in conditions in which sodium and water excretion is impaired.
- Patients with HF, cirrhosis or nephrotic syndrome have an expanded ECF volume and edema but a decreased effective arterial blood volume.
- The brain's adaptation to chronic serum hypoosmolality or hyperosmolality leads to neurologic symptoms when either hyponatremia (hypoosmolality) or hypernatremia (hyperosmolality) is corrected too rapidly.

Take Home Messages

- Hypernatremia ([Na] > 145 mEq/L) is always associated with hypertonicity and intracellular dehydration, resulting from a water deficit relative to ECF sodium content.
- Edema (clinically detectable increase in interstitial fluid volume) is usually due to heart, kidney or liver failure, or a combination of these conditions, although it can develop with a rapid decrease in serum albumin concentration along with excess fluid intake such as seen in the setting of burns or trauma.

Introduction

- Blood volume and serum osmolality are essential for normal cellular function.
- Water balance determines serum sodium concentration, and sodium balance determines volume status.
- Adequate blood volume is required for effective tissue perfusion which is required to deliver oxygen and nutrients to and remove metabolic waste products from tissues.
- Sodium osmolality is an important determinant of ICF volume.

Introduction

- Maintaining normal ICF volume in the brain is critical because alterations (rapid changes) can result in significant dysfunction and even death.
- Homeostatic mechanisms for controlling blood volume focus on controlling sodium balance.
- Homeostatic mechanisms for controlling serum osmolality ([Na]) focus on controlling water balance.

Sodium and Water Homeostasis

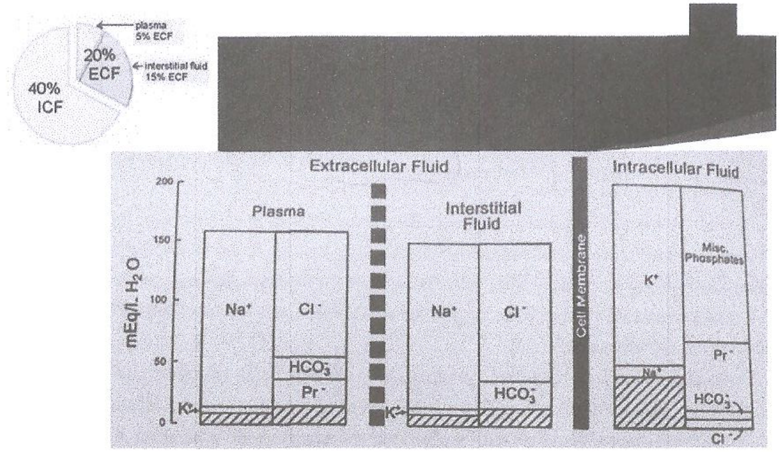
- Excessive sodium intake is a major risk factor for HTN.
- Appropriately functioning kidneys excrete excess sodium to maintain the [Na] and osmolality within a very tight range.
- The kidney can conserve Na during periods of low-sodium intake or in the presence of excessive losses.
- Both hypo- and hypernatremia are conditions of altered serum tonicity and cell volume that reflect a change in the ratio of total exchangeable body sodium to TBW.

Sodium and Water Homeostasis

- Na contributes > 90% of the ECF osmolality; whereas ICF osmolality is primarily determined by the ICF potassium concentration.
- The intra- and extracellular sodium and potassium concentrations are maintained by the sodium-potassium-adenosine triphosphatase (Na^+-K^+-ATPase) pump.
- Most cell membranes are freely permeable to water, the free flow of water between compartments ensures that the ICF and ECF osmolarities remain equal.

Sodium and Water Homeostasis

- Effective osmoles are solutes that cannot freely cross cell membranes, such as Na and K, which are kept in their compartments by Na^+-K^+-ATPase pump.
- The ECF concentration of effective osmoles determines its tonicity, which directly affects water distribution between the ECF and ICF.



Tonicity

คือการเปรียบเทียบระหว่าง Osmolarity ของสารละลายกับ Plasma ส่วนของน้ำเลือด

- isotonic สารละลายอาจมี Osmolarity = Plasma
- hypertonic สารละลายอาจมี Osmolarity > Plasma
- hypotonic สารละลายอาจมี Osmolarity < Plasma

Sodium and Water Homeostasis

- Addition of an isotonic solution (e.g. 0.9% NaCl) to the ECF will result in NO change in ICF volume because there will be NO change in the effective ECF osmolarity.
- Addition of a hypertonic solution (e.g. 3% NaCl) to the ECF will result in a DECREASE in ICF (cell) volume.
- Addition of a hypotonic solution (e.g. 0.45% NaCl) to the ECF will result in an INCREASE in ICF (cell) volume.

Sodium and Water Homeostasis

- The serum sodium concentration (135-145 mEq/L [mmol/L) is tightly regulated and thus usually varies by no more than 3%.
- Serum sodium regulation occurs via mechanisms that control serum osmolality and blood volume.
- The kidney regulates water excretion through a hypothalamic feedback mechanism, such that the serum osmolality remains relatively constant (275-290 mOsm/kg [mmol/kg]) despite day-to-day variations in water intake.

Sodium and Water Homeostasis

- Serum Osmolality can be estimated as:

$$Osm_s = (2 \times Na_s) + (glucose_s/18) + (BUN/2.8),$$

- Osm_s = [Osm] → mOsm/kg
- Na_s = [Na] → mEq/L
- $Glucose_s$ = [glucose] → mg/dL
- BUN → mg/dL

Arginine Vasopressin (AVP)

- AVP (=ADH) is synthesized in the hypothalamus and secreted by the posterior pituitary in response to both osmotic and non-osmotic regulators to maintain water balance.
- When [osm] increases by 1-2%, AVP is released and binds to the arginine vasopressin 2 (V_2) receptor (on the basolateral surface of renal collecting duct cells) results in the insertion of water channels (aquaporin 2, AQP2) into both the apical cell membrane of the collecting duct principal cells and intracellular vesicles below the apical membrane increasing permeability.

Arginine Vasopressin (AVP)

- AVP release also stimulates thirst as an additional means to return serum osmolality toward normal.
- The combined effect of increased water intake (response to thirst) and decreased water excretion (kidney's response to AVP) results in a decrease in the serum osmolality.
- Once [Osm] decreases, AVP secretion is inhibited, and renal excretion of solute-free water occurs.
- When the brain's osmoreceptors detect as little as a 6-10% reduction in the effective circulating volume or arterial blood pressure, non-osmotic AVP release occurs.

Arginine Vasopressin (AVP)

- The effective circulating volume is the portion of the ECF responsible for organ perfusion.
- A decrease in the effective circulating volume activates arterial baroreceptors in the carotid sinus and glomerular afferent arterioles, resulting in stimulation of RAS and increased angiotensin II synthesis. Angiotensin II stimulates both non-osmotic AVP release and thirst.
- Dehydration refers to a loss of TBW producing hypertonicity while hypovolemia is a symptomatic deficit in ECF volume.

Hyponatremia

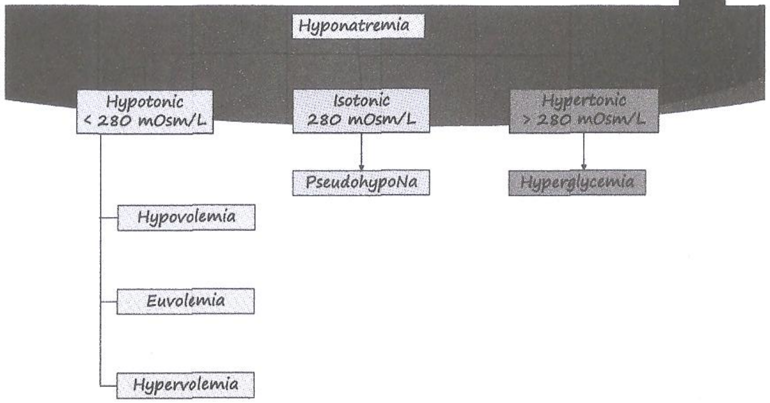
- Hyponatremia defined as a serum sodium concentration < 135 mEq/L (mmol/L) is the most common electrolyte abnormality encountered in clinical practice.
- Drug-induced hyponatremia, esp. that associated with thiazide diuretics and psychotropic medications is common.
- Advancing age is a risk factor for hyponatremia, independent of sex.
- More than 75% of hyponatremia episodes were precipitated by increased intake of hypotonic fluids either orally or through tube feeding or IV fluids.

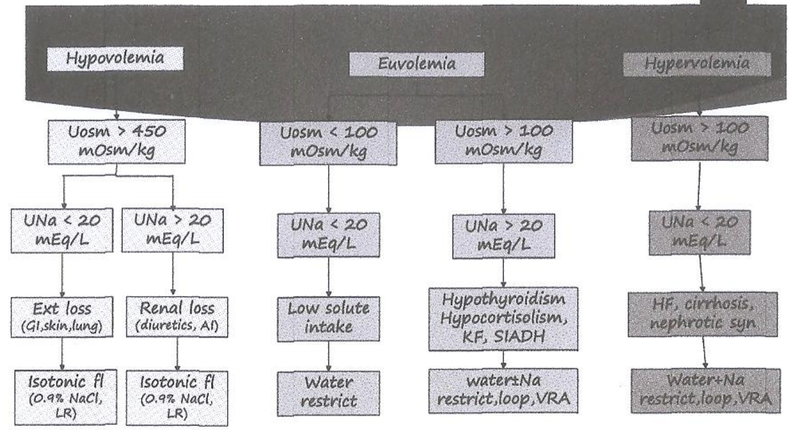
Hyponatremia

- Chronic hyponatremia has been associated with decreased cognitive function and an increased risk of falls, fractures, and bone loss, particularly in the elderly.
- Hyponatremia is predominantly the result of an excess of extracellular water relative to sodium because of impaired water excretion.
- Non-osmotic AVP release can lead to water retention and a decrease in the serum sodium concentration, despite a decrease in ECF and ICF osmolality.

Hyponatremia

- The syndrome of inappropriate antidiuretic hormone secretion (SIADH) is a common cause of hyponatremia and associated with some cancers, esp. small cell lung cancer and brain tumors, CNS damage (e.g. traumatic brain injury, meningitis), and certain lung conditions (e.g. ARDS), pneumonia and TB)





Characteristics	Hypovolemic Hyponatremia	Euvolemic (Isovolemic) Hyponatremia	Hypervolemic Hyponatremia
Water and sodium	Sodium loss >> water loss	Water gain only	Water gain > sodium gain
Causes	Renal: thiazide diuretics Nonrenal: diarrhea, cerebral salt-wasting	SIADH	Heart failure Liver cirrhosis Kidney failure
Effect on TBW	↓↓	↑	↑↑
Effect on TBNa	↓	↔	↑↑
Additional laboratory findings	Renal: UOsm high, UNa high Nonrenal: UOsm high, UNa low	Renal: UOsm low, UNa variable Nonrenal: UOsm high, UNa variable	Renal: UOsm high, UNa high
Clinical presentation	Orthostasis, hypotension, tachycardia, dry mucous membranes, CNS changes	Depends on severity of hyponatremia: seizures, lethargy	Peripheral and pulmonary edema, variable blood pressure
Treatment	0.9% NaCl until vital signs stable; *maintenance* fluids to continue fluid deficit replacement; sodium replacement if cerebral salt wasting; VRA contraindicated	Water restriction, demeclocycline, loop diuretics, VRA	Sodium and water restriction, loop diuretic, VRA

CNS, central nervous system; NaCl, sodium chloride; SIADH, syndrome of inappropriate antidiuretic hormone secretion; TBW, total body water; UNa, urine sodium; UOsm, urine osmolality; VRA, vasopressin receptor antagonist.

Drug-Induced		Nondrug-Induced
Barbiturates Bromocriptine Carboplatin Cisplatin Clofibrate Haloperidol Monoamine oxidase inhibitors	Nicotine Opioids Phenothiazines Thioridazine Thiothixene Tricyclic antidepressants	Malignancy (lung, pancreatic, duodenal) CNS (trauma, tumor, meningitis, hemorrhage, stroke) Pulmonary (pneumonia, ARDS, TB) Postoperative state Nausea Anxiety
Increased sensitivity to ADH		
Acetaminophen AVP analogs (desmopressin) Lamotrigine	NSAIDs Oxytocin Tolbutamide	
Mixed or uncertain mechanism		
ACE inhibitors Carbamazepine Chlorpropamide Cyclophosphamide Ecstasy	Moxifloxacin Omeprazole SSRIs Vinca alkaloids	

Treatment

- For both short-and long-term management, treat the underlying cause of hyponatremia.
- Appropriate treatment of hypotonic hyponatremia requires balancing the risks of hyponatremia vs the risk of osmotic demyelination syndrome (ODS).
- Patient who acutely develop moderate-to-severe hyponatremia and/or patients who have severe symptoms are at greatest risk and potentially benefit most from more rapid correction of hyponatremia.

Treatment

- Correction of hypovolemic hypotonic hyponatremia is usually best accomplished with 0.9%NaCl, as these patients have both sodium and water deficits.
- Active correction of euvolemic and hypervolemic hypotonic hyponatremia in patients who do not require rapid correction is usually best accomplished by water restriction. Demeclocycline, vasopressin receptor antagonist (VRA), or 0.9% NaCl + a loop diuretic can be used if the initial response to water restriction is not adequate.