Chapter 22
Approach to Hyponatremia

22.1 Introduction

Hyponatremia, defined as a serum sodium concentration below 135 mmol/L, is the most common electrolyte disturbance encountered in clinical practice, particularly in the intensive care unit (ICU). It is associated with a spectrum of clinical manifestations, ranging from mild, nonspecific symptoms to severe, life-threatening neurological complications. Even mild hyponatremia (serum sodium 130–134 mmol/L) has been linked to increased mortality, falls, and cognitive impairments, especially in the elderly. Effective management requires a comprehensive understanding of the underlying pathophysiological mechanisms, careful assessment, and prompt, appropriate treatment to prevent complications such as cerebral edema and osmotic demyelination syndrome [1, 2] [Ref: Algorithm 22.1].

22.2 Pathophysiological Mechanisms

Hyponatremia results from an imbalance between water intake and excretion relative to sodium [3].

22.2.1 Classification by Serum Osmolality

- Hypotonic Hyponatremia: Most common form; reflects true excess of water relative to sodium.
- Isotonic Hyponatremia: Often a laboratory artifact (pseudohyponatremia) due to hyperlipidemia or hyperproteinemia.

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- Hypertonic Hyponatremia: Caused by the presence of osmotically active substances (e.g., hyperglycemia, mannitol) that draw water into the extracellular space, diluting serum sodium.
- Hyperglycemia-Induced Hyponatremia: Elevated glucose increases plasma osmolality, causing water shift from intracellular to extracellular space, diluting serum sodium.
- **Pseudohyponatremia:** Hyperlipidemia or Hyperproteinemia: Excess lipids or proteins can interfere with laboratory measurements, falsely lowering serum sodium concentration without affecting osmolality.

22.3 Clinical Presentation

22.3.1 Initial Assessment

22.3.1.1 Rule Out Non-hypotonic Causes

- The first step in managing hyponatremia is to rule out other causes of low sodium that are not due to hypotonicity, such as hyperglycemia or the presence of other osmoles (e.g., mannitol). These conditions do not require the same treatment as true hypotonic hyponatremia, and correcting them often resolves the hyponatremia.

22.3.1.2 Severe Symptoms of Hyponatremia

Severe symptoms of hyponatremia typically arise from the effects of acute cerebral edema caused by a rapid decline in serum sodium levels. These symptoms include:

- **Seizures**: Hyponatremia can lead to neuronal swelling, which disrupts normal brain function, resulting in seizures. Seizures in hyponatremia are an emergency and indicate a critical imbalance of electrolytes in the brain.
- **Coma**: When the brain swells due to fluid shifts from the extracellular to the intracellular space, consciousness can be profoundly impaired, leading to coma. This is a life-threatening condition and requires immediate intervention.
- **Respiratory Arrest**: In extreme cases, the brainstem can be affected by the swelling, leading to respiratory arrest due to impaired autonomic control. This represents the most severe manifestation of hyponatremia.
- **Profound Confusion or Agitation**: Severe hyponatremia can cause a significant alteration in mental status, leading to agitation or severe confusion, which can progress to coma.
  - If the patient presents with severe symptoms (e.g., seizures, altered mental status), immediate treatment is required. Administer a 100 mL bolus of 3% normal saline (NS) intravenously over 10 min. This can be repeated up to two

additional times if severe symptoms persist. The goal here is rapid correction of serum sodium to alleviate life-threatening symptoms, with careful monitoring to avoid overly rapid correction, which could lead to osmotic demyelination syndrome.

22.3.1.3 Moderately Severe Symptoms of Hyponatremia

Moderately severe symptoms are less dramatic but still require prompt attention to prevent progression to more severe states:

- **Nausea and Vomiting**: These symptoms are often the first indicators of hyponatremia and result from cerebral edema.
- **Headache**: As cerebral edema progresses, intracranial pressure increases, leading to headaches. This is an early sign that the brain is being affected by the hyponatremia.
- **Confusion**: This can range from mild disorientation to severe confusion. It reflects the impact of sodium imbalance on brain function.
  - For patients with moderately severe symptoms (e.g., nausea, headache, confusion), a less aggressive approach is recommended. Administer a 100 mL bolus of 3% NS intravenously over 20 min. This approach aims to stabilize the patient while avoiding the risks associated with rapid sodium correction.

22.4 Method of Estimating Volume Status

Assessing volume status is critical in determining the etiology of hyponatremia and guiding treatment. This involves a combination of clinical examination and laboratory tests:

- **Physical Examination**: Look for signs of hypovolemia such as low blood pressure, tachycardia, dry mucous membranes, poor skin turgor, and reduced urine output. Conversely, hypervolemia may present with signs like jugular venous distension, peripheral edema, and ascites.
- **Laboratory Tests**:
  - **Blood Urea Nitrogen (BUN) and Creatinine**: These can indicate kidney function and help in assessing volume status. Elevated BUN/creatinine ratios are often seen in hypovolemic states.
  - **Hematocrit**: Hematocrit levels can rise in hypovolemia due to hemoconcentration.
  - Once immediate symptoms are managed, the next step is to assess the patient's volume status. This is a critical decision point, as the management of hyponatremia varies significantly based on whether the patient is hypovolemic, euvolemic, or hypervolemic.

- **Hypovolemic Hyponatremia:**
  - In cases of hypovolemia, where there is a deficit of both sodium and water, the cause is often due to gastrointestinal losses (e.g., vomiting, diarrhea), transdermal losses (e.g., sweating), or third-spacing (e.g., burns, pancreatitis). Urine sodium will be low (<30 mmol/L) if nonrenal causes predominate. If renal causes are responsible (e.g., diuretic use, adrenal insufficiency), urine sodium will be higher (>30 mmol/L). Treatment involves fluid resuscitation, typically with isotonic saline, to restore intravascular volume and inhibit further vasopressin release.
- **Hypervolemic Hyponatremia:**
  - Hypervolemia, characterized by fluid overload, is usually associated with conditions like heart failure, cirrhosis, or nephrotic syndrome. These patients will also have low urine sodium (<30 mmol/L) as the body attempts to retain sodium. Management includes fluid restriction, diuretics, and addressing the underlying condition.
- **Euvolemic Hyponatremia:**
  - In euvolemia, the patient appears to have normal fluid volume, but there is an inappropriate retention of water relative to sodium. This is often due to the syndrome of inappropriate antidiuretic hormone secretion (SIADH). Urine osmolality will be high (>100 mOsm/kg) and urine sodium will be elevated (>30 mmol/L). Treatment involves fluid restriction, addressing the underlying cause of SIADH, and in some cases, pharmacological agents like vasopressin receptor antagonists.

- **Role of Antidiuretic Hormone (ADH)/Arginine Vasopressin (AVP)**
- AVP plays a pivotal role in water reabsorption in the kidneys. Inappropriate secretion or action of AVP can lead to water retention and hyponatremia:
  - Euvolemic Hyponatremia: Often due to the syndrome of inappropriate antidiuretic hormone secretion (SIADH), where AVP is secreted despite normal or low plasma osmolality.
  - SIADH: Characterized by euvolemia, hyponatremia, high urine osmolality (>100 mOsm/kg), and elevated urine sodium (>30 mmol/L).

22.5 Osmolarity

Osmolarity is a measure of solute concentration in the blood and urine and is essential in understanding the type of hyponatremia:

- **Serum Osmolality**: This helps differentiate between hypotonic, isotonic, and hypertonic hyponatremia.

  - **Hypotonic Hyponatremia**: Most common and often due to excessive water retention relative to sodium. It reflects true water intoxication or sodium deficiency.
  - **Isotonic Hyponatremia**: Often a laboratory artifact, like pseudohyponatremia, where the sodium concentration appears low, but the osmolarity is normal due to high levels of lipids or proteins.
  - **Hypertonic Hyponatremia**: Occurs when other solutes like glucose or mannitol are present in high concentrations, pulling water from the intracellular space and diluting serum sodium.

- **Urine Osmolality**: This helps assess the kidneys' ability to dilute or concentrate urine.
  - **High Urine Osmolality (>100 mOsm/kg)**: Indicates that ADH (antidiuretic hormone) is being secreted and the kidneys are retaining water, which is inappropriate in cases like SIADH.
  - **Low Urine Osmolality (<100 mOsm/kg)**: Suggests that ADH is not active and points towards conditions like primary polydipsia or low solute intake.
  - **SIADH:**
    - If urine osmolality is high (>100 mOsm/kg) and urine sodium is elevated (>30 mmol/L) with a normal or low serum osmolality, SIADH is likely. Treatment focuses on fluid restriction and addressing the underlying cause.
  - **Primary Polydipsia or Low Solute Intake:**
    - If urine osmolality is low (<100 mOsm/kg), it suggests conditions like primary polydipsia or low solute intake (e.g., beer potomania). The management is primarily fluid restriction and dietary changes to increase solute intake.

22.6 Urine Sodium: Its Measurement and Interpretation

Urine sodium concentration is critical for identifying the underlying cause of hyponatremia:

- **High Urine Sodium (>30 mmol/L)**: Indicates that the kidneys are excreting sodium appropriately, which can occur in euvolemic hyponatremia (e.g., SIADH) or renal causes of sodium loss.
- **Low Urine Sodium (<30 mmol/L)**: Suggests that the kidneys are conserving sodium, which is seen in hypovolemic states due to nonrenal causes like gastrointestinal losses.

22.7 Renal Causes of Hyponatremia

Renal causes of hyponatremia are associated with impaired sodium handling by the kidneys:

1. **Diuretics (Thiazides)**
   - Thiazide diuretics impair the kidneys' ability to dilute urine by inhibiting sodium reabsorption in the distal tubules, leading to hyponatremia. This effect is more pronounced in the elderly and those with low baseline sodium intake.
2. **Renal Failure**
   - In advanced chronic kidney disease, the kidneys' ability to excrete free water is impaired, leading to dilutional hyponatremia. This is compounded by factors such as overuse of diuretics or excessive fluid intake.
3. **Adrenal Insufficiency**
   - Primary adrenal insufficiency (Addison's disease) can lead to hyponatremia due to aldosterone deficiency, which impairs sodium reabsorption in the kidneys and leads to volume depletion.
4. **Cerebral Salt Wasting**
   - This is a condition where renal sodium loss occurs due to a brain injury or neurosurgical procedure, leading to hyponatremia and hypovolemia. It is often confused with SIADH but requires volume replacement instead of fluid restriction.

22.8 Nonrenal Causes of Hyponatremia

Nonrenal causes typically involve extrarenal sodium loss or conditions that impair the body's ability to excrete water:

1. **Gastrointestinal Losses**
   - Vomiting, diarrhea, or nasogastric suctioning can lead to significant sodium loss. The kidneys respond by retaining sodium, leading to low urine sodium concentrations.
2. **Transdermal Losses**
   - Conditions such as excessive sweating, cystic fibrosis, or burns can lead to sodium loss through the skin. This is particularly significant in hot climates or during vigorous exercise without adequate sodium replacement.

3. **Third Spacing**
    - Conditions like sepsis, pancreatitis, or trauma can cause fluid to shift into nonfunctional spaces (third spacing), leading to hypovolemia and hyponatremia. This triggers the body to conserve sodium, reflected in low urine sodium levels.
4. **Primary Polydipsia**
    - Excessive water intake, often due to psychiatric conditions, overwhelms the kidneys' ability to excrete water, leading to dilutional hyponatremia. Urine osmolality is typically low due to the large volume of dilute urine.
5. **Syndrome of Inappropriate Antidiuretic Hormone Secretion (SIADH)**
    - SIADH is characterized by inappropriate secretion of ADH, leading to water retention and dilutional hyponatremia. This condition is often associated with lung diseases, CNS disorders, or certain medications.
6. **Hypothyroidism**
    - Severe hypothyroidism can lead to decreased cardiac output and renal blood flow, triggering non-osmotic release of ADH and leading to hyponatremia. However, this is a rare cause and typically only seen in severe cases.

22.9 Risk of Overcorrection

Osmotic Demyelination Syndrome (ODS)
- Mechanism: Rapid rise in serum sodium leads to demyelination in the central pontine region [4].
- Prevention:
- Correction Rate: Do not exceed 8–10 mmol/L increase in serum sodium over 24 h.
- High-Risk Patients: Lower target correction rates in patients with chronic hyponatremia or risk factors.

Use of Desmopressin
- Mechanism: Synthetic AVP analog; prevents rapid water diuresis.
- Indications: Patients at risk of overcorrection or when overcorrection has occurred.
- Dosage: Administer as per institutional protocols, with close monitoring.

22.10 Special Considerations

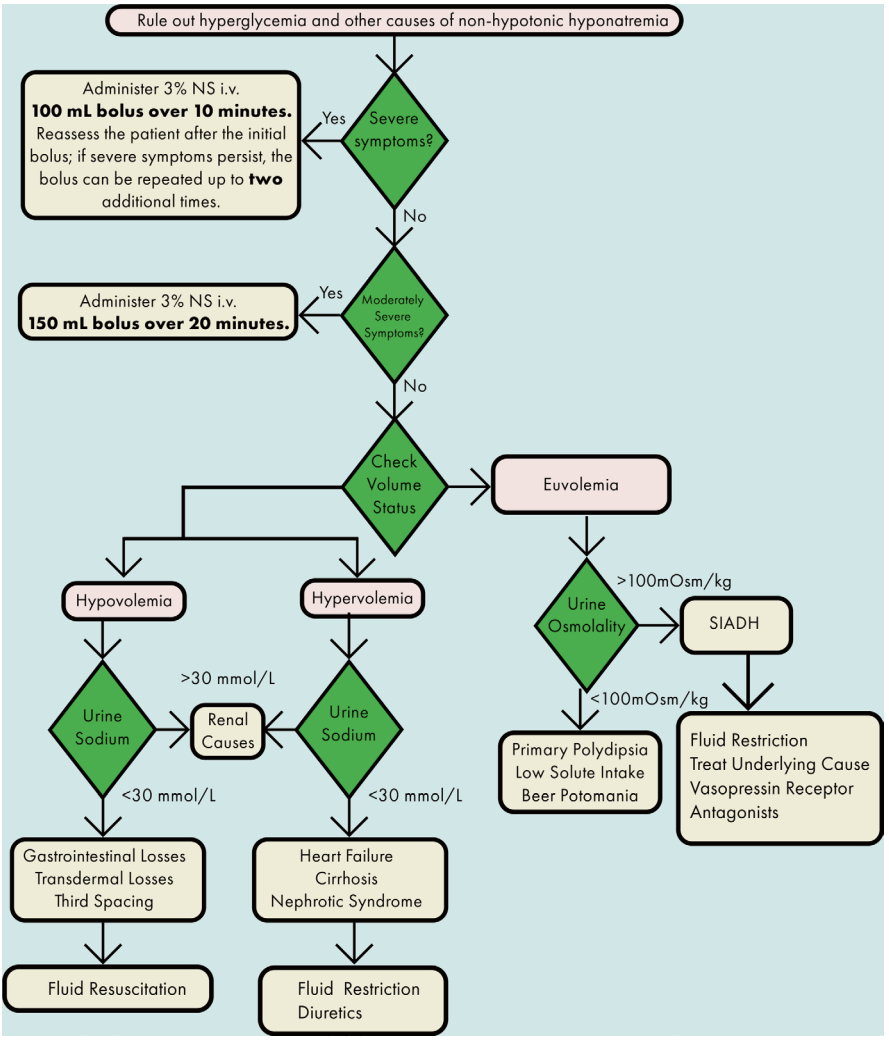
Hyponatremia in Oncology Patients
- Etiology:
- SIADH: Paraneoplastic syndromes (e.g., small cell lung carcinoma).
- Chemotherapy-Induced SIADH: Agents like vincristine, cyclophosphamide.
- Management:
- Fluid Restriction and Pharmacotherapy: Similar to SIADH management.
- Treat Underlying Malignancy: May resolve hyponatremia.
- Monitor for Recurrence: Regular assessment due to risk of SIADH relapse.

Mortality and Morbidity Data
- Elderly Patients: Increased susceptibility to hyponatremia-induced complications.
- Falls and Fractures: Hyponatremia-associated gait disturbances.
- Cognitive Impairment: Subtle neurological deficits even in mild hyponatremia.

22.11 Conclusion

The approach to hyponatremia in the ICU is a systematic process that begins with ruling out non-hypotonic causes, followed by the assessment and treatment of the severity of symptoms. Subsequent steps involve careful evaluation of the patient's volume status and targeted management of the underlying cause. The key to successful management is the balance between correcting sodium levels rapidly enough to prevent or treat severe symptoms while avoiding the risks of overly rapid correction, which can result in serious complications such as osmotic demyelination syndrome.

Algorithm 22.1: Approach to hyponatremia



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