Syndrome of Inappropriate Release of Antidiuretic Hormone

Definition

Hyponatremia is defined as a serum sodium level less than 135mmol/L. Syndrome of inappropriate release of antidiuretic hormone (SIADH) is a disorder of sodium and water balance presented with euclidean hyponatremia and impaired urinary dilution in the absence of renal disease or any identifiable non-osmotic stimulus known to release antidiuretic hormone (ADH)².

Epidemiology

Hyponatremia is common in hospitalized patients. Approximately 15 to 20 percent of patients developed mild hyponatremia and 3 to 5 percent of patients developed severe hyponatremia. SIADH is the most common cause of hyponatremia²,³. Elderly persons, especially women are more susceptible to hyponatremia because of a decrease in total body water and hormonal changes⁴.

Pathophysiology

Antidiuretic hormone or arginine vasopressin (AVP) binds to the AVP V₂ receptors on the kidney collecting tubules causing synthesis and insertion of water channels (aquaporin-2) along the luminal surface. Insertion of aquaporins promotes free water reabsorption from the renal tubules⁵.

AVP secretion is triggered by the osmotic and non-osmotic stimuli. Osmotic receptors are located on the anterior hypothalamus. These receptors monitor the serum osmolality. Small (1-2%) increases in plasma osmolality are sufficient to stimulate the osmoreceptors and trigger the secretion of AVP⁴. If serum osmolality is less than 275mOsm/kg, AVP secretion is suppressed. However, when serum osmolality is greater than 285mOsm/kg, AVP starts to release. A non-osmotic stimulus includes hypovolemia, stress, nausea, vomiting, drugs, hypoglycaemia, and/or pain⁴.

Syndrome of inappropriate release of antidiuretic hormone is resulted from inappropriate release of AVP and excessive fluid intake. Patients with SIADH may have "inappropriate thirst" due to the lowering of osmolality threshold for thirst⁶,⁷.

Causes of SIADH include tumors such as small cell lung carcinoma, pancreatic carcinoma, and lymphoma; central nervous system disorders such as multiple sclerosis, Guillain Barrè syndrome, hydrocephalus, and cerebrovascular diseases; drugs such as serotonergic reuptake Inhibitors, carbamazepine, oxcarbazepine, vincristine, cyclophosphamide; and pulmonary diseases such as tuberculosis, pneumonia, acute respiratory failure. Other causes include acquired immunodeficiency syndrome, strenuous exercise, and hyperglycemia⁵,⁶,¹¹.

Manifestations

Presentation of SIADH is primarily related to the severity and duration of hyponatremia. Patients with chronic and mild hyponatremia may be asymptomatic because of the slow process that allows the brain cells to adapt to the lower serum osmolality⁴,¹².

In mild hyponatremia, the most common symptoms are headache, nausea, fatigue, anorexia, difficulty concentrating, impaired memory, muscle cramps, weakness, dysgeusia (change in the sense of taste) and lethargy. When hyponatremia becomes more severe, neurological signs such as confusion, hallucinations, seizures, and delirium occur. If serum sodium falls below 115mmol/L coma, respiratory arrest, and death can result⁴,¹³.

Diagnostic Tests

Diagnosis of SIADH is dependent on patient presentation, physical examination, and laboratory results (see below table). Other tests include water load test, fractional excretion of sodium and saline infusion study¹,⁴,¹⁴.

Laboratory tests include both serum and urine tests (see below table).

Table: Diagnostic criteria for SIADH⁴,¹³.

<table>
<thead>
<tr>
<th>Essential features</th>
<th>Serum osmolality &lt;275 mOsm/kg</th>
<th>Urine osmolality &gt;100 mOsm/kg</th>
<th>Urine sodium &gt;40 mmol/L</th>
<th>No recent use of diuretic agents</th>
<th>Clinical euvolemia</th>
<th>Normal thyroid and adrenal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Supplementary features</td>
<td>Serum uric acid &lt;4mg/mL</td>
<td>BUN &lt;10 mg/mL</td>
<td>Fractional sodium excretion &gt;1%</td>
<td>Failure to correct hyponatremia after 0.9% saline infusion</td>
<td>Elevated serum AVP levels</td>
<td>Abnormal water load test result</td>
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Treatment Options

Management for patients with SIADH includes elimination of the underlying causes and correcting the electrolyte imbalance. When selecting interventions to correct hyponatremia, the severity and duration of hyponatremia and the symptoms of patients should be considered⁴.

If patients develop symptoms of acute hyponatremia (hyponatremia developed within 48 hours), the goal is to raise serum sodium level by 1-2mmol/L/H. Hypertonic sodium chloride (3%) is commonly used to correct hyponatremia¹³,¹⁵. Correction of sodium in the first 48 hours should be gradual. In the first 24 hours, serum sodium correction should be less than 8 to 10mmol/L, and in the first 48 hours serum sodium correction should be between 18 to 25mmol/L. In clinical practice, the most commonly used calculation for 3% hypertonic saline infusion rate is 1 ml/kg/h. This will increase serum sodium level by 1 mmol/L/h²,¹⁴. Administration of furosemide to promote water excretion is also recommended¹⁶.
During treatment, serum sodium should not be raised greater than 12mmol/L/day. Monitor for symptoms of central pontine and extrapontine myelinolysis. These include tremors, incontinence, hyporeflexia, mutism or dysarthria, dysphagia, cranial nerve palsies, seizures, spastic quadriparesis, pseudobulbar palsy, and/or locked-in syndrome. Isotonic (0.9%) saline may be administered when patients have mild and asymptomatic hyponatremia. However, if patients have severe and acute hyponatremia, isotonic saline should be avoided because patients with SIADH will excrete most of the sodium in the saline solution and retain the water component resulting in worsened hyponatremia.

Fluid restriction is usually the first treatment for SIADH. Most often, total fluid intake is limited to 0.8L to 1L/day or daily urine output minus 500mL.

In the acute phase of treatment, serum electrolyte levels should be assessed every 2 to 4 hours to avoid overcorrection.

A newer drug group known as the Vaptans (Conivaptan and Tolvaptan) has been used in SIADH. Vaptans are V₂ receptors antagonists (blockers). When V₂ receptors are blocked, it inhibits the action of AVP and prevents free water reabsorption. Vaptans do not affect or increase the excretion of urine solutes such as sodium or potassium.

Urea is the major osmotic constituent of urine, administering urea orally can act as osmotic diuresis because it increases the renal filtrate osmolality. Urea also promotes reabsorption of sodium in the ascending limb of the loop of Henle and reduces sodium excretion. However, the bitter taste of urea keeps some patients away from using this option.

**Nursing Implications**

Monitor patients' vital sign closely for any hypotensive effects if patients are on Conivaptan.

If patients are receiving intravenous infusion of hypertonic (3%) sodium chloride, assess the intravenous insertion site regularly, hypertonic saline may cause irritation and phlebitis.

Patients with SIADH may have “inappropriate thirst”. This change may cause patient to be non-compliant with fluid restrictions. Explain to the patient the rationale for fluid restriction and encourage patients to adhere to the fluid intake restriction. Provide hard candy or ice chips to ameliorate the “thirsty” feeling.

Maintain a strict fluid intake and output record and monitor daily body weights. When patients are on fluid restrictions, calculate the total fluid intake carefully. All types of fluid intakes such as intravenous fluid, medication, oral fluid intake, and tube feeding formula should be included. Note that when patients are on tube feeding formulas, some feeding formulas have different dry weights. Please consult the manufacturer’s manual for the exact fluid volume or use the calculator on the [www.neuro4nurses.com](http://www.neuro4nurses.com) website to calculate the oral fluid allowed when patients are on tube feeding formulas. Consult a registered dietitian when a more concentrated feeding formula is required.

**Reference**


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