

## Syndrome of inappropriate secretion of antidiuretic hormone and hyponatremia after spinal surgery

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Hyponatremia caused by an inappropriately high level of antidiuretic hormone secretion after spinal surgery is an uncommon and self-limiting phenomenon that resolves within 2 or 3 weeks. During the early postoperative period, the patient's urine output and serum level of sodium should be monitored closely to prevent possible serious complications of the syndrome of inappropriate secretion of antidiuretic hormone. Symptoms vary depending on the severity of the hyponatremia and can range from mild headache, muscle cramps, nausea, and vomiting to convulsions, coma, and death. Treatment options include fluid restriction, oral intake of salt, and hypertonic saline. It is important that spine surgeons recognize this phenomenon early and treat it appropriately and conservatively to prevent possible serious complications.

**KEY WORDS** • syndrome of inappropriate secretion of antidiuretic hormone • hyponatremia • spinal surgery

The SIADH was first described in patients with bronchogenic carcinoma by Schwartz and colleagues<sup>19</sup> in 1957. Since that time, it has been reported in association with many surgical procedures, anesthetic agents, brain injury, spinal surgery, and tumors.<sup>3,5,6,15,17,18,24</sup> In these patients, loss of sodium and water retention have been attributed to sustained endogenous production and release of ADH or ADH-like substances without any physiological or pharmacological stimuli to ADH release. The SIADH is defined as retention of water, loss of sodium, and inappropriately concentrated urine in normovolemic or hypervolemic patients in whom renal and adrenal function is normal.

Physiological and abnormal secretion of ADH during the perioperative period has been described by many different authors.<sup>2,4,16,23</sup> In this paper, we will discuss hyponatremia and SIADH together as a complication of spinal surgery. We will review the literature and discuss the diagnosis, pathophysiology, and management of SIADH after spinal surgery.

### HYPONATREMIA AND SIADH

Hyponatremia is a very common disturbance of fluid and electrolyte balance in the critically ill patient. Hyponatremia is defined as a sodium value of 135 mEq/L or less. Total body sodium may be increased or decreased in the presence of excess extracellular free water. In depletion, or hypertonic hyponatremia, the total body concen-

tration of sodium is decreased in the presence of decreased or normal extracellular fluid. In dilutional, or hypotonic, hyponatremia, the total body concentration of sodium is either normal or increased in the presence of increased total body water. In the latter case SIADH is defined and is characterized by hypotonic hyponatremia and impaired urinary dilution in the absence of any known nonosmotic stimulus to ADH secretion, such as hypovolemia, hypotension, or adrenal insufficiency.<sup>9,10</sup> In 1957, Schwartz and colleagues<sup>19</sup> described the clinical parameters required for a diagnosis of SIADH (Table 1).

The SIADH is seen in patients with a variety of medical conditions, including carcinoma of the bronchus, prostate, and ovary; agenesis of the corpus callosum and cleft lip and palate; closed or penetrating head trauma; infectious processes such as an abscess or tuberculosis of the lung or brain, encephalitis, or bacterial or viral meningitis; asthma; reliance on positive-pressure ventilation; and neurological conditions such as Guillain-Barré syndrome, multiple sclerosis, hydrocephalus, cerebrovascular occlusion or hemorrhage, and cavernous sinus thrombosis.<sup>8-11</sup> The SIADH has also been reported as a postoperative complication of cardiothoracic, brain, or spine surgery. In most of these conditions, SIADH is caused by either ectopic production or osmotically inappropriate secretion of ADH by the neurohypophysis. Postoperative SIADH has been attributed to stress<sup>16</sup> and, in cases of neurological or spinal surgery, to invasion of the dura mater and traction on the neural pathways.<sup>12</sup> Callewart, et al.,<sup>5</sup> have reported the development of SIADH in patients who had undergone revision surgery or had experienced a blood volume loss greater than 10%. On the other hand, Lieh-Lai, et al.,<sup>12</sup> found no relationship between blood loss or type of spinal surgery and the development of SIADH.

*Abbreviations used in this paper:* ADH = antidiuretic hormone; cAMP = adenosine 3',5'-cyclic monophosphate; CNS = central nervous system; CPEM = central pontine and extrapontine myelinolysis; CVP = central venous pressure; SIADH = syndrome of inappropriate secretion of ADH.

TABLE 1

*Clinical parameters used to diagnose SIADH*

decreased plasma osmolality (<275 mOsm/kg H <sub>2</sub> O)
inappropriate urinary concentration (>100 mOsm/kg H <sub>2</sub> O)
clinical euvoolemia/hypervolemia or absence of signs of hypovolemia or hypervolemia
elevated urinary excretion of sodium w/ a normal salt & water intake
absence of other causes of increased ADH such as hypothyroidism, hypoadrenalism, kidney problem, & diuretic use

**Pathophysiology of SIADH**

Antidiuretic hormone, a product of the hypothalamus, is stored in the posterior pituitary gland and controls the metabolism of water. It is synthesized as a prohormone in the supraoptic and paraventricular nuclei and is cleaved into its active form during transportation to the posterior pituitary. Under normal conditions, ADH is secreted in response to a decreased intravascular volume and serum hyperosmolality. This hormone acts on cells of the distal renal tubules and the collecting duct via the cAMP pathway. An increased level of cAMP increases the permeability of cells to free water, inducing free water absorption.<sup>13</sup> Antidiuretic hormone is also a potent vasoconstrictor at levels between 2.5 and 20 pg/mL, which is above the physiological range. In patients with SIADH, excess water is retained in the extracellular and intracellular compartments, decreasing the concentration of sodium and other solutes such as uric acid and plasma urea. In addition, the expansion of plasma and extracellular volume decreases the level of aldosterone and of renin activity, and increases the urinary excretion of sodium as an appropriate response. The combination of excess fluid retention by inappropriate levels of ADH and a loss of sodium due to a normal response to increased body fluid provides a description of SIADH.

The causes of SIADH can be divided into four major groups: tumors, drugs, pulmonary conditions, and CNS disorders. In tumors, the cause of SIADH is usually ectopic secretion of ADH. Pharmacological agents have been shown to stimulate secretion of vasopressin, potentiate the antidiuretic effect of vasopressin, activate V2 renal receptors, or work through a combination of mechanisms. In pulmonary conditions, hypoxia and decreased venous return have been thought to be the mechanism leading to SIADH. The mechanism by which CNS disorders cause SIADH is not well understood. Most authors hypothesize that injury to the CNS disrupts or alters the osmoregulation of ADH release by the neurohypophysis, stimulating inappropriate release of ADH. The exact mechanism by which this occurs is not well known; however, SIADH seems to be an acute and self-limited disorder that lasts only a few days or weeks.

**SPINAL SURGERY AND SIADH**

The SIADH has been reported after spinal surgery by many authors.<sup>2,5,7</sup> Elster<sup>7</sup> reported a 5% incidence of postoperative SIADH in a retrospective review of 161 patients who underwent spinal surgery. Callewart, et al.,<sup>5</sup> reported a postoperative incidence of 6.9% SIADH in their pro-

spective study of 116 patients who underwent spinal surgery. Lieh-Lai, et al.,<sup>12</sup> reported a postoperative incidence of 33% SIADH in a prospective cross-sectional study of 30 pediatric patients. In their prospective study of 10 patients, Bell and associates<sup>2</sup> reported a 100% incidence of SIADH in patients who underwent spinal fusion.

Although these reported incidences range from 5 to 100%, it is important to recognize the risk of postoperative SIADH in patients undergoing spinal surgery. Close observation and early diagnosis are very important in the appropriate treatment of patients with SIADH.

**Symptoms and Diagnosis**

Symptoms of SIADH may vary, depending on its rate of development from mild headache, muscle cramps, and anorexia to nausea, vomiting, confusion, coma, convulsions, and death. The first sign of developing SIADH usually is a decrease in urine output with an associated increase in urine specific gravity.<sup>12</sup> Lieh-Lai, et al.,<sup>12</sup> found that the ADH level was elevated immediately and 6 hours postoperatively, and that it returned to preoperative values within 12 hours. They also found that serum osmolality decreases below normal within 6 hours after surgery. These findings indicate that SIADH develops in patients immediately postoperatively. Hence, a close observation of decreases in urine output and the serum level of sodium may help diagnose SIADH early. It should be noted that the level of ADH may rise postoperatively as a physiological response to hypovolemia or hypotension. Hence, to diagnose SIADH, the specific constellation of signs that Schwartz and colleagues<sup>19</sup> originally described (Tables 1 and 2) should be used. These include serum hypoosmolality (< 275 mOsm/kg), inappropriate urinary concentration (urine osmolality > 100 mOsm/kg), and elevated urinary excretion of sodium in the absence of hypovolemia. In addition, other medical causes of hyponatremia, such as hypovolemia and renal, adrenal, or thyroid dysfunction, should be excluded. Any medication that might cause hyponatremia should also be excluded.

Any decrease in urine output should prompt the clinician to perform an additional workup. The serum level of sodium should be measured. If the level is less than 130 mEq/L, serum and urine osmolality should be checked. If these values are less than 275 mOsm/kg H<sub>2</sub>O and more than 100 mOsm/kg H<sub>2</sub>O (Table 2), respectively, the patient's fluid status should be accessed. Intravascular fluid volume can be assessed either directly by measuring CVP or indirectly by challenging the patient with a bolus of fluid. If CVP is high or the urine osmolality does not change in response to the fluid challenge, other causes of SIADH should be ruled out. In the presence of normally

TABLE 2

*Clinical comparison of SIADH and the normal ADH response*

Parameter	SIADH	Normal-Response ADH
plasma sodium	low (<130 mEq/L)	low
plasma osmolality	low (<275 mOsm/kg H <sub>2</sub> O)	normal-low
urine sodium	high (>20 mEq/L)	low
urine osmolality	high (>100 mOsm/kg H <sub>2</sub> O)	high
plasma uric acid	low	high

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functioning kidneys, adrenals, and thyroid gland, the diagnosis of SIADH can be made.

### Treatment of SIADH

It is very important to distinguish between SIADH and appropriate-response ADH because the management of the two conditions is markedly different. In the face of SIADH, volume expansion should be avoided. In patients with a known cause of SIADH, the disorder can be cured by eliminating the cause, for example, the tumor, drug, or disease responsible for the syndrome. In CNS and spine disorders, SIADH can be an acute self-limited disorder that remits spontaneously within 2 or 3 weeks.

In patients whose SIADH is related to a CNS or spinal disorder, depending on the severity of the hyponatremia, it is important to correct the salt and water imbalance while waiting for the inappropriate release of ADH to cease. In mild hyponatremia with minimal symptoms, reducing total intake of free water and increasing the oral intake of salt often is sufficient to reduce the amount of body water and raise the serum level of sodium. In patients with significant hyponatremia and CNS manifestations, it is important to decide how fast and to what level the plasma osmolality should be increased. Correcting severe hyponatremia too rapidly could be devastating because it might cause CPEM, a demyelinating disease that causes severe morbidity and mortality, including quadriparesis, mutism, pseudobulbar palsy, seizures, behavioral disturbances, and movement disorders.<sup>1,21,24</sup>

There is great debate over how fast and how much the serum level of sodium should be corrected. Early studies found less risk of CPEM with increases in serum sodium less than 25 mEq/L over the first 24 to 48 hours of treatment.<sup>20,25</sup> Authors of later studies, however, have suggested that the risk of CPEM is much higher if the serum level of sodium is corrected faster than 12 mEq/L in 24 hours or 18 mEq/L in 48 hours.<sup>22</sup> In addition, the duration of hyponatremia is important in its treatment. Perioperative hyponatremia, often an acute process (< 48 hours), is associated with a higher risk of developing complications from hyponatremia and is rarely associated with demyelinating complication with rapid correction. Hence, if hyponatremia has developed acutely after surgery, it should be corrected rapidly. If hyponatremia is a chronic process, however, it should be corrected in a controlled and limited fashion. Some authors have suggested correcting the serum level of sodium at a rate of 1 to 2 mEq/L per hour, while keeping the total magnitude of correction to less than 25 mEq/L over the first 48 hours.<sup>20,25</sup> Nevertheless, we use more conservative parameters: a maximal correction rate of 0.5 mEq/L per hour and overall magnitudes of correction less than 12 mEq/L in the first 24 hours and 18 mEq/L in the first 48 hours.<sup>22</sup>

When treating hyponatremia with an intravenous administration of 3% saline solution, the serum level of sodium and urine output should be monitored closely to ensure prompt recognition and discontinuation of treatment if SIADH acutely remits. Lithium carbonate and demeclocycline have been shown to increase the excretion of free water by blocking the effect of ADH at the level of the collecting duct. Both of these drugs carry the risk of severe complications, however, and should be used only

in patients who cannot comply with water restriction and a high dietary salt intake or in whom this therapy fails. Although ADH antagonists are still in the experimental stages, they offer the promise of treating severe hyponatremia quickly.<sup>15,24</sup>

### CONCLUSIONS

The SIADH is the principal cause of postoperative hyponatremia in patients who have undergone spinal surgery. Early recognition of signs and symptoms is very important for a prompt diagnosis and treatment of postoperative SIADH. Special attention should be given to the aggressiveness of and length of treatment for the correction of hyponatremia to avoid the serious possible complication of overtreatment of hyponatremia.

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