Central neurogenic diabetes insipidus, syndrome of inappropriate secretion of antidiuretic hormone, and cerebral salt-wasting syndrome are secondary events that affect patients with traumatic brain injury. All 3 syndromes affect both sodium and water balance; however, they have differences in pathophysiology, diagnosis, and treatment. Differentiating between hypernatremia (central neurogenic diabetes insipidus) and the 2 hyponatremia syndromes (syndrome of inappropriate secretion of antidiuretic hormone, and cerebral salt-wasting syndrome) is critical for preventing worsening neurological outcomes in patients with head injuries. (Critical Care Nurse. 2012;32[2]:e1-e8)

Traumatic brain injury (TBI) in adults continues to be a major cause of death and disability in the United States. An estimated 1.7 million persons in the United States will sustain TBI; of these, approximately 52,000 will die of the injury, 275,000 will be hospitalized, and 1.4 million will be treated and released from an emergency department. Although young children (0-4 years old) and adolescents (15-19 years old) have the highest risk of TBI, older adults (≥75 years) have the highest rates of TBI-related hospitalization and death. Patients who survive the initial injury are likely to have secondary complications that can result in permanent disability. Approximately 80,000 to 90,000 patients experience long-term disability each year because of TBI.

The most common causes of TBI are falls (35.2%), motor vehicle accidents (17.3%), being struck by or against objects (16.5%), assaults (10%), and sports-related injuries and penetrating trauma (21%).

Central neurogenic diabetes insipidus, syndrome of inappropriate secretion of antidiuretic hormone, and cerebral salt-wasting syndrome are secondary events that affect patients with traumatic brain injury. All 3 syndromes affect both sodium and water balance; however, they have differences in pathophysiology, diagnosis, and treatment. Differentiating between hypernatremia (central neurogenic diabetes insipidus) and the 2 hyponatremia syndromes (syndrome of inappropriate secretion of antidiuretic hormone, and cerebral salt-wasting syndrome) is critical for preventing worsening neurological outcomes in patients with head injuries. (Critical Care Nurse. 2012;32[2]:e1-e8)

This article has been designated for CE credit. A closed-book, multiple-choice examination follows this article, which tests your knowledge of the following objectives:

1. List potential causes of central neurogenic diabetes insipidus (CNDI), syndrome of inappropriate secretion of antidiuretic hormone (SIADH), and cerebral salt-wasting syndrome (CSWS)
2. Compare the signs, symptoms, and laboratory values for CNDI, SIADH, and CSWS
3. Discuss the treatment and nursing management for CNDI, SIADH, and CSWS

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initial trauma, is the result of biochemical processes that occur at
the cellular level when neurons are
damaged. Hypotension, hypoxia,
cerebral edema, and electrolyte
imbalance further worsen neurolo-
gical outcomes and markedly affect
morbidity and mortality. In this
article, we discuss how electrolyte
imbalances caused by injury of the
pituitary gland complicate the
recovery of patients with TBI.

Pathophysiology of TBI

Primary TBI is caused by 2 main
mechanisms: direct impact (ie, an
object strikes the head or the brain)
and acceleration-deceleration injury
(ie, the force of the impact causes
the brain to ricochet inside skull,
resulting in shearing of cerebral
axons). Direct impact caused by
blunt trauma, falls, or penetrating
injuries can result in cerebral edema
and intracranial hemorrhage, which
can lead to severe deterioration in
a patient’s clinical condition and
even death.

Acceleration-deceleration injuries
often cause diffuse axonal injury.
The rotational shearing of gray and
white brain matter results in micro-
scopic damage of the axons of the
brain. Initially, diffuse axonal injury
usually is not visible on imaging
studies; however, because of axonal
degeneration, abnormal findings
such as edema, atrophy, and
petechial hemorrhages eventually
are visible on magnetic resonance
images. Acceleration-deceleration
forces can also cause injuries of the
cranial nerves, the hypothalamus,
and the pituitary stalk. The damage
that occurs with the primary injury
is soon overtaken by the secondary
injury from the cerebral edema,
hemorrhage, or the hypoxia caused
by a chain of ischemic events at the
cellular level.

Ischemic Cascade of
Neuronal Cell Death

Secondary injury of the brain is
the damage that occurs seconds,
minutes, hours, or even days after
the traumatic event and may even
be superimposed on a mechanical
injury. Because of the primary
injury, oxygen and nutrients are not
delivered to brain cells. Hypoxia due
to decreased cerebral blood flow
results in biochemical processes
involving a cascade of ischemic
events. This hypoxia causes dysfunc-
tion in normal cellular metabolism,
and neurons die. The sequence of
events begins with a lack of oxygen
and cerebral perfusion, which causes
the cellular ion pumps to fail, lead-
ing to anaerobic metabolism and
buildup of lactic acid. Active trans-
port of cellular ions becomes
impaired, and calcium ions flow
into the neurons. Excitatory neuro-
chemical transmitter substances such
as glutamate are released, allowing
even more calcium into the cells.
This excess calcium causes release
of oxygen free radicals and excess
enzymes. The cell membrane is
damaged by these enzymes, the
mitochondria break down, and cel-
lar death occurs. When cells die,
more glutamate is released, more
cells in the area are injured, edema
increases, and the cascade spreads
to undamaged neurons.

Fluid and Electrolyte Imbalances

In addition to events at the cellu-
lar level, injury of the hypothalamus
and the pituitary gland from forces
transmitted to the head on impact,
along with cerebral edema, often
results in fluid and electrolyte dis-
turbances that profoundly affect
morbidity and mortality in TBI
patients. Three common electrolyte
imbalances are associated with the
hypothalamic-pituitary dysfunction
experienced by patients with TBI:
central neurogenic diabetes insipidus
(CNDI), syndrome of inappropriate
secretion of antidiuretic hormone
(SIADH), and cerebral salt-wasting
syndrome (CSWS). CNDI is associ-
ated with hypernatremia, whereas
SIADH and CSWS are associated
with hyponatremia. Early recog-
nition of all 3 syndromes is important
in patients with TBI to prevent fur-
ther neurological deterioration.

The pituitary gland, the pitu-
itary stalk, and the hypothalamus
are vulnerable to injury from head
trauma. The hypothalamic-neuro-
hypophyseal system is a collection
of nuclei and tracts located in the
hypothalamus and the pituitary
gland that regulate body water bal-
ance. The paraventricular and
supraoptic nuclei located in the

Authors

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hypothesis for osmoregulation or baroregulation. ADH release is increased, resulting in conservation of body fluids. When serum osmolality is less than 280 mOsm/kg, an excess of body water occurs (the blood is diluted) and ADH is not secreted. When osmolality is greater than 295 mOsm/kg, a loss of body water occurs (the blood is more concentrated). ADH is then secreted to stimulate the collecting tubules of the kidney to increase water reabsorption to maintain water balance. ADH is controlled by 2 principal negative-feedback mechanisms: osmoregulation and baroregulation. Osmoregulation is the mechanism used by the body to maintain water balance. Normal serum osmolality is 280 to 295 mOsm/kg. Even slight changes in serum osmolality can markedly affect ADH release. When serum osmolality is less than 280 mOsm/kg, an excess of body water occurs (the blood is diluted) and ADH is not secreted. When osmolality is greater than 295 mOsm/kg, a loss of body water occurs (the blood is more concentrated). ADH is then secreted to stimulate the collecting tubules of the kidney to increase water reabsorption to maintain water balance. ADH release is also affected by changes in blood volume and pressure. Baroreceptors located in the chest, left atrium, aortic arch, and carotid sinuses are sensitive to changes in blood pressure and circulating blood volume. Impulses from the baroreceptors are transmitted through the vagus and glossopharyngeal nerves to the paraventricular and supraoptic nuclei in the hypothalamus. Increases in blood volume and blood pressure result in decreased ADH secretion. In patients with hypotension and hypovolemia (common in patients with TBI), secretion of ADH is increased, resulting in conservation of body fluids. Even a 5% to 10% decrease in blood volume or a 5% decrease in mean arterial pressure can stimulate the release of ADH.

In general, the body first regulates ADH secretion in response to osmoregulation (concentration of body fluids). However, in severe volume depletion (hypotension or blood loss) baroreceptor stimulation of ADH takes precedence over osmoregulation.

Central Neurogenic Diabetes Insipidus

CNDI is characterized by an abnormal increase in urine output, an increase in fluid intake, and thirst due to decreased secretion of ADH, resulting in elimination of extracellular fluid. In trauma patients, CNDI is usually due to damage of the posterior part of the pituitary gland where ADH is stored and secreted. In patients with neurological conditions, CNDI is often associated with neurosurgery, tumors, increased intracranial pressure, brain death, and central nervous system infections such as meningitis or encephalitis. CNDI occurs in up to 16% of all brain-injured patients and usually occurs 5 to 10 days after trauma. CNDI usually occurs in 3 phases. The first phase consists of polyuria due to the inhibition of ADH that lasts a few hours or up to several days. The second phase (5-6 days) is characterized by near-normal urinary output because of the release of stored ADH. The third phase is transient or permanent excessive urinary output due to depletion of stored ADH or loss of functioning of the cells that produce ADH. If the lack of ADH is uncorrected in patients with TBI, CNDI results in severe dehydration and further worsening of electrolyte balance.

Signs and Symptoms. Signs and symptoms of CNDI include polyuria (large volumes of dilute urine, 250 mL/h), polydipsia (extreme thirst in patients who are awake and alert), hypovolemia, and hypernatremia. Urinary specific gravity is less than 1.005 (normal, 1.005-1.030), urine osmolality is less than 200 mOsm/kg, serum osmolality is elevated (>295 mOsm/kg), the serum level of sodium is elevated (>145 mEq/L), and the urine level of sodium is markedly decreased. Marked urinary losses of other electrolytes (potassium and magnesium) may occur simultaneously. Patients may also have weight loss of approximately 3% to 5% of body weight. Hypovolemia associated with CNDI in patients with TBI must be corrected. Other assessment findings may include indications of dehydration: confusion, irritability, poor skin turgor, dry mucous membranes, hypotension, and/or tachycardia.

Diagnosis. Diagnosis of CNDI in patients with TBI is based on clinical signs and symptoms and laboratory findings, specifically polyuria, low urinary specific gravity, low urine osmolality, hypernatremia, and elevated serum osmolality (see Table).
**Table**  Comparison of central neurogenic diabetes insipidus, syndrome of inappropriate secretion of antidiuretic hormone, and cerebral salt-wasting syndrome

<table>
<thead>
<tr>
<th>Feature</th>
<th>Central neurogenic diabetes insipidus</th>
<th>Syndrome of inappropriate secretion of antidiuretic hormone (ADH)</th>
<th>Cerebral salt-wasting syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Definition</strong></td>
<td>Fluid imbalance due to decreased secretion of ADH in the posterior lobe of the pituitary gland or to renal unresponsiveness to the release of ADH</td>
<td>Persistent production or overproduction of ADH resulting in water intoxication and a volume-expanded state</td>
<td>Renal loss of sodium leading to true hyponatremia and a volume-contracted state in which the kidneys do not reabsorb sodium</td>
</tr>
<tr>
<td><strong>Cause</strong></td>
<td>Hypotension, stress, pain, anxiety, and an upright position Trauma, surgery, or damage of the hypothalamus</td>
<td>Head trauma, brain tumor, abscess, subarachnoid hemorrhage, hydrocephalus, meningitis, encephalitis, Guillain-Barré syndrome Pneumonia Drugs associated with increased ADH secretion (oral hypoglycemic agents, nonsteroidal anti-inflammatory agents, opiates, anesthetics)</td>
<td>Cause unclear but often occurs in patients with intracranial abnormalities (head trauma, stroke, subarachnoid hemorrhage, brain tumors) Loss of both intravascular fluid and sodium</td>
</tr>
<tr>
<td><strong>Serum level of sodium, mEq/L</strong></td>
<td>Hypernatremia &gt;145 (high)</td>
<td>Hyponatremia &lt;135 (low)</td>
<td>Hyponatremia &lt;135 (low)</td>
</tr>
<tr>
<td><strong>Serum osmolality, mOsm/kg</strong></td>
<td>&gt;295 (high)</td>
<td>&lt;275 (low)</td>
<td>&lt;275 (low)</td>
</tr>
<tr>
<td><strong>Urinary osmolality, mOsm/kg</strong></td>
<td>Decreased (&lt;200)</td>
<td>Elevated (&gt;100)</td>
<td>Elevated (&gt;100)</td>
</tr>
<tr>
<td><strong>Urinary level of sodium, mEq/L</strong></td>
<td>Within normal reference range or decreased</td>
<td>Within normal reference range or elevated (&gt;25)</td>
<td>Elevated (&gt;25)</td>
</tr>
<tr>
<td><strong>Urine output</strong></td>
<td>Increased (&gt;250 mL/h)</td>
<td>Decreased (400-500 mL/24 h)</td>
<td>Decreased</td>
</tr>
<tr>
<td><strong>Urinary specific gravity</strong></td>
<td>&lt;1.005 (very dilute)</td>
<td>&gt;1.010 (concentrated, dark)</td>
<td>&gt;1.010 (concentrated, dark)</td>
</tr>
<tr>
<td><strong>Extracellular fluid volume</strong></td>
<td>Decreased</td>
<td>Increased</td>
<td>Decreased</td>
</tr>
<tr>
<td><strong>Serum urea nitrogen</strong></td>
<td>Elevated</td>
<td>Normal or low (dilutional)</td>
<td>Elevated</td>
</tr>
<tr>
<td><strong>Mental status</strong></td>
<td>Normal to impaired</td>
<td>Confusion Lethargy</td>
<td>Decreased level of consciousness, agitation, coma</td>
</tr>
<tr>
<td><strong>Body weight</strong></td>
<td>Decreased</td>
<td>Normal or increased</td>
<td>Decreased</td>
</tr>
<tr>
<td><strong>Heart rate</strong></td>
<td>Tachycardia</td>
<td>Slow or normal</td>
<td>Resting or postural tachycardia</td>
</tr>
<tr>
<td><strong>Blood pressure</strong></td>
<td>Normal to mildly hypertensive progressing to hypotension</td>
<td>Hypertensive</td>
<td>Postural hypotension</td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
<td>Fluid replacement (0.45% saline intravenously replaced milliliter for milliliter, or greater) ADH replacement with desmopressin acetate intranasally or orally, lypressin intranasally, or aqueous vasopressin intravenously</td>
<td>Fluid restriction (800-1000 mL/24 h) Slow sodium replacement with normal saline or hypertonic (3%-5%) saline intravenously</td>
<td>Replacement of fluid volume and sodium No restriction of fluids Slow sodium replacement with hypertonic (3%) saline intravenously</td>
</tr>
</tbody>
</table>

*Treatment.* The goal in CNDI is to correct the ADH deficiency and restore fluid balance by promoting sodium and water reabsorption. In the acute phase of CNDI, exogenous ADH is provided, and fluid equivalent to the amount of urine output is given either orally, if the patient can tolerate adequate oral intake, or intravenously. Patients with intact thirst centers who are able to take fluids orally are encouraged to drink as much as possible when thirsty to keep up with fluid losses. However, in patients with TBI, complications from impaired level of consciousness, sensory and motor deficits, and dysphagia often preclude oral
Intake, and intravenous solutions are required to meet the fluid demands. Intravenous hypotonic solutions most often used to replace lost body fluids include 0.45% saline titrated hourly to replace urine output. Exogenous ADH, either desmopressin (DDAVP), vasopressin, or lyspressin, may be administered. Desmopressin can be administered nasally 5 to 2 μg/d in divided doses or parenterally 5 to 40 μg/d in daily divided doses. Vasopressin (aqueous Pitressin) can be administered intravenously 0.5 to 2 U every 3 hours for patients who have urine output of more than 300 mL/h for 2 consecutive hours. Urinary output greater than 200 mL/h for more than 2 consecutive hours should be reported to a physician. Urinary specific gravity should be determined every 1 to 2 hours; low specific gravity (<1.005) indicates that the kidneys are not concentrating urine. Serum osmolality and electrolyte levels, specifically sodium and potassium levels, should be measured at least daily, and frequently more often, depending on the findings and the patient’s hemodynamic stability. Body weight should be determined daily, and patients should be assessed daily for signs and symptoms of worsening dehydration such as decreased skin turgor, dry mucous membranes, tachycardia, and hypotension. Trends are important. Is the patient getting worse? Or is the patient getting better? What do the laboratory values indicate?

**Syndrome of Inappropriate Secretion of Antiuretic Hormone**

SIADH is characterized by abnormally high levels or continuous secretion of ADH, causing renal reabsorption and retention of water. Water is continually being reabsorbed by the kidneys, leading to concentrated urine, fluid retention, and hyponatremia. Hyponatremia is the most common electrolyte problem in patients with neurological problems and is particularly common after TBI; up to 33% of patients with TBI have hyponatremia. Pathophysiologically, the negative feedback mechanisms that control the release of ADH do not function. In the general population of hospitalized patients, many precipitating factors can cause SIADH: bronchogenic carcinoma, lung disease, pneumonia, positive-pressure breathing during mechanical ventilation, and certain medications (eg, morphine, chlorpromazine, chlorpropamide, chlorothiazide, carbamazepine, and acetaminophen). Conditions that cause SIADH in patients with TBI include traumatic subarachnoid hemorrhage, increased intracranial pressure, and injury of the hypothalamic-neurohypophyseal system. The damage of the hypothalamic-pituitary region that causes ADH dysfunction results in increases in water reabsorption by the renal tubules, decreases in urine volume, fluid retention, and extracellular volume expansion. Patients experience excessive water retention and dilutional hyponatremia with a 5% to 10% increase in body weight due to expansion of extracellular volume.

**Signs and Symptoms.** The signs and symptoms of SIADH include decreased urinary output, to less than 400 to 500 mL/24 hours, and generalized weight gain due to excess fluid retention. Laboratory findings include low serum levels of sodium (<135 mEq/L), serum hypoosmolality (<275 mOsm/L), elevated urinary levels of sodium (>25 mEq/L), and elevated urine osmolality (greater than serum osmolality).

**Diagnosis.** Diagnosis of SIADH is based on the clinical signs and symptoms and laboratory findings. Complications due to SIADH and hyponatremia include fluid retention, headache, nausea, vomiting, muscle twitching, fatigue, confusion, lethargy, and, possibly, seizures.
(usually in patients with a serum level of sodium <120 mEq/L). In patients with TBI, the underlying pathological changes result in hyponatremia due to excessive ADH release, which causes renal reabsorption of water and expansion of extracellular volume.

Treatment. The treatment of SIADH is focused on fluid restriction (<1000 mL/24 h) and slow, careful replacement of sodium with an intravenous hypertonic solution of sodium chloride (3% saline) and/or diuretics such as furosemide. Medications to suppress ADH activity (demeclomycin hydrochloride) or inhibit renal response to ADH (lithium carbonate) are also options. Administration of hypertonic intravenous solutions such as 3% sodium chloride requires careful titration because a too-rapid correction of hyponatremia can result in central pontine myelinolysis, an irreversible demyelination of the neurons in the pons of the brain stem. The exact mechanism that causes demyelination is unknown; the recommended rate of serum sodium correction is 10 to 20 mEq/d.

Nursing Management. Nursing management for patients with SIADH and hyponatremia is comparable to the management of patients with CNDI. Intake of fluids, urinary output, and urinary specific gravity should be determined every 1 to 2 hours. Urinary and serum levels of electrolytes and osmolality should be monitored. Patients should be assessed for signs and symptoms of worsening outcome. Accurate body weights should be recorded daily for the purpose of monitoring fluid retention. Patients with SIADH require frequent oral care because fluid restriction causes dry mouth. Indications of improvement include correction of low serum levels of sodium, lowered urine osmolality, lowered urinary levels of sodium, and increased serum osmolality.

Cerebral Salt-Wasting Syndrome

Unlike SIADH, CSWS is characterized by a true hyponatremia, that is, hyponatremia that results in a loss of both sodium and extracellular fluid. Even though ADH levels are elevated in patients with CSWS, the body loses extracellular fluid and plasma volume decreases, resulting in decreased body weight (volume-contacted state). The pathophysiology of CSWS is unclear but is thought to be due to multiple mechanisms that affect sodium and water balance. The primary pathogenic mechanism is renal loss of sodium, which leads to hyponatremia and a decrease in extracellular volume. Although the syndrome occurs most often in patients with stroke, intracerebral hemorrhage, subarachnoid hemorrhage, and intracranial surgery, it may develop in patients with TBI who have increased intracranial pressure.

Signs and Symptoms. Patients with CSWS may report headache and increased thirst. Clinical indications include orthostatic hypotension, tachycardia, dehydration, weight loss, dry mucous membranes, lethargy, decreased level of consciousness, seizures, and coma.

Diagnosis. The diagnosis of CSWS is based on the clinical manifestations and the following laboratory findings: primary hyponatremia, serum hypoosmolality, elevated urine osmolality, elevated urinary levels of sodium, increased levels of serum urea nitrogen, increased hematocrit, and increased urinary specific gravity. Even though the mechanism of CSWS is not well understood, the primary distinction between CSWS and SIADH is volume status. Indications of volume depletion (hypotension, weight loss, and decreased skin turgor) occur with CSWS, whereas indications of volume expansion occur with SIADH (decreased urine output and generalized weight gain due to fluid retention).

Treatment. Determining the cause (SIADH or CSWS) of hyponatremia in trauma patients is important. SIADH requires strict fluid restriction and/or slow, judicious administration of hypertonic saline, whereas CSWS requires replacement of fluid volume with physiological saline and intravenous replacement with hypertonic 3% sodium chloride solution. As in treatment of SIADH, hypertonic solutions (3% sodium chloride) must be administered slowly because too-rapid correction of hyponatremia can result in central pontine myelinolysis. In patients who tolerate oral intake, fluid can be replaced orally, often with salt tablet supplements.

Restriction of fluids is contraindicated in patients with CSWS. If fluids are restricted, patients will be at risk for cerebral vasospasm, cerebral ischemia, and/or infarction. Other medical interventions may include treatment with fludrocortisone acetate to increase absorption of sodium by the renal tubules.

Nursing Management. Nursing management of patients with CSWS is comparable to that of patients with CNDI or SIADH. Isotonic or hypertonic fluids are administered intravenously to obtain positive fluid...
balance and correct volume depletion. Sodium can also be replaced orally. Cardiac status should be monitored to detect side effects of medications and fluid volume status. The goal of treatment of CSWS is to replace sodium and fluid volume with intravenous saline or salt tablets. Fluid restriction is definitely contraindicated and can worsen neurological outcomes.

Summary

Caring for patients with complex neurological problems, specifically patients with TBI and electrolyte imbalances, can be challenging. Understanding and recognizing the signs and symptoms of CNDI, SIADH, and CSWS will guide nurses in the appropriate actions to take to avoid deterioration in a patient’s condition. In summary, CNDI is a hypernatremia characterized by elevated serum levels of sodium and serum osmolality, but low urine specific gravity. Patients have large-volume urinary output and extreme thirst. Treatment is replacement of fluid volume either orally or intravenously or treatment with ADH.

SIADH and CSWS are both characterized by hyponatremia. Signs and symptoms are remarkably similar; however, patients with CSWS experiences a true loss of sodium and intravascular fluid. Both sodium and fluid must be replaced to correct the imbalance. In patients with SIADH, sodium is replaced, but fluid is restricted. Monitoring patients for trends in neurological status, laboratory findings, and physiological parameters will guide nurses in determining whether treatment is effective or not.

References