WATER-ELECTROLYTE IMBALANCE IN PATIENTS WITH TRAUMATIC BRAIN INJURY: CLINICAL MANIFESTATION AND TREATMENT

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ABSTRACT

Traumatic brain injuries represent a direct injury to the central nervous system. The presentation depends on the location, type, and severity of the injury. Fluid and electrolyte imbalance are common after traumatic brain injury and may manifest as abnormalities in sodium, potassium, chloride, and calcium levels. Changes in serum sodium levels are the most common and critical electrolyte abnormality. Plasma sodium concentration is a major determinant of plasma osmolality and is maintained by the secretion of antidiuretic hormone or arginine vasopressin and the sensation of thirst. For decades, disturbances in salt and water balance due to impaired secretion of arginine vasopressin have been recognized after traumatic brain injury. Which can be manifest as arginine vasopressin deficiency, formerly called central diabetes insipidus, leading to hypernatremia, or arginine vasopressin excess, leading to the syndrome of inappropriate antidiuretic hormone secretion and hyponatremia. Dysnatremia is associated with a higher risk of secondary brain injury from the resulting changes in brain fluid levels, greater morbidity, and longer hospital stays. Posterior pituitary dysfunction following traumatic brain injury, along with alterations in arginine vasopressin release and dysnatremia, most commonly occurs in the acute phase of injury, is often transient, and resolves in most patients after recovery from the initial injury. Most importantly, in both hypo and hypernatremia, early detection and prompt appropriate treatment often save lives.

Key words: traumatic brain injury, water-electrolyte imbalance, diabetes insipidus, SIADH, CSWS

INTRODUCTION

Traumatic brain injury is one of the most common causes of death among individuals at the age ranging from 1 to 35 years that leads to various disabilities with a high socioeconomic burden. The total incidence of traumatic injuries is estimated at 538.3 per 100,000 population (1).

Traumatic brain injury is classified into primary and secondary. The usual mechanisms of primary traumatic brain injury include direct impact, rapid acceleration/deceleration, penetrating injury, and blast-related injury. Although these mechanisms are heterogenous, they share the common characteristic of externally applied mechanical forces to the brain. The resulting trauma includes focal cerebral contusions, hematomas, and diffuse axonal lesion, all of which are

associated with cerebral edema. Secondary brain injury develops as a result of complex molecular mechanisms initiated at the time of the primary trauma and evolve over hours or days. Some of these mechanisms include excessive glutamate-mediated stimulation, free radical-induced cell membrane damage, mitochondrial dysfunction, damage to the vascular wall, inflammatory reactions, apoptosis, ischemia due to vasospasm, local microcirculatory occlusion, and electrolyte abnormalities (2,3).

Serum electrolyte imbalances in patients with traumatic brain injury are considered preventable secondary complications. They may result directly from brain injury, iatrogenic factors, or other coexisting conditions such as renal insufficiency, cirrhosis, and congestive heart failure (4,5). The risk of electrolyte imbalance in patients with traumatic brain injury depends on injury severity, the presence or absence of comorbidities, patient age, and initial treatment strategies, such as adequate choice of fluids for resuscitation, administration of mannitol or diuretics and hyperventilation (6). Early recognition of serum electrolyte disturbances may reduce mortality and morbidity rates associated with primary and secondary brain trauma.

The aim of this paper is to present the common serum electrolyte imbalances and their clinical manifestations in patients with traumatic brain injury.

MATERIAL AND METHODS

In this review article, a comprehensive literature research was performed using PubMed and Google Scholar databases. The following key words or medical subject headings were used: “traumatic brain injury”, “water-electrolyte imbalance”, “diabetes insipidus”, “SIADH”, “CSWS”. The most relevant and recent literature, were examined and summarized.

DISCUSSION

Patients with traumatic brain injury frequently develop electrolyte imbalances that may be manifested as abnormalities in the levels of sodium, potassium, chloride, and calcium. Among these, serum sodium disorders are the most common and clinically significant electrolyte abnormalities (7).

Serum sodium concentration is the principal determinant of plasma osmolality, and is maintained in a close physiological range by central osmoregulation through the secretion of antidiuretic hormone or arginine vasopressin (AVP) and thirst mechanisms. Arginine vasopressin is released in response to increased plasma osmolality (8). Traumatic brain injury is defined as any brain injury caused by external force and can lead to dysfunction of hypothalamic-pituitary axis.

By examining autopsy samples after fatal head injury, Kibayashi et al. identified infarction or hemorrhage of the pituitary gland in 40.9% of cases, as well as hypothalamic infarction (9). The supraoptic and paraventricular nuclei were most commonly affected sites of injury leading to denervation of the posterior hypophysis and impaired arginine vasopressin release (9,10). For decades, salt and water imbalance due to altered secretion of arginine vasopressin have been

recognized following traumatic brain injury, and they may manifest as arginine vasopressin deficiency (formerly known as central diabetes insipidus). It leads to hypernatremia, or excess arginine vasopressin, resulting in the syndrome of inappropriate diuresis (SAID) and hyponatremia (11). Dysfunction of the posterior hypophysis most often occurs after acute traumatic brain injury and resolves in the majority of cases (12).

The pattern of water-electrolyte and endocrine abnormalities after brain trauma vary depending on the site of injury. Hypothalamic injury may cause anterior hypopituitarism, diabetes insipidus, or inappropriate secretion of antidiuretic hormone (13). Damage to the posterior hypophysis alone does not usually lead to permanent diabetes insipidus, as ADH synthesized in the hypothalamic nuclei may still be found into the peripheral circulation. After transection of the pituitary stalk, a three-phase response has been described (initially DI, followed a few days later by transient SIADH and later recurrence of DI, either transient or permanent) (14).

Post-traumatic diabetes insipidus

Diabetes insipidus (DI) is a hormonal disorder caused by reduced secretion or impaired action of antidiuretic hormone (ADH, vasopressin). It is classified into central and nephrogenic diabetes insipidus. Central diabetes insipidus occurs following damages to vasopressinergic neurons due to trauma, neoplasms, neurosurgical procedures, or autoimmune inflammations that involve neurons secreting vasopressin (15).

Diabetes insipidus is a rare disorder with a prevalence of 1 per 25,000 individuals considering all causes. However, its incidence reaches up to 20% of patients with moderate or severe traumatic brain injury. The onset of diabetes insipidus is associated with brain death, and is present in 80% of brain-dead patients (16). No clear age or sex predisposition has been identified. It is noteworthy that post-traumatic diabetes insipidus may persist from several days to several weeks and is associated with high mortality rates (57%-69%), particularly when it develops very early after traumatic injury (86%-90%) (17).

Many reports confirm diabetes insipidus often following the criteria proposed by Seckl and Dunger (polyuria >3l, urine osmolality below 300 mOsm/kg, hypernatremia >145 mmol/L) (18).

Patients with DI lose their ability to concentrate urine and excrete large volumes of dilute urine (polyuria) resulting in polydipsia. Predominant manifestations of diabetes include hypotonic polyuria with diuresis exceeding 50 mL/kg within 24 hours and polydipsia with fluid intake greater than 3 L/day. Most patients with diabetes insipidus are in a poor health condition and frequently present with impaired consciousness (due to the direct traumatic effect, cerebral edema, intracranial hemorrhage or sedative medications used in intensive care units) on their admission to the intensive care unit. They may be unable to express their feeling of thirst or to maintain adequate oral intake. In such cases, the excessive volume of inadequately dilute urine output and hypernatremia are key indicators for establishing the diagnosis**.** Inadequate fluid intake combined with rapid renal water loss may lead to severe dehydration and hypovolemic hypernatremia (with hypotension and reduced cerebral perfusion pressure) (19).

The diagnosis of PTDI is not always simple. Patients in intensive care units often require interventions such as shock management, blood product transfusion, and correction of circulating volume, as well as treatment of the increased intracranial pressure with hyperosmolar substances or barbiturate administration, that is, therapeutic procedures that may influence on establishing the diagnosis of DI.

Once polyuria is identified, it is necessary to exclude other causes for large urine loss (often encountered in patients with trauma as a result of hypercatabolic condition and medications), administration of hyperosmolar agents (e.g., mannitol or hypertonic saline solution), or diuretic therapy (20).

However, confirming of diagnosis of DI includes 24-hour urine collection with measurement of urine volume, urine and plasma osmolality, as well as serum sodium concentration, and copeptin levels. Plasma osmolality > 280 mOsm/kg and sodium levels > 147 mEq/L support the diagnosis of diabetes insipidus. The water deprivation test has been used as a standard method for diagnosing DI for years, although its diagnostic accuracy is approximately 70%. Following the water deprivation test no increased ADH release has been identified, and hypotonic urine continues to be excreted. For definitive establishment of the diagnosis of diabetes insipidus, additional tests may be necessary such as administration of hypertonic saline infusion or testing the arginine stimulation. The test with hypertonic physiological solution can be used for differentiation between patients with primary polydipsia and patients with central diabetes insipidus, with 93% sensitivity and 100% specificity. This test is performed with infusion of 250 mL 3% hypertonic physiological saline within 15 minutes, followed by measuring the copeptin and sodium levels every 30 minutes. The infusion is stopped once the plasma sodium concentration reaches ≥147–150 mmol/L, at which point the final copeptin sample is taken and value above 4.9 pmol/L indicates a condition of primary polydipsia (PP). Regarding the arginine test, if serum copeptin is <3.8 pmol/L after a 60-minute arginine infusion, then the diagnosis is central diabetes insipidus. Intravenous infusion of arginine had a diagnostic accuracy of 93% in the differential of CDI and PP. In situations where it is necessary to distinguishes between central and nephrogenic diabetes insipidus, copeptin values ≤ 4.9 pmol/L are specific for central diabetes insipidus, while levels ≥ 21.4 pmol/L indicate nephrogenic diabetes insipidus. Also, magnetic resonance (MRI) has been applied as diagnostic tool. Pituitary stalk hematoma or loss of the bright signal intensity of the pituitary posterior lobe on T1-weighted scans are occasionally seen. An ectopic bright spot in cases with stalk transection has been rarely described. In some cases, cerebral CT/MRI do not show any abnormal findings, meaning that some hypoxic damage or diffuse axonal injury has occurred (21,22).

Treatment of patients with diabetes insipidus in intensive care units follows the same general intensive care principles as for the other critically ill patients, including careful monitoring of vital signs, blood pressure, pulse, diuresis, cerebral perfusion pressure, intracranial pressure, GCS, oxygenation status, hydration status, standard laboratory parameters, urine specific weight, plasma and urine osmolality, serum sodium levels (23,24).

After diagnosing DI, the initial approach is aimed at fluids compensation to avoid dehydration (related to negative outcome in patients with acute injury to the head) (25). In conscious patients,

with preserved thirst mechanisms and good general physical condition, oral fluid intake may adequately compensate for renal water losses. In patients with impaired consciousness, which is most commonly seen in patients in intensive care units with associated neurological deficit, dysphagia or changes in the thirst mechanism, hypotonic polyuria may rapidly lead to hypovolemia and hypernatremia. Initially, hypovolemia should be corrected with intravenous administration of fluids and evaluation of the volume status is mandatory. Five percent dextrose solution is recommended for free water replacement (26).

Fluid correction must be made with close clinical monitoring and CVP measurement to avoid both under-resuscitation (related to hypovolemia and reduced CPP) or over-resuscitation (that can exacerbate cerebral edema, increase intracranial pressure and may cause lung edema). The free water deficit may be calculated using the following formula:

(0.6[weight in kilograms])x(serum sodium-140):140=body water deficit (in liters) (27).

By fluids correction, serum sodium levels would be reduced. In cases of severe hypernatremia (>150 mmol/L), the correction should be carefully made as the brain tissue is too sensitive to rapid osmotic changes that lead to aggravation of cerebral edema. The recommended rate of sodium reduction should not exceed 0.5 mmol/h or 10-12 mmol/L/24 hours. The treatment should include hormone substitution with desmopressin, particularly in patients with urine output exceeding >250 mL/hour (28,29).

Desmopressin is the treatment of choice for central diabetes insipidus and may be administered orally, intranasally, subcutaneously, or intravenously. Oral doses of desmopressin range from 0.05 mg to 0.8 mg (in divided doses) daily. The oral form is weaker than the nasal one since only 5% is reabsorbed by the intestines. Intranasal dosing typically ranges from 10 mcg to 20 mcg per day. Intravenous or subcutaneous administration is used for acute diabetes insipidus (30).

Syndrome of inappropriate antidiuretic hormone secretion (SIADH)

Syndrome of inappropriate antidiuretic hormone secretion (SIADH) is a condition characterized by excessive release or action of antidiuretic hormone (ADH), which results in water retention and subsequent hyponatremia. SIADH is associated with various etiologies, and is most commonly combined with lung malignant tumors, surgical interventions, medications and central nervous system disorders. Traumatic brain injury is the cause of approximately 2.5% of SIADH cases (31). This disorder usually originates from injuries to the osmoreceptors or volume receptors of the hypothalamus and hypophysis, where ADH is produced and secreted. However, it may also result from changes in the renal tubules, specifically the collecting ducts, and their inappropriate reaction to ADH (32). Regarding traumatic brain injury, there are basically limited data related to specific injury sites associated with SIADH and the mechanisms of its onset (33).

It is estimated that in 33% of patients with traumatic brain injury, hyponatremia and SIADH develop. The clinical presentation of SIADH in patients with TBI depends on the type of trauma and Na+ concentration. According to the study by Moro et al., the incidence of SIADH varied depending on injury type, where 47.9% of patients had cerebral contusions, 34.8% had acute

subdural hematomas, 25% had acute epidural hematomas and 15.9% had chronic subdural hematomas (34). Majority of hyponatremia cases occur within first four to ten days after injury, but rare cases of persistent hyponatremia lasting for years have been reported (35).

With regards to hyponatremia, the severity of symptoms correlates with the rapidity of onset of hyponatremia and with its severity. As hyponatremia develops, all cells absorb water causing cellular swelling. This process is problematic to the brain, which is enclosed within an inextensible skull. Astrocytes are especially sensitive to osmotic stress, although the excretion of potassium and other electrolytes within 6 to 12 hours and organic osmolytes, including glutamine and taurine within 24 to 48 hours, reduce the content of cellular soluble substances and help in diminishing edema in case of hyponatremia. Taking into consideration the time course, acute hyponatremia is defined as a condition in which hyponatremia develops within 48 hours, whereas chronic hyponatremia persists for a longer period and develops in majority of cases. In severe hyponatremia, Na+ <125 mEq/L, which develops within less than 48 hours, and absorption of water in the brain overwhelm compensatory mechanisms, symptoms are primarily neurological and progress to mild clinical picture involving nausea, vomiting, lethargy, headaches, confusion and muscle spasms. Severe complications of acute deep hyponatremia involve cerebral edema, seizures, coma, brainstem herniation, and neurogenic pulmonary edema. It is considered that long-term hyponatremia may be symptomatic if severe, although many patients with chronic mild to moderate hyponatremia remain asymptomatic (36).

The diagnosis of SIADH is based on clinical signs and symptoms and laboratory findings. Laboratory findings include low serum sodium levels (<135 mEq/L), low plasma osmolality (<275 mOsm/L), increased urine sodium levels (>25 mEq/L), and increased urine osmolality (greater than serum osmolality) (37).

Osmotic demyelination syndrome (ODS) is associated with rapid correction of hyponatremia. In patients with acute hyponatremia, it develops within 24 to 48 hours, and in patients with initial sodium [Na+] levels >125 mEq/L, treatment is not associated with osmotic demyelination syndrome. On the other hand, chronic hypotonic hyponatremia and [Na+] serum levels of <105 mEq/L represent major risk factors for ODS.

In acute hyponatremia, Na+ normalization does not carry a risk of ODS; the correction rate need not be restricted when hyponatremia duration is less than 48 hours. In chronic hyponatremia, [Na+] levels should be increased to prevent the risk of severe complications such as seizures or brain herniation while minimizing the risk of ODS. Studies have shown that in patients with chronic hyponatremia no post-therapeutic neurological complications occurred when [Na+] correction was <12 mEq/L within 24 hours or <18 mEq/L within 48 hours. Also, no post-therapeutic neurological symptoms were observed in patients where [Na+] increased to <0.55 mEq/L per hour until a sodium concentration of 120 mEq/L was reached (38).

Initially, SIADH is treated by water intake restriction (<1000 mL/24 hours). Practical guidelines from Italian Society of Endocrinology (SIE) and U.S. guidelines indicate that urine osmolality greater than 500 mOsm/kg is a strong predictor of a poor response to fluid restriction. According to SIE Practice Guidelines, U.S. and British guidelines, the expected effectiveness rate of fluid

restriction can be estimated using the Furst formula, which calculates the ratio of the sum of urine potassium and sodium concentrations to serum sodium concentration. A ratio >1 requires the need for strict water restriction (<500mL/d), and at the same time, predicts treatment failure of fluid and water restriction alone, leading to worsening hyponatremia (39,40,41).

Fluid restriction alone is not efficient in many cases of SIADH where the underlying cause persists.

Sodium supplementation using intravenous sodium chloride is another therapeutic option. Fluids of varying tonicity (isotonic saline, 3% physiological solution) can be used in treatment of different types of hyponatremia. Which fluid would be selected depends on the etiology, severity of hyponatremia, and the presence of symptoms. In general, isotonic solution is used in treatment of hypovolemic hyponatremia. In some cases of severe hyponatremia (serum sodium <120 mEq/l), hypertonic saline is needed. Patients with acute severe hyponatremia are treated with a rapid increase in serum sodium level of 4-6 mmol/l within 4 hours, which results in reducing intracranial pressure and managing herniation in approximately 50% per hour. In practice, this can be achieved by administering a 100 ml bolus of 3% physiological solution over 15 minutes, which may be repeated up to three times. In patients with mild or moderate symptoms, infusion of 3% physiological solution at a rate of 0.5–2 ml/kg/h is the initial approach, with frequent measurements of serum sodium levels (42).

Two pharmacological treatment options for hyponatremia, vaptans and urea osmotic agent, deserve more detailed discussion. Conivaptan is a non-selective inhibitor of vasopressin V1 and V2 receptors, whereas tolvaptan selectively inhibits V2. The results of placebo-controlled randomized clinical trials showed that conivaptan increased Na+ level by approximately 8 mEq/L within several days, and tolvaptan by approximately 5 mEq/L within four days after administration of an initial dose of 15 mg and titrated up to 60 mg daily. The initial expectation was that with their ability to antagonize the effect of excess vasopressin, would make them more efficient and consequently, they would be widely used. However, as expected, not a single agent can be used long-term. Conivaptan is a potent CYP3A4 inhibitor with many drug-drug interactions, and is approved by the U.S. Food and Drug Administration only for short-term intravenous use. Long-term use of tolvaptan is restricted due to concerns about hepatic damage. In Europe, only oral tolvaptan is approved for treatment of SIADH.

Urea is a long-established and cost-effective alternative to vaptans in treatment of SIADH. It is excreted in urine, increases urinary soluble substances and enhances electrolyte-free water clearance. Retrospective studies suggest that administration of 7.5 to 90 g/d urea is associated with Na+ level of ~6 mEq/L over 4 to 5 days. Urea therapy is generally not associated with serious side effects such as overly rapid correction of Na+.

It is important to emphasize that vaptans or urea should be taken into consideration only in patients with euvolemic or hypervolemic hyponatremia with mild to moderate symptoms, and not in cases where [Na+] should be rapidly increased. In addition, vaptans should not be used in combination with hypertonic saline, according to reported cases associated with ODS (43).

Demeclocycline, an antibiotic drug (600-1200 mg/day), and lithium carbonate, an antidepressant (600-900 mg/day) can cause nephrogenic diabetes insipidus, and this effect has historically been used in the treatment of hyponatremia in SIADH. Also, loop diuretics may be used for treatment of SIADH to increase water excretion (44).

A personalized treatment approach to SIADH based on the severity of hyponatremia, symptoms and individual patient risk factors are of crucial significance to ensure safe and efficient treatment.

Cerebral Salt Wasting Syndrome CSWS

Cerebral salt wasting syndrome (CSWS) is characterized by hyponatremia caused by renal sodium wasting, and the primary distinguishing feature from similar conditions is decreased extracellular fluid volume. CSWS was first described by Peters et al. in 1950. Together with the syndrome of inappropriate antidiuretic hormone (SIADH), CSWS represents one of the most common causes of hyponatremia in neurologic patients. Some authors define CSWS to be a subtype of SIADH. It is of crucial importance to make accurate differentiation between these two disorders to ensure appropriate treatment. Evaluating volemia is an important clinical characteristic that helps in distinguishing between the two syndromes. CSWS is a hypovolemic hyponatremia, induced by increased natriuresis and diuresis (45) (Table 1) (46).

Table 1. Differences in clinical manifestation between SIADH and CSWS

Feature Clinical	SIADH	CSWS
Central venous pressure	Normal or increased	Decreased
Orthostatic hypotension	Absent	Present
Body weight	Increased	Decreased
Fluid balance	Positive	Negative
Plasma volume	Increased	Decreased

Any form of cerebral aggression has the potential to lead to hypernatremia syndrome. In most cases, CSWS is associated with subarachnoid hemorrhages (SAH); however, it has also been observed in neurological and meningeal tuberculous infections, as well as postoperative complications following tumor resection (47). CSW syndrome has been reported in patients with severe traumatic brain injury, most frequently resulting from road traffic accidents, but also injuries from firearms. Several theories have been proposed to explain the causality of sodium wasting in CSWS. One of the current theories suggests reduced sympathetic stimulation of juxtaglomerular apparatus, which leads to decreased reabsorption of sodium, urates and water. In addition, it is associated with reduced secretion of renin and aldosterone (47,48). Another theory proposes elevated levels of brain natriuretic peptide (BNP) and atrial natriuretic peptide (ANP) in patients with SAH, resulting in renal sodium and water loss (47).

The diagnosis is based on clinical manifestations (Table 1) and biochemical analyses.

Biochemical criteria for CSWS are: low or normal serum sodium levels, elevated or normal serum osmolality, increased or normal urine osmolality, elevated hematocrit, urea, bicarbonate and albumin levels as a consequence of hypovolemia.

However, these criteria are often inconclusive. In CSWS, the total daily urinary sodium excretion exceeds sodium intake.

Additional parameters contributing to establishing the diagnosis of CSWS, and differentiating it from SIADH include monitoring the fractional excretion of uric acid and fractional excretion of phosphates. Fractional excretion of uric acid (FEUA) exceeds 10% in both syndromes. After hyponatremia correction in patients with SIADH, it decreases, but in patients with CSWS it remains high. Fractional excretion of phosphate (FEP) is normal (<10%) in patients with SIADH and increased (>20%) in patients with CSWS, making it a useful criterion for differentiation between these pathological conditions (45).

Treatment of CSWS consists of correcting hypovolemia and hyponatremia. First-line therapy includes hydration with saline solutions, either isotonic or hypertonic, depending on the severity of symptoms. Sodium supplementation should be gradual, avoiding an increase in sodium of more than 10 mmol/L within the first 24 hours (47). Other drugs studied in cases of neurocritical hyponatremia are fludrocortisone at doses of 0.1 to 0.4 mg, which has a direct effect on the proximal renal tubules, enhancing sodium reabsorption (47,49,50). If hypothalamic-pituitary region is affected, refractory polyuria may occur, and treatment with 1-deamino-8-D-arginine vasopressin (DDAVP) can be useful. However, its use remains controversial, as it may reduce urine volume, while simultaneously increasing production of natriuretic peptide, thereby worsening hyponatremia (51,52).

Regarding other electrolyte disturbances, it has to be pointed out that hyperkalemia has been reported in 17.77% of patients with traumatic brain injury, with a prevalence of 29% within the first 12 hours after admission. It is considered to be the result of catecholamine release, blood product transfusions, pharmacologic agents such as succinylcholine, acidosis and tissue ischemia. In contrast, hypokalemia typically occurs immediately after injury and reaches its peak during the first few days, primarily due to potassium shifts induced by catecholamines, renal

potassium loss, fluid deficit, and hyponatremia. Disturbances in calcium and chloride levels are also important in patients with traumatic brain injury. Hypercalcemia frequently occurs as a consequence of prolonged immobility or hyperparathyroidism. Hypocalcemia may develop during massive transfusions and is associated with severe coagulopathy and higher mortality. Hyperchloremia may develop acutely during the first days following TBI, which coincides with the phase of hyperemia characterized by increased cerebral blood flow and reduced arterio-jugular venous oxygen differences. Hypochloremia as well as the other electrolyte abnormalities has also been observed in patients with severe TBI and is associated with increased mortality (53).

CONCLUSION

Electrolyte disturbances are common in patients with traumatic brain injury. They are important but correctable cause of neurologic deterioration. Imbalance in sodium level show the highest incidence, and electrolyte abnormalities usually occur in the first days after injury. Their early recognition and appropriate management as well as timely treatment not only improve patient neurological status, but also reduce morbidity, mortality and socioeconomic losses in the country.

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REFERENCES

1.Rutland-Brown W, Langlois JA, Thomas KE, Xi YL. Incidence of traumatic brain injury in the United States, 2003. J Head Trauma Rehabil. 2006; 21(6):544-8. [DOI:10.1097/00001199-200611000-00009] [PMID]

2.Williamson C, Rajajee V. Traumatic brain injury: Epidemiology, classification, and pathophysiology. UpToDate. 2021. [Link]

3.Buhary BM, Alrajhi SM, Abukhater M, Kyadudyn AM, SM AF, Rahman AK, et al. Acid Base Electrolyte Imbalance and Survival Outcome of Low Glasgow Coma Scale (GCS) patients in the Medical Intensive Care Unit. Ann Med Health Sci Res. 2017; 7:10-5. [Link]

4.Stocchetti N, Pagan F, Calappi E, Canavesi K, Beretta L, Citerio G, et al. Inaccurate early assessment of neurological severity in head injury. J Neurotrauma. 2004; 21(9):1131-40. [DOI:10.1089/neu.2004.21.1131] [PMID]

5.Stratton SJ. Glasgow coma scale score in trauma triage: A measurement without meaning. Ann Emerg Med. 2018; 72(3):270-1. [DOI:10.1016/j.annemergmed.2018.06.036] [PMID]

6.Ali Z, Prabhakar H. Fluid management during neurosurgical procedures. J Neuroanaesth Crit Care. 2016; 3(04):S35-40. [DOI:10.4103/2348-0548.174733]

7. Saurabh, S.; Neeraj, K.; Singh, Y.; Kumar, Ghanshyam, S.Y.; Gupta, B.K.; EYa, R.; Ey, S. Evaluation of Serum Electrolytes in Traumatic Brain Injury Patients: Prospective Randomized Observational Study. J. Anesth. Crit. Care Open Access 2016, 5.

8. Sterns RH, Silver SM. Brain volume regulation in response to hypo-osmolality and its correction The American Journal of Medicine. 2006;119(7):S12-16 Volume 119, Issue 7, Supplement 1, July 2006, Pages S12-S16

9. Tomkins M, Green D, O'Reilly MW, Sherlock M. Fluid and electrolyte disorders following traumatic brain injury. Best Practice & Research Clinical Endocrinology & Metabolism. 2025:39(3):102014

10.Januszewska A, Kluczyński L, Hubalewska-Dydejczyk A.Traumatic brain injuries induced pituitary dysfunction: a call for algorithms Endocr Connect.2020 May;9(5):R112-R123. doi: 10.1530/EC-20-0117.

11.Martin-Grace J, Tomkins M, O'Reilly MW, Thompson JC, Sherlock M. Approach to the patient: hyponatremia and the syndrome of inappropriate antidiuresis (SIAD).J Clin Endocrinol Metab. 2022 Jul 14;107(8):2362-2376. doi: 10.1210/clinem/dgac245.

12. Hoffman H, Jalal M, Lawrence S. Effect of hypernatremia on outcomes after severe traumatic brain injury: a nationwide inpatient sample analysis. World neurosurgery.2018;118:e880-886

13.Yuan X.Q., Wade C.E. Neuroendocrine abnormalities in patients with traumatic brain injury. Front. Neuroendocrinol. 1991;12:209–230. [PubMed] [Google Scholar]

14.Hensen J., Henig A., Fahlbusch R., Meyer M., Boehnert M., Buchfelder M. Prevalence, predictors and patterns of postoperative polyuria and hyponatraemia in the immediate course after transsphenoidal surgery for pituitary adenomas. Clin. Endocrinol. (Oxf.) 1999;50:431–439. doi: 10.1046/j.1365-2265.1999.00666.x. [DOI] [PubMed] [Google Scholar]

15.Tomkins, M.; Lawless, S.; Martin-Grace, J.; Sherlock, M.; Thompson, C.J. Diagnosis and Management of Central Diabetes Insipidus in Adults. J. Clin. Endocrinol. Metab. 2022, 107, 2701. [Google Scholar] [CrossRef]

16.Ranasinghe A.M., Bonser R.S. Endocrine changes in brain death and transplantation. Best. Pract. Res. Clin. Endocrinol. Metab. 2011;25:799–812. doi: 10.1016/j.beem.2011.03.003. [DOI] [PubMed] [Google Scholar]

17.Karali V., Massa E., Vassiliadou G., Chouris I., Rodin I., Bitzani M. Evaluation of development of diabetes insipidus in the early phase following traumatic brain injury in critically ill patients. Crit. Care. 2008;12:S51–S52. doi: 10.1186/cc6351. [DOI] [Google Scholar]

18.Seckl J.R., Dunger D.B., Lightman S.L. Neurohypophyseal peptide function during early postoperative diabetes insipidus. Brain. 1987;110:737–746. doi: 10.1093/brain/110.3.737. [DOI] [PubMed] [Google Scholar]

19.Stern R.H. Disorders of plasma sodium. N. Engl. J. Med. 2015;372:55–65. doi: 10.1056/NEJMra1404489. [DOI] [PubMed] [Google Scholar]

20.Adrogue H.J., Madias N.E. Hypernatremia. N. Engl. J. Med. 2000;342:1493–1499. doi: 10.1056/NEJM200005183422006. [DOI] [PubMed] [Google Scholar]

21.Su D.H., Chang Y.C., Chang C.C. Post-traumatic anterior and posterior pituitary dysfunction. J. Formos. Med. Assoc. 2005;104:463–467. [PubMed] [Google Scholar]

22.Shin J.H., Lee H.K., Choi C.G., Suh D.C., Kim C.J., Hong S.K., Na D.G. MR imaging of central diabetes insipidus: A pictorial essay. Korean J. Radiol. 2001;2:222–230. doi: 10.3348/kjr.2001.2.4.222. [DOI] [PMC free article] [PubMed] [Google Scholar]

23.Helmy A., Vizcaychipi M., Gupta A.K. Traumatic brain injury: Intensive care management. Br. J. Anaesth. 2007;99:32–42. doi: 10.1093/bja/aem139. [DOI] [PubMed] [Google Scholar]

24.John C.A., Day M.W. Central neurogenic diabetes insipidus, syndrome of inappropriate secretion of antidiuretic hormone, and cerebral salt-wasting syndrome in traumatic brain injury. Crit. Care Nurse. 2012;32:e1–e7. doi: 10.4037/ccn2012904. [DOI] [PubMed] [Google Scholar]

25.Clifton G.L., Miller E.R., Choi S.C., Levin H.S. Fluid thresholds and outcome from severe brain injury. Crit. Care Med. 2002;30:739–745. doi: 10.1097/00003246-200204000-00003. [DOI] [PubMed] [Google Scholar]

26.Haddad S.H., Arabi Y.M. Critical care management of severe traumatic brain injury in adults. Scand. J. Trauma Resusc. Emerg. Med. 2012;20:12. doi: 10.1186/1757-7241-20-12. [DOI] [PMC free article] [PubMed] [Google Scholar]

27.Urdan L, Stacy K, Lough M, eds. Endocrine disorders and therapeutic management. In: Thelan's Critical Care Nursing: Diagnosis and Management. (5th ed) . St Louis, MO: Mosby-Elsevier; 2006:918–966. Google Scholar

28.Stern R.H. Disorders of plasma sodium. N. Engl. J. Med. 2015;372:55–65. doi: 10.1056/NEJMra1404489. [DOI] [PubMed] [Google Scholar]

29.Overgaard-Steensen C., Ring T. Clinical review: Practical approach to hyponatraemia and hypernatraemia in critically ill patients. Crit. Care. 2013;17:206. doi: 10.1186/cc11805. [DOI] [PMC free article] [PubMed] [Google Scholar]

30.Christ-Crain, M.; Winzeler, B.; Refardt, J. Diagnosis and management of diabetes insipidus for the internist: An update. J. Intern. Med. 2021, 290, 73–87. [Google Scholar] [CrossRef]

31. Cuesta M, Garrahy A, Thompson CJ. SIAD: practical recommendations for diagnosis and management. J Endocrinol Invest. (2016) 39:991–1001. doi: 10.1007/s40618-016-0463-3

32.Martin-Grace, J.; Tomkins, M.; O'Reilly, M.W.; Thompson, C.J.; Sherlock, M. Approach to the Patient: Hyponatremia and the Syndrome of Inappropriate Antidiuresis (SIAD). J. Clin. Endocrinol. Metab. 2022, 107, 2362–2376. [Google Scholar] [CrossRef] [PubMed]

33.Dick, M.; Catford, S.R.; Kumareswaran, K.; Hamblin, P.S.; Topliss, D.J. Persistent syndrome of inappropriate antidiuretic hormone secretion following traumatic brain injury. Endocrinol. Diabetes Metab. Case Rep. 2015, 2015, 150070. [Google Scholar] [CrossRef]

34.Moro, N.; Katayama, Y.; Igarashi, T.; Mori, T.; Kawamata, T.; Kojima, J. Hyponatremia in patients with traumatic brain injury: Incidence, mechanism, and response to sodium supplementation or retention therapy with hydrocortisone. Surg. Neurol. 2007, 68, 387–393. [Google Scholar] [CrossRef]

35.Chen L, Xu M, Zou Y, Xu L. Clinical analysis of brain trauma-associated SIADH. Cell Biochem Biophys. (2014) 69:703–6. doi: 10.1007/s12013-014-9856-0

36.Kengne FG, DecauxG. Hyponatremia and the Brain.Kidney Int Rep(2018)3,24–35; https://doi.org/10.1016/j.ekir.2017.08.015

37.Byrum D, Kirkwood PL. Pituitary, thyroid, and adrenal disorders. In: Carlson KK, ed. AACN Advanced Critical Care Nursing. St Louis, MO: Saunders/Elsevier; 2009:939–965. Google Scholar

38.Tandukar S, Sterns RH, Rondon-Berrios H. Osmotic Demyelination Syndrome following Correction of Hyponatremia by ≤10 mEq/L per Day.Kidney360. 2021 Jul 8;2(9):1415–1423. doi: 10.34067/KID.0004402021

39.Cuesta M, Garrahy A, Thompson CJ. SIAD: practical recommendations for diagnosisand management. J Endocrinol Invest. (2016) 39:991–1001. doi: 10.1007/s40618-016-0463-3

40.Verbalis JG, Goldsmith SR, Greenberg A, Korzelius C, Schrier RW, Sterns RH, et al. Diagnosis, evaluation, and treatment of hyponatremia: expert panel recommendations. Am J Med. (2013) 126:S1–S42. doi: 10.1016/j.amjmed.2013.07.006

41.Furst H, Hallows KR, Post J, Chen S, Kotzker W, Goldfarb S, et al. The urine/plasma electrolyte ratio: a predictive guide to water restriction. Am J Med Sci. (2000)319:240–4. doi: 10.1097/00000441-200004000-00007

42.Koenig M.A, Bryan M, Lewin J.L, Mirski M.A, Geocadin R.G, Stevens R.D. Reversal of transtentorial herniation with hypertonic saline. Neurology, 70 (2008), pp. 1023-1029http://dx.doi.org/10.1212/01.wnl.0000304042.05557.60 | Medline

43. Cuesta M, Thompson C.The relevance of hyponatraemia to perioperative care of surgical patients. Surgeon, 13 (2014), pp. 163-169 http://dx.doi.org/10.1016/j.surge.2014.09.005 | Medline

44.Gross P. Clinical management of SIADH.Ther Adv Endocrinol Metab. 2012 Apr;3(2):61–73. doi: 10.1177/2042018812437561

45. Rudolph A, Gantioque R.Differentiating between SIADH and CSW using fractional excretion of uric acid and phosphate: a narrative review. Neurosci Med. 2018;9:53–62. [Google Scholar]

46.Tisdall, M · Crocker, M · Watkiss, J.Disturbances of sodium in critically ill neurologic patients.J Neurosurg Anesthesiol. 2006; 18:57-63

47. Bouchlarhem A, Haddar L, Berrichi H, et al. Cerebral salt wasting syndrome (CSW): An unusual cause of hypovolemia after spontaneous cerebral hemorrhage successfully treated with fludrocortisone. Radiol Case Rep 2021; 17(1):106–110.

48. Mullaguri N, Omer T, George P, et al. Refractory polyuria secondary to cerebral salt wasting successfully treated with DDAVP and hypertonic saline. Interdiscip Neurosurg 2020; 22:100814.9. Mohamed H, Shorten G. Distinguishing cerebral salt wasting syndrome and syndrome of inappropriate ADH in a patient with traumatic brain injury. BMJ Case Rep 2021; 14(3):e237027.

49. Taylor P, Dehbozorgi S, Tabasum A, et al. Cerebral salt wasting following traumatic brain injury. Endocrinol Diabetes Metab Case Rep 2017; 2017:16-0142.

50. Makoveev SA, Grudina ES, Tsarionova DV, et al. Combination of central diabetes insipidus and salt wasting syndrome in a patient with severe traumatic brain injury. Russ J Anesthesiol Reanimatol 2024; (1):57–63.

51. Costa MM, Esteves C, Castedo JL, et al. A challenging coexistence of central diabetes insipidus and cerebral salt wasting syndrome: a case report. J Med Case Rep 2018; 12(1):212.

52. Shah A, Sabir S, Artani M, et al. Significance of hyponatremia as an independent factor in predicting short-term mortality in patients with hemorrhagic stroke. Cureus 2019; 11(4):e4549.

53.Suman S., Kumar N., Singh Y., Kumar V., Yadav G. Evaluation of Serum Electrolytes in Traumatic Brain Injury Patients: Prospective Randomized Observational Study. J. Anesth. Crit. Care Open Access. 2016;5:00184. [Google Scholar]