Perioperative Management of the Pediatric Patient with Craniopharyngioma

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Goals:

1. Discuss the perioperative anesthetic management of a pediatric patient with craniopharyngioma, specifically preoperative assessment of hypothalamic/pituitary dysfunction.
2. Understand the perioperative management of central diabetes insipidus in pediatric patients undergoing both major and minor procedures under general anesthesia.
3. Understand the different possible etiologies of delayed emergence and altered mental status after general anesthesia, particularly for neurosurgical procedures, and the approach to diagnosis and management.
4. Recognize risk factors for perioperative seizures in pediatric patients and discuss possible etiologies and management.

Case:

A 4 year old male with craniopharyngioma status post resection four months prior resulting in panhypopituitarism is admitted with new right hand weakness that has worsened over the past two weeks and is found to have recurrence of craniopharyngioma. The patient is scheduled to undergo a left frontal craniotomy for tumor resection.

Past Medical History:

Born at 34 weeks gestation, spent two months in the NICU. History of craniopharyngioma, obstructive hydrocephalus, central diabetes insipidus (DI) with intact thirst, adrenocorticotropic hormone (ACTH) insufficiency, and hypothyroidism. History of a single seizure after prior resection, has been maintained on levetiracetam since that time with no further recurrence.

Medications:

Desmopressin (DDAVP), hydrocortisone, levothyroxine, levetiracetam

Social History:

Lives with parents and siblings. No second hand smoke exposure

Past Surgical/Anesthetic History: Endoscopic drainage of cystic suprasellar mass and placement of Ommaya reservoir, with subsequent removal of Ommaya and craniotomy for tumor resection earlier this year. Multiple prior imaging studies under general anesthesia with no complications.

Physical Examination: Awake and alert, lying comfortably in bed, follows commands appropriately
Neurological Examination: Left eye ptosis, dysconjugate gaze, left cranial nerve (CN) II and III palsy, moving all extremities with diminished right hand strength (4/5) noted on exam, normal sensation and reflexes

Vitals: BP 116/70 | Pulse 122 | Temp 37 °C (98.6 °F) | Resp 29 | Ht 97 cm (38.19") | Wt 16.7 kg (36 lb 13.1 oz) | SpO2 98% | BMI 17.75 kg/m²

Imaging (MRI): Large 5.2 x 6.0 x 5.8cm cystic and solid suprasellar mass effacing the third ventricle and extending into the left mesial temporal region and prepontine cistern. There is effacement of the fourth

ventricle with extensive distortion and mass effect on the ventral midbrain and anterolateral pons. The lateral ventricles are markedly increased in size since the prior study. No acute large infarct.

IMPRESSION:
Marked increase in the partially cystic suprasellar mass with progressive mass effect and new hydrocephalus. No large acute infarct.

Labs:
Na 133 mEq/L (24 hour range 126 to 137 mEq/L), K 4.3 mEq/L, Chloride 95 mEq/L, Bicarb 20 mEq/L, Glucose 128 mg/dL, BUN: 6 mg/dL, Creatinine: 0.24 mg/dL, Calcium 9.3 mg/dL.
WBC 9.9 thou/µL, H/H 11.2 g/dL /35.3%, Plt 335 thou/µL

Questions:

- What are the most common pediatric pituitary tumors? What pediatric tumor is highly associated with the development of central diabetes insipidus?
- How does the surgical approach affect the incidence of central DI?
- How is the diagnosis of central DI made?
- How can you assess if a patient's central DI is well managed prior to surgery?
- What additional preoperative information or studies would you require prior to anesthetizing this patient?

Case Continued:
The patient was started on dexamethasone therapy by neurosurgery given his enlarging mass noted on imaging. His sodium values were extremely labile prior to surgery and he required escalating doses of DDAVP for break-through episodes of polyuria associated with polydipsia, thought to be secondary to increased glucocorticoid administration.

Questions:

- If the serum sodium was down trending prior to surgery would you proceed with surgery? What is your sodium threshold for proceeding versus delaying surgery?
- How would you manage this patient's DDAVP on the day of surgery?
- What fluids would you plan to use for intraoperative resuscitation?
- How would you adjust your administration of intravenous fluids if the patient received DDAVP prior to surgery?

Case Continued:
He is started on maintenance fluids with dextrose 5% and 0.9% sodium chloride with 20 mEq/L potassium chloride to account for insensible fluid loss in addition to urine output replacement with dextrose 2.5% with sodium chloride 0.2% at a 1:1 ratio while NPO. His sodium level is 137 mEq/L on the morning of surgery and DDAVP is administered per the endocrinology service.

Question:

- Would you give this patient a premed?
- How would you induce this patient? Would you perform an inhalational induction if this patient's intravenous access malfunctioned prior to surgery?
- What lines and monitors would you require for this case?
- How would you maintain anesthesia in this patient?

Case Continued:
The patient undergoes an uncomplicated intravenous induction with propofol, fentanyl, and rocuronium. After induction, additional intravenous and arterial access is obtained. The surgeon does not plan for intraoperative neurophysiological monitoring. The patient is maintained on sevoflurane with additional doses of opioid analgesia and muscle relaxant as needed. Intraoperatively, the case is complicated by acute surgical blood loss necessitating fluid resuscitation and blood transfusion to maintain hemodynamic stability. Serial arterial blood gases are monitored and the patient's serum sodium is noted to be down trending to the low 130s (mEq/L).

Questions:
- Why might this patient develop hyponatremia? How would you adjust your management for hyponatremia?
- How would you adjust your management if the patient developed hypernatremia intraoperatively?

Case continued: After undergoing subtotal resection of his tumor and insertion of an Ommaya reservoir, the patient remains obtunded and is not following commands.

Questions:
- What is your postoperative plan for this patient?
- Would you extubate if the patient is not following commands but has intact airway reflexes?
- What is on your differential for a patient with altered mental status after general anesthesia? What steps would you take to further evaluate? What is your threshold to proceed with additional investigations versus giving patient more time?

Case continued: The patient undergoes additional imaging that is unrevealing and is transported to the intensive care unit. He remains unresponsive. In the intensive care unit, he is noted to become increasingly hypertensive, tachycardic, and with rightward eye deviation.

Questions:
- How would you determine if the patient is having nonconvulsive status epilepticus?
- What risk factors does this patient have for developing seizures postoperatively? How would you treat suspected seizures?

Case Continued:
The patient's mental status initially improves with lorazepam and he is subsequently loaded with fosphenytoin. He develops worsening hyponatremia over the course of the next several hours with serum sodium levels of 128-130 mEq/L.

Questions:
- What is your differential diagnosis for this patient's hyponatremia? How would you treat hyponatremia in this patient?

Case Continued: He remains encephalopathic despite adequate treatment with antiepileptic drugs and no epileptiform activity seen on electroencephalogram, and his Ommaya reservoir is noted to be malfunctioning. He is scheduled to return to the OR for removal of the Ommaya and placement of an external ventricular drain (EVD).

Questions:

- How would you alter your anesthetic plan in the setting of altered mental status and concern for elevated intracranial pressure?
- How would you manage his intraoperative fluids in the setting of transient SIADH?

Discussion:

Epidemiologic considerations

Pituitary tumors are rare in childhood and adolescence, and virtually all tumors of this region are benign. Tumors occupying the pituitary fossa are of two main types: craniopharyngiomas, the most common tumor causing hypopituitarism in childhood, and pituitary adenomas. Craniopharyngiomas account for 80-90% of neoplasms arising in the pituitary region.[1] They are rare neuroectodermal tumors that make up 5-13% of pediatric and 1-4% of adult brain tumors.[2] The incidence is bimodal and peaks at ages 5-14 years and 65-74 years.[1] Although classified as a benign tumor with no metastatic potential, due to their sellar and/or suprasellar location in close proximity to critical neural and vascular structures, there can be considerable morbidity both at the time of diagnosis and when the tumor is partially or completely resected. Preoperative central diabetes insipidus (DI) has been reported in 8-35% of patients affected with craniopharyngioma, whereas postsurgical and permanent DI accounts for up to 80% of patients; 13% of cases are transient.[3] Compared to adults with craniopharyngioma, children undergoing craniopharyngioma resection have a significantly higher incidence of permanent DI and the management of postoperative DI is more difficult due to wider serum sodium fluctuations and a higher incidence of hyponatremia.[4]

The management of pediatric craniopharyngioma was traditionally via a transcranial approach with the goal to achieve complete resection, however this aggressive strategy was associated with greater injury to vital tissues, resulting in a high frequency of visual impairment, hypothalamic dysfunction, central diabetes insipidus, and anterior pituitary hormone deficiencies.[2] In recent years, less invasive surgical approaches followed by adjuvant therapies have gained acceptance. This includes an endoscopic endonasal rather than open approach to tumor resection, partial resection with or without radiation therapy to eradicate residual tumor, or procedures aimed at tumor decompression in patients with a significant cystic component, including endoscopic cyst fenestration or placement of an Ommaya reservoir into the tumor cyst for drainage with or without subsequent instillation of antineoplastic agents. This shift in surgical treatment approach away from gross total resection has led to better preservation of the pituitary stalk and improved endocrine outcomes, with a significant reduction in the occurrence of central DI in a recent meta-analysis from 80% to 65%, comparable to other published studies.[2,5]

Craniopharyngioma Perioperative Considerations

Clinical presentation of patients with craniopharyngioma will depend on the size and site of the tumor, with many symptoms resulting from compression of adjacent structures and increased intracranial pressure. These include headache, visual deficits, endocrine deficiencies such as diabetes insipidus or panhypopituitarism from compression of the pituitary gland or stalk, hypothalamic dysfunction resulting in abnormalities in sleep, appetite or thermal regulation, and symptoms of hydrocephalus from obstruction of cerebral spinal fluid pathways.[6] At time of diagnosis 20-50% of children will have hormonal insufficiencies; preoperative endocrine evaluation including measurement of growth hormone, thyroid stimulating hormone, cortisol, follicular stimulating hormone/luteinizing hormone, prolactin, and serum electrolytes should be performed and corrected as indicated prior to surgery.

Consultation with an endocrinologist is recommended and preoperative considerations include administration of stress dose steroids and assessment of volume status and electrolyte disturbances.

Many of these patients will present with intravenous access prior to surgery, however an inhalational induction could be considered in appropriately fasting patients without evidence of significant intracranial hypertension. Options for maintenance of anesthesia should prioritize a rapid awakening at the completion of surgery to allow for neurological examination and take into consideration any planned intraoperative neurophysiological monitoring.

Vascular access for surgical resection should include at least two large-bore peripheral intravenous lines for rapid resuscitation due to the close proximity to the internal carotid artery and other vessels of the circle of Willis. Arterial cannulation should be considered for both close hemodynamic monitoring as well as the ability to closely monitor blood gases and serum electrolytes in these patients at high risk for the development of intraoperative diabetes insipidus. Placement of a urinary catheter is recommended for the early detection of DI as well.[7]

As the treatment paradigm for craniopharyngioma has evolved over time from "curative" tumor resection to less aggressive approaches, anesthesiologists caring for pediatric patients may frequently encounter these patients after initial tumor resection for medical imaging, adjuvant radiation treatment, and neurosurgical procedures for tumor regrowth/recurrence. There has been an overall general reduction in the prevalence of postoperative endocrinopathies with the increase in less invasive treatment modalities, however it still remains a major perioperative consideration for patients with craniopharyngioma undergoing subsequent procedures. In particular, the development of hypothalamic obesity represents a major concern, as the rapid weight gain associated with craniopharyngioma has not been significantly reduced despite hypothalamic sparing strategies.[2]

Perioperative Management of Central Diabetes Insipidus

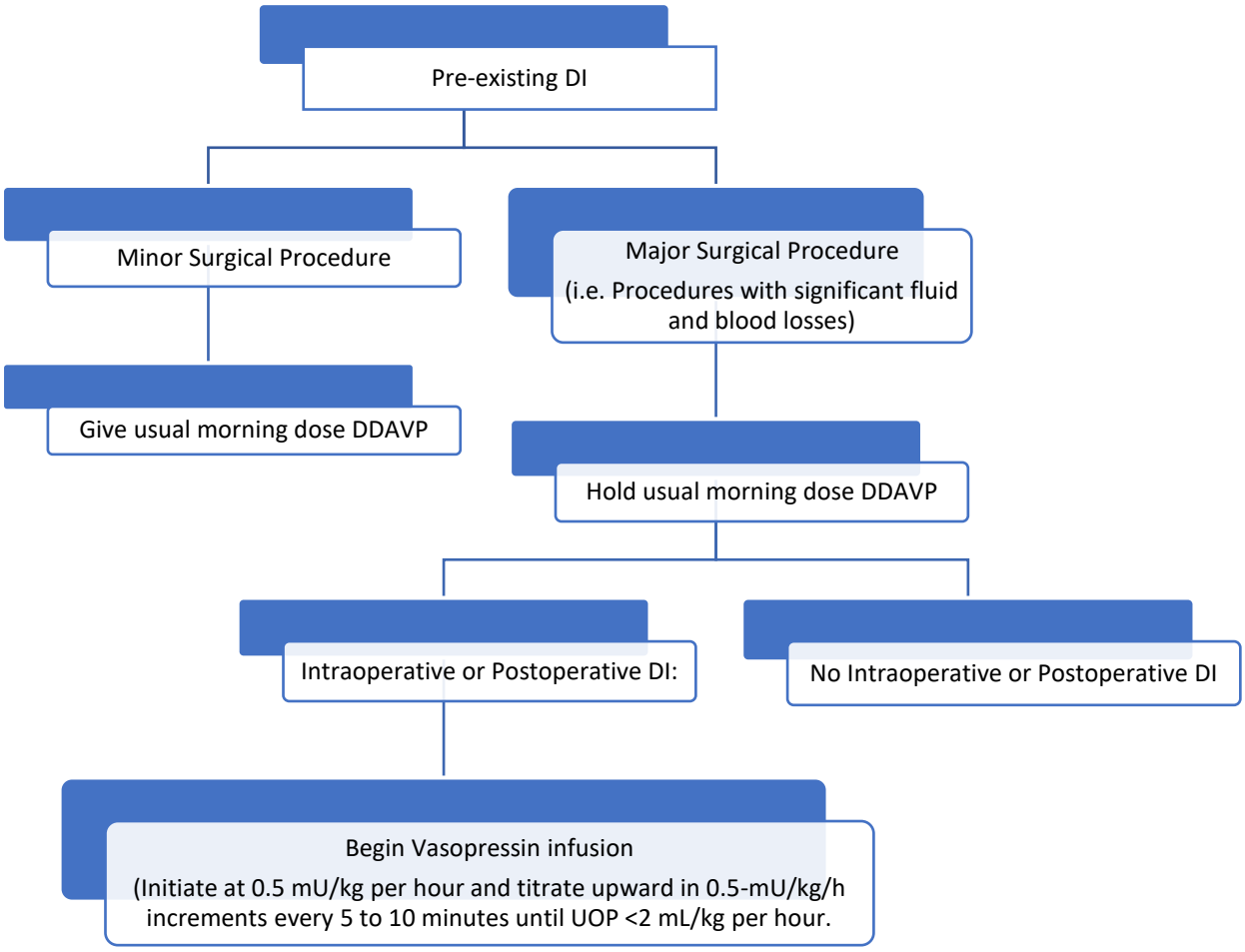
Central DI is characterized by the inability to concentrate urine secondary to vasopressin deficiency resulting in polyuria and subsequent polydipsia. Polyuria is defined as excretion of a urinary volume greater than 2 L/m^2/day, 150 ml/kg/day in neonates, 100–110 ml/kg/day in children up to age 2, and 40–50 ml/kg/day in older children.[8] A serum osmolality (Sosm) > 300mOsm/kg at the same time as inappropriately dilute urine (Uosm <300mOsm/kg) are indicative of DI.[8] In children with central DI with an intact thirst mechanism, the mainstay of treatment is free access to water combined with a pharmacologic agent, typically synthetic vasopressin (desmopressin/DDAVP). The most common side effect of DDAVP is hyponatremia which can be avoided by allowing for adequate breakthrough urine output (UOP), defined as >4 ml/kg/hr of urine for two or more hours, specific gravity <1.005 and normal to increasing serum sodium.

The intra- and early postoperative course of children with craniopharyngioma is often complicated by temporary or permanent abnormalities in water homeostasis, including the development of central DI and syndrome of inappropriate secretion of antidiuretic hormone (SIADH). There are published standard approaches to treatment of both DI and SIADH, however the optimal perioperative management to prevent or control these complications are less clear. There are no large evidence-based studies that determine optimal fluid management in children with central DI requiring IV fluids. Prior approaches for the perioperative management of central DI relied on the replacement of fluid losses volume for volume to match urinary output plus insensible losses utilizing hypotonic fluids. This approach was felt to be more useful in young children who were at highest risk of developing

hyponatremia with vasopressin therapy.[9] At our institution, insensible fluid replacement is frequently initiated perioperatively with D_5 + 0.45NS with 20 mEq/L potassium chloride at 300–500 ml/m^2/day in addition to UOP replacement with 1 ml of $D_{2.5}$ + 0.2NS for every 1 ml of UOP while patients with central DI are restricted access to free water, with fluid rates adjusted based on sodium trends and ongoing losses.[8] Treatment with low-dose DDAVP is considered in cases where it is difficult to replace ongoing losses. However, in many situations perioperative use of intravenous vasopressin in children with central DI is considered the treatment modality of choice, resulting in lesser fluctuations in serum sodium as long as care is taken to limit fluid intake while under full anti-diuresis and to avoid iatrogenic water intoxication with hypotonic fluids.[9,10]

One published approach to the intraoperative management of children undergoing craniopharyngioma surgery found reduced frequency of intra- and early postoperative complications of fluid and electrolyte disturbances after instituting a standard set of guidelines.[11] According to this algorithm, when polyuria is detected, fluid replacement is adjusted to match urinary output plus insensible fluid loss using sodium-free solutions exclusively. If evidence for DI persists for more than 2h at a stretch or urinary output cannot be replaced, DDAVP is given intravenously at a low dose in conjunction with restriction of fluid intake and only high-salt-concentration fluids are used (0.7-0.9% NaCl). Higher doses of DDAVP are given if polyuria persists. In this retrospective study, DI was diagnosed preoperatively in 14 of the 39 patients and all of these patients were treated with DDAVP, however no further specifics were given on the management of this subset of patients.

In an effort to standardize the perioperative management of children with pre-existing DI in addition to those undergoing procedures associated with significant risk for the development of DI, authors at a different institution developed a safe and effective algorithm for the management of perioperative central DI.[10] Eighteen children were prospectively managed according to a standard protocol and compared to nineteen historical controls at a major academic pediatric center. Patients managed according to this protocol had less significant fluctuations in serum sodium concentrations and a lower occurrence of hyponatremia, in addition to generally improving provider satisfaction regarding overall management. In this study, the management of patients with pre-existing central DI was dependent on the surgical procedure planned, as demonstrated in the diagram below. Urine output and serum electrolytes were closely monitored in these patients. It is unclear the optimal interval for monitoring electrolytes perioperatively in at-risk patients, however prior published guidelines in the pediatric literature have recommended serum and urine electrolytes and osmolality testing immediately postoperatively and at least every 8 hours, with changes in serum sodium of >5mmol/l assessed more frequently (every 4 to 6 hours).[12] It may be prudent to monitor more frequently intraoperatively due to the dynamic nature of the patient's volume status while undergoing major surgical procedures.



Adapted from FIGURE 1[10]

Wise-Faberowski, et al. *Perioperative Management of Diabetes Insipidus in Children.* J Neurosurg Anesthesiol, 2004. **16**(3): p. 220-225

IV fluids in both major and minor procedures were administered as normal saline at two-thirds maintenance rates and additional IV saline was given, as needed, to maintain hemodynamic stability and replace blood loss. The authors cautioned regarding the risks of intravascular volume overload in the setting of a vasopressin infusion and the avoidance of hypotonic fluids, as this can result in dangerous hyponatremia. Normal saline was the only intravenous fluid administered until normal oral intake resumed. Perioperative serum sodium concentrations were generally maintained between 130 and 150 mEq/L and the mean change in sodium concentrations was significantly less as compared to historical controls. In children with known DI, DDAVP therapy was resumed once an intact thirst mechanism returned and the resumption of adequate oral intake was established.

Normal saline (NS) has historically been the fluid of choice for intraoperative use, however, a small retrospective-prospective study recently showed increased risk of negative outcomes using NS in patients undergoing craniopharyngioma resection, with the best outcomes using 0.45NS.[13] In the prospective portion of this study, patients undergoing transcranial resection of craniopharyngioma were randomly assigned to receive NS, 0.45NS, or D5W. Postoperative DI was managed with subcutaneous desmopressin according to a standard protocol. All patients received fluid boluses intraoperatively with comparable fluid amounts. In the postoperative period, patients who received NS had sodium values

significantly higher in the first 48 hours than preoperative values. In the D5W group, hyponatremia, hyperglycemia and seizures were negative complications associated with D5W use. The postoperative sodium was independent of use of desmopressin and glucocorticoid therapy. The authors concluded it is favorable to use half NS as the sole intraoperative fluid in patients undergoing craniopharyngioma surgery. This very small study excluded patients with preoperative DI and cannot comment on appropriate management in these patients.

In patients with coexisting vasopressin and cortisol deficits (e.g. in combined anterior and posterior hypopituitarism following neurosurgical treatment of craniopharyngioma), symptoms of DI may be masked because cortisol deficiency impairs renal free water clearance. In such cases, the institution of glucocorticoid therapy alone may precipitate polyuria, leading to the diagnosis of DI. Conversely, excessive amounts of cortisol, due to endogenous release during stress or to treatment with exogenous drug, may inhibit the insertion of water channels. This may explain why patients with central DI treated with desmopressin become "resistant" and require an increased dosage during times of stress or treatment with glucocorticoids.[9]

All patients having surgery in the area of the pituitary need close monitoring of fluid intake, UOP and serum sodium levels. UOP can be greater than 4 ml/kg/hr with dilute urine in the setting of normal serum osmolality secondary to post-operative fluid shifts in the first 24–48 h after surgery. Administration of osmotic diuretics such as mannitol can result in a brisk diuresis and cloud the diagnosis or management of central DI. Monitoring serial serum and urine osmolality and electrolyte levels can be helpful in differentiating the etiology of polyuria.

<u>Perioperative Management of Hyponatremia</u>

Intraoperative hyponatremia may occur iatrogenically from excessive intravenous fluid administration, particularly if hypotonic fluids are administered in the setting of concomitant DDAVP. Hyponatremia is a known complication of DDAVP administration, and there exists reports of symptomatic DDAVP-associated hyponatremia that resulted from hypotonic fluid administration or failure to fluid restrict in the setting of concurrent DDAVP, with the result of hyponatremic encephalopathy and significant neurologic injury if the sodium levels are corrected too quickly.[14] The development of hyponatremia may particularly be a concern in patients with pre-existing central DI previously managed on stable doses of DDAVP requiring escalating doses prior to surgery.

SIADH is an important consideration for evolving hyponatremia in a patient with craniopharyngioma in the perioperative period. SIADH is defined by hyponatremia and hypo-osmolality due to inappropriate ADH secretion which results in impaired water excretion despite a normal or increased plasma volume.[15] It has occasionally been described before craniopharyngioma resection as a result of inappropriate ADH release by direct mechanical stimulation of the tumor mass or ischemic changes on the osmoreceptor/ADH-secreting neurons.[15] Additionally, preoperative endocrinopathies such as severe secondary/tertiary hypothyroidism and hypocorticolism has been described in patients with craniopharyngiomas with resultant hyponatremia, highlighting the importance of a thorough preoperative endocrine assessment.[15]

SIADH can occur in the postoperative period due to damage to neurons with release of intracellular antidiuretic hormone. Transient SIADH can be isolated or can occur as part of a classic triphasic pattern, in which the initial phase of central DI is followed by a second phase of oliguria due to inappropriate vasopressin secretion, followed by a third and final phase of permanent central DI. Isolated SIADH

typically occurs in patients with limited damage to the neurohypophysis and has been reported in 8-21% of patients after pituitary surgery.[15] SIADH can be treated by fluid restriction and, in severe cases, with an infusion of 3% saline, taking care to avoid overcorrection.

Cerebral salt wasting (CSW) is reported in 4% of children following neurosurgery and is characterized by polyuria and natriuresis, resulting in hyponatremia. CSW is defined by the development of extracellular volume depletion due to a renal sodium transport abnormality in patients with intracranial disease and appropriate adrenal and thyroid status.[15] It is postulated that inappropriate secretion of natriuretic peptides (NP) released from the injured brain and loss of sympathetic stimulation to the kidney may be a pathogenic mechanism for CSW. It is typically managed with fluid administration to restore intravascular volume and sodium supplementation.

The principal defining feature distinguishing CSW from SIADH is the patient's volume status, with CSW identified by high urine output and hypovolemia. Laboratory analysis may be similar in acute clinical circumstances, with low serum osmolality, inappropriately high urine osmolality, and significant natriuresis (>40 mEq/L) in both conditions. The chart below summarizes the main clinical and biochemical differences between the two conditions. Making the distinction between CSW and SIADH as etiologies of perioperative hyponatremia is very important, as the treatment for the two conditions is very different.

	SIADH	CSW
Extracellular Fluid Volume	Normal to high	Low
Evidence of volume depletion	No	Yes
Serum Sodium	Low	Low
Urine Sodium	High	High
Net sodium loss	Normal	High
Serum Osmolality	Low	Low
Urine Osmolality	High	High
Urine Output	Usually low	Very high

Clinical and biochemical differences between SIADH and CSW. Adapted from Table 3[15]

Edate, et al. *Management of Electrolyte and Fluid Disorders after Brain Surgery for Pituitary/Suprasellar Tumours.* Horm Res Paediatr, 2015. **83**: p. 293-301

Delayed Recovery after Anesthesia

Delayed emergence from anesthesia presents a challenge to the anesthesiologist, as pharmacological as well as nonpharmacological causes must be considered. The time to emerge from anesthesia is affected by patient factors, anesthetic factors, duration of surgery, and painful stimulation. Delayed awakening after general anesthesia is most commonly caused by anesthetic factors including residual drug effects from opioids, benzodiazepines, IV anesthetic agents, neuromuscular blockade, and drug interactions.[16] In addition, organic causes such as metabolic disorders, electrolyte imbalances (including hypo- and hypernatremia), hypothermia, and respiratory causes, including hypoxemia and hypercarbia, must be considered. Unexpected delayed emergence after general anesthesia may also be due to neurological complications that can have devastating effects leading to death or severe disability, including cerebral edema, seizures, postoperative intracranial hemorrhage, and cerebral ischemia.

An early diagnosis of postoperative neurological complications is particularly important after neurosurgical procedures to limit potentially devastating consequences and improve patient outcome, highlighting the importance of an early postoperative neurologic exam and timely evaluation of delayed recovery after anesthesia. Postoperative neurologic complications should be higher on the differential diagnosis of patients with delayed awakening after anesthesia in those undergoing neurosurgical procedures, particularly intracranial surgeries. If, after surgery, a patient does not rapidly recover consciousness or a focal neurological deficit becomes apparent, a head CT should be performed as soon as possible to rule out a neurosurgical complication and to allow for timely intervention.[17]

Susceptible patients at risk for seizures may present with delayed emergence after anesthesia. In a retrospective review of 223 previously seizure-free children with brain tumors undergoing intracranial tumor resection at a large academic children's hospital, the authors found an incidence of 7.4% of patients experienced at least one clinical seizure during the surgical admission.[18] Independent factors associated with perioperative seizures included supratentorial tumor location, accounting for over half of all patients, age<2 years, and postoperative hyponatremia. Perioperative seizures were not associated with tumor pathology, size, or frontotemporal location. Most episodes classified as seizure activity consisted of eye deviation and unresponsiveness with only 2 patients presenting with generalized tonic-clonic seizures.

Diagnosis of altered mental status after general anesthesia includes ensuring normal vital signs, review of administered drugs and patient medical history, and assessment of metabolic abnormalities including glucose and electrolyte levels. In neurosurgical patients with unexplained delayed recovery from anesthesia, a lower threshold for additional imaging is indicated, and empiric treatment for nonconvulsive seizures may be initiated if there is a high clinical suspicion while awaiting EEG correlation.

Nonconvulsive Status Epilepticus

Nonconvulsive status epilepticus (NCSE) has been defined as a cognitive or behavioral change that lasts for at least 30 minutes with evidence of seizures on electroencephalogram (EEG).[19] In children, the diagnosis of NCSE is often under-recognized and requires a high index of suspicion as its presentation may only include nonspecific signs such as changes in behavior or altered mental status, and continuous EEG monitoring is thought to be essential for diagnosing NCSE. In children, NCSE can be observed in acute neurologic injuries, specific childhood epilepsy syndromes and other nonprogressive encephalopathies, and in individuals with certain learning difficulties. Treatment is dependent on the subtype of NCSE based on EEG features, however most subtypes are treated with benzodiazepines and antiepileptic drugs such as fosphenytoin or valproic acid.[19]

Additionally, in children undergoing craniotomy of sellar or suprasellar tumors, large fluctuations of plasma sodium levels, particularly the development of hyponatremia, is highly associated with altered mental status and seizures. Patients with permanent central DI showed the most severe fluctuations in plasma sodium concentration during the early postoperative period.[20] In these patients, the treatment of altered mental status and seizure activity should include close electrolyte monitoring and correction of plasma sodium levels.

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