HYPONATREMIA AND ANESTHESIA

In general, hyponatremia does not affect anesthesia per se, but may cause significant complications of confusion, seizures, sedation, respiratory depression, and protracted unconsciousness that may be confused with other issues in the recovery post-operative period. In neurosurgical cases or preoperative altered levels of consciousness, hyponatremia may cause central edema and elevated ICP therefore avoidance of agents and techniques leading to further ICP elevations may be useful.

Hyponatremia is a serum sodium level less than 135 mEq/l. Mild hyponatremia is common and asymptomatic but severe hyponatremia may manifest itself with severe hyponatremic symptoms.

The treatment for hyponatremia is not always additional sodium chloride. Certain hyponatremic conditions can be made worse by additional sodium chloride. A slow correction of hyponatremia is generally thought to be safer than a rapid correction due to the occurrence of a rare complication known as central pontine myelinolysis (osmotic demyelination syndrome). This syndrome has some of the same symptoms as hyponatremia, and may be difficult to delineate. It is associated with confusion, delirium, hallucinations, ataxia, tremor, difficulty swallowing, drowsiness or lethargy, slurred speech, weakness in the face/arms/legs bilaterally. After a correction of hyponatremia, one should always look for these symptoms prior to initiating an anesthetic, regional, MAC, TIVA, or general.

KEY POINTS FOR ANESTHESIA for HYPONATREMIA and SUGGESTIONS:

1. **Elective surgery** should be postponed for serum sodium levels of 128 or less until the sodium level has been corrected to at least 129 or until severe symptoms attributed to hyponatremia (confusion, ataxia, seizures, obtundation, coma, respiratory depression) have resolved. Over-rapid correction may lead to central pontine neurolysis (Cureus. 2018 Sep 4;10(9):e3252), therefore corrections of sodium from profound hyponatremia (<120) may require many days. Mild symptoms (headache, lethargy, dizziness) with a sodium level of 129 or higher are not a contraindication to elective surgery. For patients scheduled for elective surgery and have sodium levels of 128 or less, a full workup including determination of serum and urinary osmolality is indicated in order to effect the appropriate treatment pathway, that may not include administration of additional sodium and in some cases involves sodium restriction. Typically internal medicine is involved with the evaluation and treatment of hyponatremic patients presenting for elective surgery.

2. **Urgent surgical patients may have anesthesia with sodium levels of 125 or greater as long as severe hyponatremic symptoms (confusion, ataxia, seizures, obtundation, coma, respiratory depression) are not present.** If severe symptoms are present, then an IV bolus of 100-150ml of 3% hypertonic saline may be administered (avoid in CHF or cirrhosis) (Verbalis JG, et al. Diagnosis, evaluation, and treatment of hyponatremia: expert panel recommendations. Am J Med.)
3. **True emergency surgery should not be postponed for hyponatremia** however the risk of postoperative complications including infection rate, prolonged hospitalization, major cardiac events, and death increase substantially. If the patient has a sodium level of 125 or less, then treatment with an IV bolus of 100-150ml of 3% hypertonic saline (avoid if the patient has CHF or cirrhosis) at the initiation of surgery or if time permits, prior to surgery, may be implemented even without severe hyponatremic symptoms, then recheck a sodium level after an hour. Hyponatremia, unless extreme (<120 mEq/l) or in the absence of severe preoperative hyponatremic symptoms, generally causes few symptoms or signs related to the administration of the anesthetic or in the immediate post operative period that cannot be controlled but correction of severe or profound hyponatremia may be initiated during the anesthetic. Hyponatremia is more of a marker of the extent of other diseases rather than an entity causing severe pathology itself in most patients unless the sodium levels are profoundly low, then hyponatremia may cause severe symptoms.

4. **In situations of severe hyponatremia (125 or less)** or if severe symptoms of hyponatremia are present, take extra precautions to avoid elevation of ICP during intubation/extubation, and avoid agents that elevate ICP (e.g. Desflurane, succinylcholine, hypoventilation, suctioning of the oropharynx, fentanyl). Agents that do not increase intracranial pressure include propofol, sevoflurane, ketamine, lidocaine, rocuronium, vecuronium.

5. **Use normal saline (154 mEq/l sodium)** instead of lactated ringsers (130mEq/l sodium) intraop for fluid maintenance. **Restrict volume used in renal failure, CHF, nephrosis, cirrhosis when possible.** Other solute sodium content: Plasmalyte A contains 140 mEq/l sodium. Hydroxyethyl starch (Hetastarch/Hespan/Voluvem) is 154 mEq/l. Volulyte contains 137mEq/l sodium. Albumen contains 130-160 mEq/L sodium. 3% sodium chloride has a sodium content of 513 mEq/l.

6. **If 3% or 5% saline IV infusion has been initiated preoperatively to correct hyponatremia, continue the infusion at the same rate during surgery but check the sodium level every 6 hours if this is being infused.** This should be infused via an IV infusion pump and never given without controlled programmed infusion rates. Correction of severe hyponatremia may require many days of hypertonic saline infusion and elimination of causative factors.

7. **Avoid worsening hyponatremia by avoiding diuretics (mannitol, sorbitol, furosemide) during surgery when possible and correct adrenal insufficiency** (due to any glucocorticosteroids given as injection or "dose pack" within 3 weeks prior to surgery). Also correct any hyperglycemia (>200mg/dl) as this may be a cause of hyponatremia. Avoidance of diuretics may not be possible during neurosurgery but reduction of CSF pressure may be accomplished using alternative methods. You cannot completely correct hyponatremia during surgery.
but you may be able to avoid worsening it. Too rapid of a correction of plasma sodium results in central pontine neurolysis.

8. **Symptoms of hyponatremia are usually subtle pre, intra, and post-operatively and are masked by sedation or general anesthesia** - there are **usually no signs of hyponatremia during sedation or general anesthesia**. There are usually no ECG changes with hyponatremia unless the sodium levels are profoundly low (<100) that may manifest with severe ST segment elevation or complete AV block (Am J Med Oct 2016, 129(10), e243-44). AV block has also been reported in 3 patients with sodium levels between 108 and 120 mEq/l (Clin Cardiol 1991; 14 165-68). P wave alternating morphologies normal progressing to inverted have been reported with hyponatremia 125 mEq/l (Hellenic J Cardiol 57(3) May-June 2016, 188-90). Overall, ECG changes are rare with hyponatremia, even with profound hyponatremia.

9. **Severe hyponatremia (<125mEq/l) may manifest with seizures and altered sensorium post operatively, or nausea/vomiting**. RAPID changes in sodium levels resulting in hyponatremia cause much more common and severe issues than chronic hyponatremia. RAPID onset hyponatremia symptoms including severe cerebral edema, coma, brainstem herniation, seizures, altered sensorium, or agitation. RAPID CHANGES in sodium levels during anesthesia may be induced via the use of mannitol or furosemide IV or with large amounts of gastric fluids suctioned during anesthesia.

10. **There should be a high index of suspicion of symptomatic hyponatremia in patients that do not awaken within the usual bands of timeframes after anesthesia, and may therefore require post-operative ventilation.** Those patients with pre-operative severe symptoms of hyponatremia should have planned postoperative ventilation in the ICU. In patients without severe preoperative symptoms of hyponatremia and in whom extubation is performed, be prepared to treat seizure activity in the PACU (propofol) or reintubate with respiratory failure or continued obtundation. Warn the PACU nurses that the patient may exhibit seizure activity or require re-intubation for ventilatory failure, and to call anesthesiology early in cases of respiratory failure, seizure activity, or in cases of prolonged obtundation.

11. **There is a risk of developing or worsening hyponatremia post-operatively due to SIADH that is commonly seen after surgical procedures.** Frequently this occurs after the period in PACU so be aware of changes in sensorium or severe symptoms of hyponatremia when making post op rounds on the patient the next day. (N Engl J Med. 1986 Jun 12;314(24):1529-35)

**OUTCOMES OF PATIENTS WITH HYponATREMIA**

Preoperative hyponatremia occurs in 1 out of 13 patients undergoing major surgery. Hyponatremia results in a 44% increased risk of 30-day perioperative mortality compared to normonatreic patients, and is directly related to the degree of hyponatremia. Hyponatremia increases the risk of a major coronary event from
0.7% to 1.8%, wound infections from 4.6% to 7.4%, and pneumonia from 1.5% to 3.7%. (Arch Intern Med. 2012;172(19):1474-81). Other populations show a high incidence of hyponatremia with 30% of ICU patients having hyponatremia. One large study showed an incidence of 14% hyponatremia in hospitalized patients with 2.7% of those hyponatremic patients having levels of 120-125 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5864034/)

Postoperative hyponatremia may also develop over 24-48 hours in 30% of patients having major surgery and is more common in general anesthesia (72%) than regional anesthesia (28%). The most common associated symptoms post operative with hyponatremia were nausea, drowsiness, vomiting, lethargy, and abdominal distension. Headache and altered sensorium was less common. (Mujtaba, Gen Med Open Access Feb 25, 2016)

CAUSES:
Most hyponatremia is chronic and is iatrogenic- primarily due to excessive diuretics, however there are many other medications that may cause hyponatremia including carbamazepine, SSRIs, SNRIs, opioids, methotrexate, NSAIDs, PPIs, ACE inhibitors, antiepileptic drugs including gabapentin and others, amiodarone, and vasopressin analogs. MDMA (Ecstasy) may also cause hyponatremia. SIAD is the most common primary cause in the elderly being responsible for 50% of all cases of hyponatremia (Clin Interv Aging 2017;12:1957-65) Other common causes of hyponatremia include vomiting or diarrhea, diabetes, infections, cerebral disorders (tumors), pneumonia, ADH secretion (e.g. solid tumors, small cell lung cancer), CHF, cirrhosis, hypothyroidism, alcoholism, excessive water ingestion, etc. Hyponatremia is age related. Hyponatremia causes are almost always multifactorial.

HYponATREMIA WORKUP
A workup for the treatment of hyponatremia before an elective surgery is important because the treatment pathways are radically different, and may not involve giving the patient additional sodium. Failure to recognize the need for an appropriate treatment path may lead to a worsening clinical situation such as giving IV hypertonic saline to CHF or cirrhosis patients.
Mild hyponatremia is serum sodium <135 mEq/L and >129 mEq/L. Moderate hyponatremia is 125-129 mEq/L and profound hyponatremia is less than 125 mEq/L. In most cases of hyponatremia the total body water is increased relative to the amount of sodium present (low plasma osmolality <285 mOsm/kg). Those with a low plasma osmolality are further evaluated by assessing the extracellular volume status and urine sodium levels. Decreased extracellular volume are subdivided into renal sodium losses (>20mEq/L) or extrarenal losses (urine Na<10mEq/L- primarily GI losses). Those with normal extracellular volumes (lack of edema or hypovolemia) are primarily due to adrenal insufficiency, hypothyroidism, medication, and SIADH. Those with increased extracellular volume (edema on exam) occur due to CHF, cirrhosis, nephrotic syndrome and renal failure.
**Hypovolemic Hyponatremia:** Head injury including TBI and intracranial hemorrhage are important causes that can result in cerebral salt wasting. Sodium is the main salt that is lost in urine. Many different hormones like mineralocorticoid deficiency impart a profound impact on urine osmolality that can raise more than 20 mEq/L. Various central and renal causes are responsible for this. Addison’s disease, hypopituitarism, and hypothalamic failure are the most frequent causes of this class. Simple and common conditions like diarrhea and vomiting can result in significant loss of sodium, which may result in dropping urinary osmolality below 20 mEq/L with serum hyponatremia. Other causes like elevated glucose levels and use of sorbital or mannitol can also result in this type of hyponatremia.

Clinical features in this type of hypovolemia are mainly because of volume depletion. These include vomiting, diarrhea, and tachycardia. Lab studies demonstrate elevated BUN/creatinine ratios that accurately predicts hypovolemia in 68%. Treatment generally consists of volume repletion with normal (0.9%) saline, occasional use of salt tablets, and treatment of the underlying condition. Most common side effect of over hydration can be avoided by monitoring urinary output, maintaining below 110 ml/h.

**Euvolemic hyponatremia:** In this hypovolemic type, plasma volume remains in normal limits but sodium level drops. Most common causes of this are SIADH, hypothyroidism and glucocorticoid deficiency. Diagnosis is made on urinary sodium level which is greater than 20 mEq/L. Along with it low serum uric acid levels and normal blood urea nitrogen to creatinine ratio helps in making diagnosis. Different contributory factors like use of diuretic therapy and low-salt diet can artificially influence the sodium levels. Treatment generally consists of fluid restriction and correcting the underlying cause. Fluid restriction should be limited to 500 ml less than the daily urinary volume.

**Hypervolemic hyponatremia:** Main causes of this are renal, cardiac and liver dysfunction. Hyponatremia is seen in 50% of those with cirrhosis of the liver. It results in retention of fluid and electrolytes. In volume overload states, the effective arterial blood volume is decreased compared with venous volume, resulting in excess ADH secretion. Treatment consists of correcting the underlying cause, sodium and fluid restriction, and diuretic therapy.

**Severe symptomatic hyponatremia:** Rapid fall of plasma sodium levels in quick succession of time results in this type of hyponatremia. It occurs classically when serum sodium levels fall below 120 mEq/L. However it can also occur even in serum sodium at 125 mEq/L. Seizures are main clinical manifestation. This dilutional hyponatremia can be treated by excretion of excess water from body with drugs Furosemide. Other pharmacological agents like vaptans seem to have no role in it. To avoid drastic complication like central pontine demyelination the rate of sodium correction should be 6 to 12 mEq/L in the first 24 hours and 18 mEq/L or less in 48 hours. An increase of 4 to 6 mEq/L is usually sufficient to reduce symptoms of acute hyponatremia.

**Pseudohyponatremia:** There are actual normal sodium levels in this form of hyponatremia. Many different clinical entities like hyperglycemias, hyperproteinemias and use of drugs e.g. mannitol, contributes in it. Laboratory errors also play a part. Patients with form of hyponatremia usually have normal volume status and urinary osmolality is also unchanged.