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Sodium disturbances in neurosurgery

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Normal physiology of sodium and water regulation

Sodium and volume are regulated by neural, humoral, and renal mechanisms. These systems integrate information regarding extracellular fluid (ECF) osmolality, intravascular volume, circulatory haemodynamics, as well as sodium and water intake. Neural and humoral messengers are then used to modify the intake and excretion of sodium and water, as well as regulate vascular tone. While regulation of sodium and water involve separate systems, they do not operate independently.

Water regulation

Two-thirds of total body water remain intracellular with the remainder in the extracellular space. The primary extracellular solutes are sodium, its anions (chloride and bicarbonate), glucose, and urea. Intracellular osmolality is primarily dependent on potassium and its anions. The osmolality of intracellular fluid and ECF are the same because most cell membranes allow free movement of water. Large changes in ECF osmolality can result in water shifts leading to cell shrinkage or swelling, which can alter cell function considerably. Solutes that do not freely cross cell membranes such as sodium and glucose determine the tonicity of the ECF.[1,2] The contribution of these solutes to ECF osmolality can be estimated with the following formula:

(Na [mEq/L] x 2) + (Glucose [mg/dL]/18 + (BUN [mg/dL]/2.8)

Osmolarity is the major determinant of water movement between the extra- and intracellular compartments and is maintained between 285 and 295 mOsm/kg.[1,3] Changes in ECF osmolality are usually as a result of an increase or a decrease in water volume but occasionally may result from a change in the amount of solute. Changes in osmolality are monitored by neurons in the hypothalamus called osmoreceptors and are relayed to the magnocellular neurons in the supraoptic and paraventricular nuclei of the hypothalamus where arginine vasopressin (AVP), also known as antidiuretic hormone (ADH), is synthesised and transported to the posterior lobe of the pituitary gland.[2,4,5]

The magnocellular neurons also react to information concerning intravascular volume and pressure. Cardiac and vascular baroreceptors detect blood pressure and volume variations and communicate this information to the hypothalamus such that hypotension or hypovolaemia can lead to the release of AVP (Table I).[7]

Sodium regulation

Sodium regulation is controlled via renal mechanisms that are influenced by both sympathetic innervation and natriuretic factors. Renal baroreceptors respond to sympathetic activation,

Table I: Differences between osmoregulation and volume regulation[6]

Differences between osmoregulation and volume regulation		
	Osmoregulation	**Volume regulation**
What is being sensed	Plasma osmolality	Effective circulating volume
Sensors	Hypothalamic osmoreceptors	Carotid sinus
		Afferent glomerular arteriole
		Atria
Effectors	ADH	Sympathetic nervous system
		Renin-angiotensin-aldosterone
		Natriuretic peptides
		Pressure natriuresis
		ADH
What is affected	Water excretion (via ADH)	Sodium excretion
	Water intake (via thirst)	

ADH – antidiuretic hormone

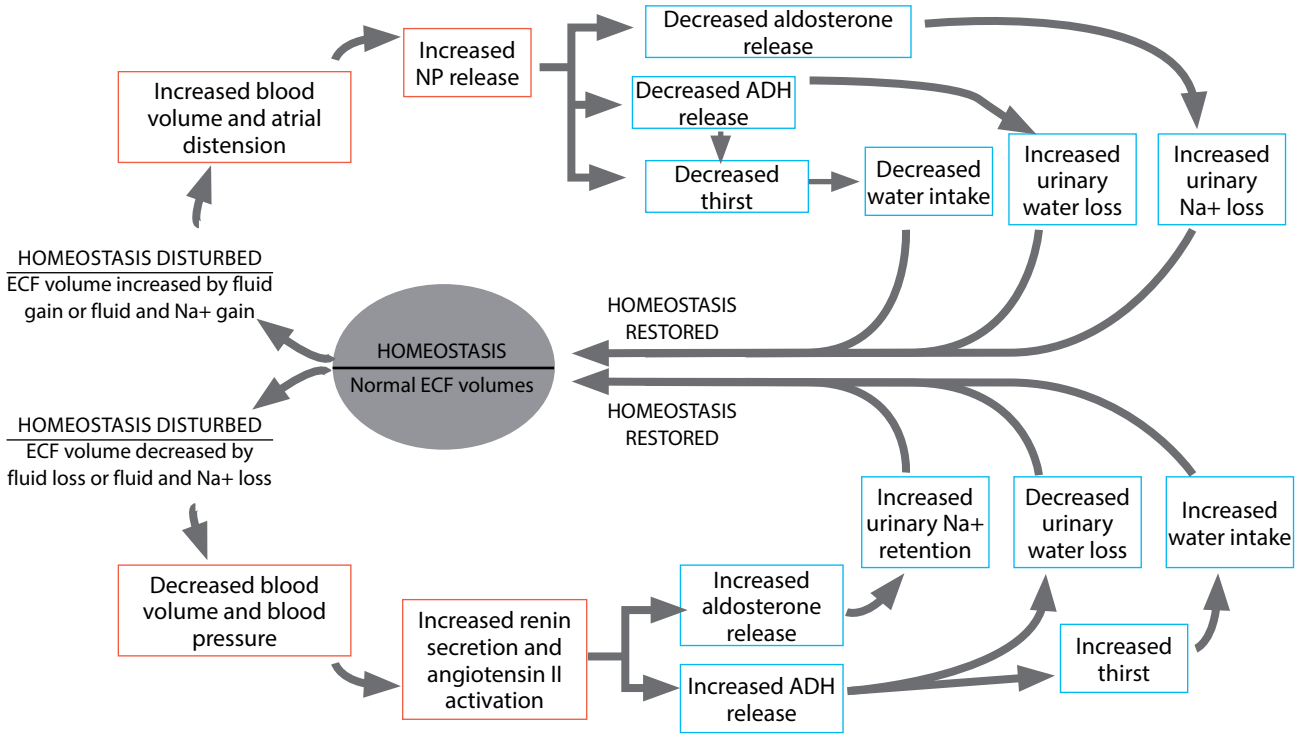

Figure 1: Electrolyte fluid balance[9]

hypotension, and/or reduced sodium delivery to the distal tubule of the kidney by increasing the secretion of renin. Renin stimulates the production of angiotensin II, which not only stimulates receptors in the subfornical organ to induce thirst but also stimulates a non-osmotic release of AVP. Angiotensin II stimulates aldosterone synthesis. Aldosterone acts in the distal tubule of the nephron to promote reabsorption of sodium and water (Figure 1).[8]

The natriuretic peptide family (atrial natriuretic peptide [ANP], brain or B-type natriuretic peptide [BNP], C-type natriuretic peptide [CNP], dendroaspis natriuretic peptide [DNP], and urodilatin) promotes natriuresis by inhibiting sodium reabsorption in the inner medullary collecting duct. ANP, BNP, and urodilatin are not only able to inhibit sodium reabsorption but also can stimulate sodium secretion. In addition, circulating ANP and BNP can inhibit renin, aldosterone, and AVP release.[1]

Hypernatraemia: Pathophysiology/aetiology

Hypernatraemia is defined as serum sodium greater than 145 mEq/L, which results when there is a shift in the ratio of sodium to water, which favours less water and/or more sodium. Hypernatraemia can be a result of increased free water loss without adequate replacement (diarrhoea, osmotic diuresis), a lack of circulating AVP (neurogenic DI), or an inadequate renal response to AVP (nephrogenic DI).[1,2,7] Hypernatraemia could also be a result of excessive sodium retention as seen with primary hyperaldosteronism, Cushing's syndrome, or with the administration of hypertonic solutions. In hypernatraemia, an increase in ECF osmolality promotes movement of water out of the cellular compartment with resultant cell shrinkage.

Within several hours of the rise in ECF osmolality, the brain cells begin to generate intracellular osmolytes to increase intracellular tonicity. This adaptation will promote the return of water into the intracellular space and return the cell to normal size. If a rapid decline in extracellular osmolality occurs once intracellular osmolytes form, the likelihood of harmful cerebral swelling increases. Common symptoms include weakness, confusion, seizures, and even coma. The severity of symptoms is correlated with the degree and rapidity of the hypernatraemia. In rare cases, severe hypernatraemia can result in brain shrinkage which is significant enough to produce mechanical disruption of blood vessels and haemorrhage.[7]

Management of hypernatraemia

Clinical assessment of the patient's volume status allows differentiation between the inability to appropriately conserve water (DI) and excessive accumulation of sodium (administration of hypertonic solutions). The clinical combination of hypernatraemia and hypotonic urine indicates that the kidneys are unable to appropriately conserve water.

Possible aetiologies include an impaired renal response to AVP (nephrogenic DI), osmotic diuresis, or an insufficient release of AVP (neurogenic DI). Nephrogenic DI can be congenital or acquired through drug toxicity (lithium, demeclocycline, furosemide, gentamicin, amphotericin B) or renal disease. It is distinguishable from neurogenic DI by the lack of response when exogenous AVP is administered.[1] The choice of intravenous fluid depends on the intravascular volume and serum sodium concentrations. Volume contracted patients should have their intravascular volume repleted with 0.9% sodium chloride to correct hypovolaemia and improve hypoperfusion. Once

intravascular volume is restored and/or haemodynamic stability achieved, the water deficit can be roughly estimated:

Water deficit in liters = (0.6 weight [kg] x (serum Na/140 – 1).

To determine the rate at which to replace the water deficit, take half of the total calculated water deficit and administer over 12 to 24 hours. The remainder of the deficit should then be given over the next 48 to 72 hours. The preferred replacement solution is sodium chloride 0.45% if sodium loss is ongoing; whereas dextrose 5% water is preferred if the sodium losses have been stopped or when there is no sodium deficit. In addition to replacing the water deficit, ongoing urinary and insensible losses should also be considered.[1,5]

The rate of sodium correction depends on the rapidity with which the hypernatraemia developed. Hypernatraemia that develops over less than 48 hours may be safely corrected at a rate of 1 mEq/L per hr; whereas a correction rate of 0.5 mEq/L per hr should not be exceeded if the hypernatraemia occurred more gradually. Slower correction of the hyperosmolar state is done to prevent acute cellular swelling and prevent serious consequences, most notably cerebral oedema.[10] Serial serum sodium measurements should be drawn every few hours during the first 12 to 24 hours to ensure the sodium concentration is not declining at an unsafe rate. Hormone replacement, with aqueous vasopressin or its analogue 1-Desamino-D- AVP (dDAVP), should be considered in patients with acute DI when the urine output is greater than 8 L/d. Aqueous vasopressin has a shorter duration of action and increased vasopressor activity compared to its analogue dDAVP. Doses of the injectable formulation of dDAVP between 0.5 and 4 mcg are commonly administered and produce an antidiuretic effect for 8 to 12 hours. In transient DI, allowing the development of hypotonic, polyuria prior to each dose (urine output > 300 mL/h and specific gravity < 1.005) can confirm the persistence of the disorder.[10]

Neurogenic diabetes insipidus

Neurogenic DI, also referred to as central DI, is a failure of adequate release of AVP from the posterior pituitary. The disruption of AVP secretion is transient in 50% to 60% of cases with return to normal osmoregulation in three to five days. Clinical manifestations include excessive excretion of inappropriately dilute urine (> 30 ml/kg per d), low urine osmolality (< 300 mOsm/kg and specific gravity < 1.005), high serum osmolality, and subsequent elevations in serum sodium levels.[1,5] This excessive loss of dilute urine can lead to dehydration if fluids and/or AVP replacement is not instituted.

Tumours, such as pituitary adenomas or craniopharyngiomas, can produce either chronic DI as the tumour enlarges or acute symptoms following surgical resection. Treatment with hormone and fluid replacement is generally successful to normalise serum sodium levels. Monitoring of urine output, urine-specific gravities, and serum sodium levels after surgery is critical. During this time, a transitory release of vasopressin from the injured pituitary occurs and causes hyponatraemia. Syndrome of inappropriate secretion of antidiuretic hormone (SIADH) is generally considered the aetiology of the hyponatraemic phase; however, cerebral salt wasting syndrome (CSW) and secondary adrenal insufficiency have also been suggested and should be considered.[2,5] Depletion of vasopressin stores leads to insufficient vasopressin release and symptoms of DI return. Acute hormone and fluid replacement is commonly required and chronic hormonal replacement is often necessary. Common vascular aetiologies of DI include expanding aneurysms, arteriovenous malformations, sinus thromboses, and intrathalamic haemorrhages. DI is common following head

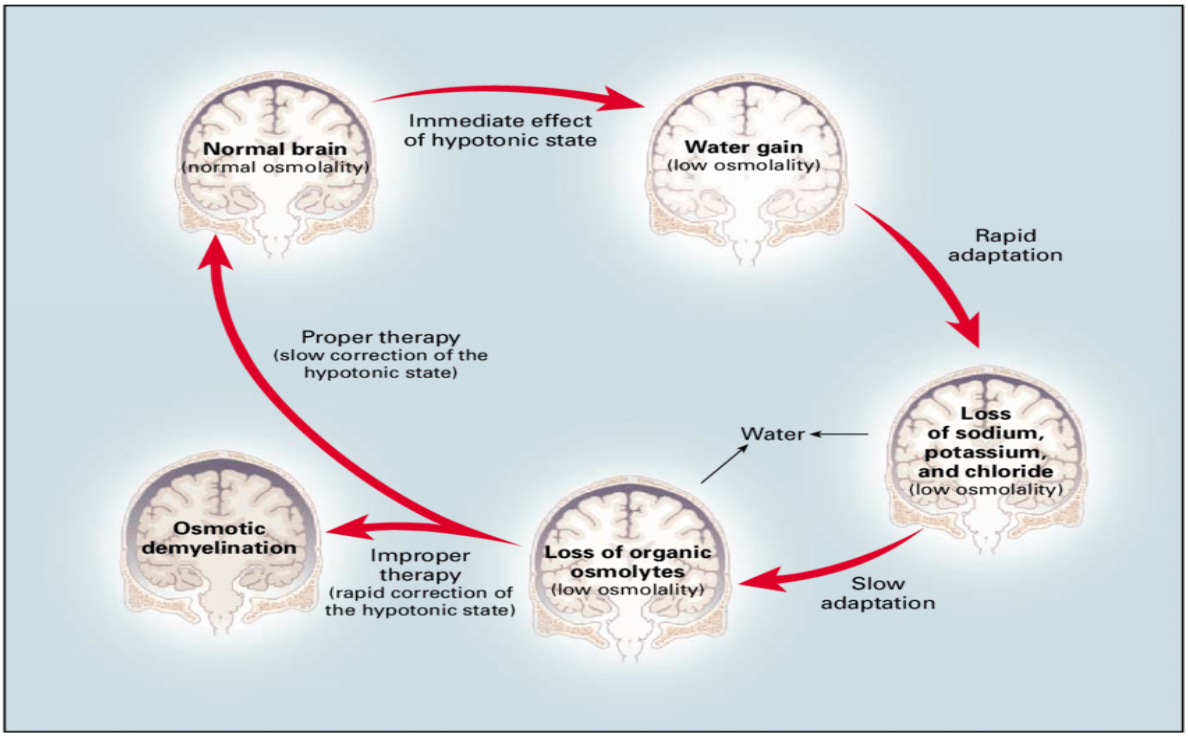

Figure 2: Effects of hyponatraemia on the brain[13]

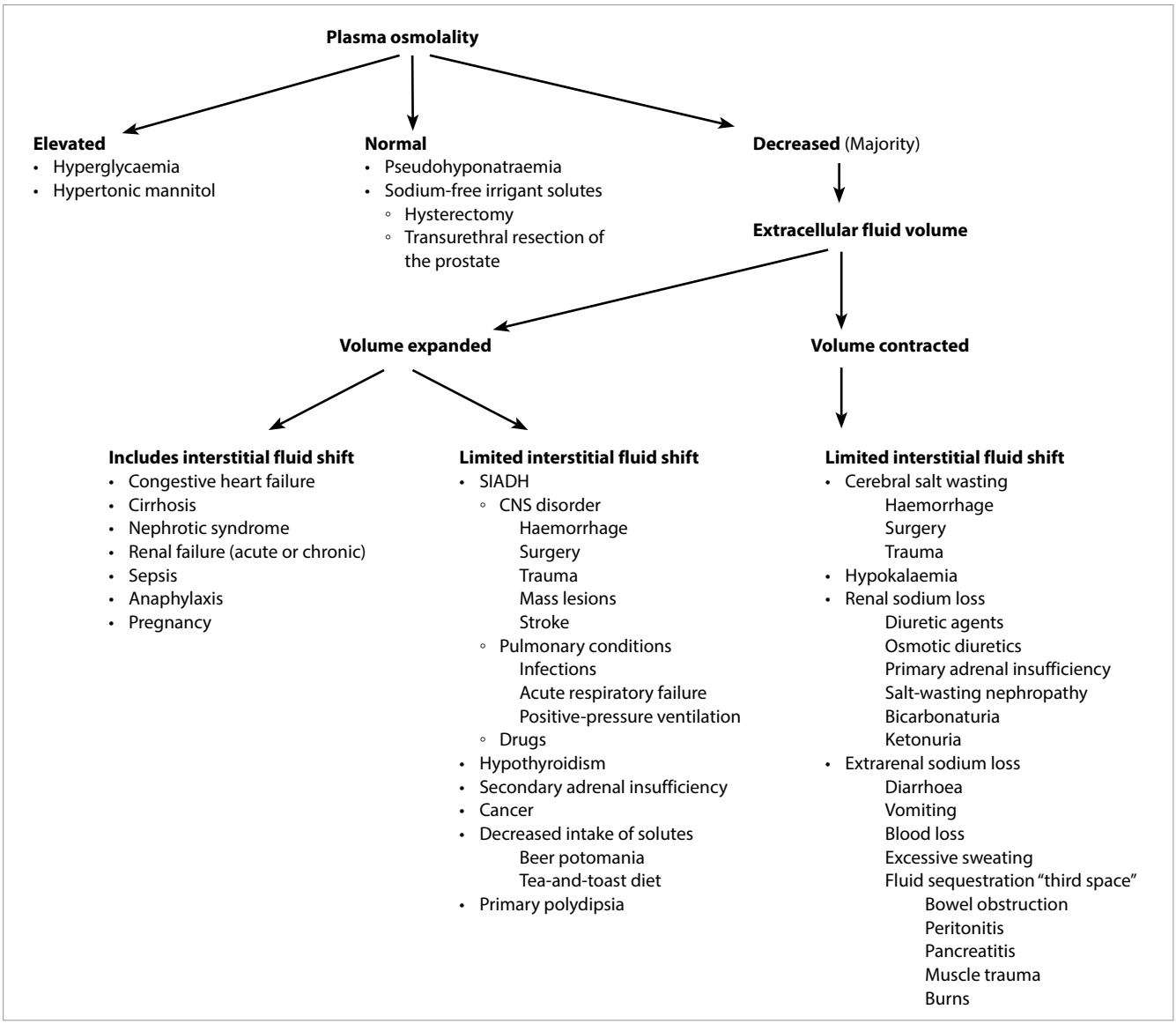

Figure 3: Approach to hyponatraemia[14]

trauma and is often seen in patients who progress to brain death.[11]

Hyponatraemia: Pathophysiology/Aetiology

Hyponatraemia is defined as a serum sodium less than 135 mEq/L and is the most common electrolyte abnormality in hospitalised patients. The aetiological range of this electrolyte disorder can be subcategorised into hyponatraemia associated with high, normal, or low osmolality.[1,11] Patients in whom the serum sodium concentration is greater than 125 mmol/L are usually asymptomatic, whereas those in whom these values are lower may have symptoms that include headache, nausea, vomiting, muscle cramps, lethargy, restlessness, disorientation, and depressed reflexes.[1,2,5] If, however, the disorder has developed rapidly, complications of severe and rapidly evolving hyponatraemia include seizures, coma, permanent brain damage, respiratory arrest, brainstem herniation, and death.

Hypotonic hyponatraemia is predominantly the result of an excess of extracellular water relative to sodium. This disturbance may be secondary to impaired renal water excretion, excessive water intake, or excessive sodium loss; each resulting in the dilution of sodium in the ECF. Shifts in water from the ECF into the intracellular compartment causes cellular swelling and can acutely increase brain volume. Large, rapid shifts that cause acute cerebral oedema may lead to herniation and even brain death (Figure 2).[12] Compensation of this acute increase in intracellular volume begins first by reducing intracellular potassium (rapid adaptation) followed by a decline in the production of intracellular osmolytes (slow adaptation).

Neurological dysfunction is the principal manifestation of hyponatraemia, which may be exacerbated by other disease processes or underlying conditions, especially in those patients in whom a pathological condition is located intracranially. Awareness of other potential causes of hyponatraemia is required to provide appropriate management and avoid deleterious outcomes, which may occur when the electrolyte deficiency is overcorrected or corrected too rapidly. Therefore, early diagnosis and effective treatment of hyponatraemia is critical for hyponatraemic patients.

Hyperosmotic hyponatraemia: In hyperosmotic hyponatraemia disorders, solutes confined to the extracellular compartment induce shifts in transcellular water.[2] As an example, hyperglycaemia or the retention of hypertonic mannitol may result in hyponatraemia because water shifts from the intracellular to the extracellular space, causing dehydration of cells.

Isosmotic hyponatremia: May be observed in patients who undergo transurethral resection of the prostate or hysterectomy. During these procedures, patients may absorb large quantities of hypoosmotic glycine or sorbitol irrigating solutions leading to a dilutional reduction in the plasma sodium concentration. The extent of isosmotic hyponatraemia is related to both the quantity and rate of fluid that is absorbed.[1,11] A less common condition of hyponatraemia associated with normal serum osmolality is seen in patients with extreme hyperlipidaemia and hyperproteinaemia. Also known as "pseudohyponatraemia".

Hypoosmotic hyponatraemia: Most hyponatraemic disorders are associated with hypoosmolality. Also known as "dilutional hyponatraemia", these disorders may be caused by excessive water intake, but are more commonly caused by water retention. This subcategory of hyponatraemia may be further differentiated according to volume status (Figure 3).[1]

Volume-expanded hyponatraemia occurs when the intake of salt and water exceeds renal and extrarenal losses. The sodium and water retention may be primary, from an increased ECV, or secondary, in response to a decreased ECV, including congestive heart failure, cirrhosis, nephrotic syndrome, sepsis, anaphylaxis, and pregnancy.[1,11] Other causes of volume-expanded hyponatraemia are due to a reduced rate of salt resorption by the diluting segment of the kidney (hypothyroidism, secondary adrenal insufficiency, cancers), sustained non-osmotic release of ADH (SIADH), or a combination of these two factors.[11]

Euvolaemic hyponatraemia accounts for 60% of all cases of hyponatraemia and is described by an increase in water content without a concomitant increase in total body sodium. SIADH is the leading cause of euvolaemic hyponatraemia and a major cause of hyponatraemia in patients with central nervous system (CNS) disease.

Syndrome of inappropriate secretion of antidiuretic hormone (SIADH)

It is characterised by excessive plasma levels of AVP that are not adequately suppressed in response to low plasma osmolality. This unrestricted AVP release leads to excessive water retention by the kidney which produces ECF volume expansion and ultimately dilutional hyponatraemia. Volume expansion from water retention initially results in a brief period of natriuresis, which accounts for the brief "salt-wasting" phase of SIADH.[11,12,15] Fluid restriction is the treatment of choice in SIADH. There is the potential for an administration of intravenous saline in patients with SIADH to result in symptomatic hyponatraemia, because renal handling of water is impaired but renal management of sodium is not.

In SIADH, neither hyperosmolality nor volume contraction is the stimulus behind the release of ADH. In cases of SIADH, excessive levels of ADH occur as a result of disease- or drug-induced pituitary release of ADH or the ectopic production of ADH. Because of these excessive ADH levels, the diagnosis of SIADH is based on the presence of a low serum level of sodium, an inappropriately concentrated urine compared with serum osmolality, a high urinary sodium level, and the absence of

Table II: Comparison between DI, CSW and SIADH[19]

Features	Central neurogenic diabetes insipidus	Syndrome of inappropriate secretion of ADH	Cerebral salt-wasting syndrome
Cause	Decreased secretion of ADH or renal unresponsive to ADH	Over-production of ADH	Renal sodium transport abnormality
Serum level of sodium, mEq/L	Hypernatraemia > 145 (high)	Hyponatraemia < 135 (low)	Hyponatraemia < 135 (low)
Serum osmolality, mOsm/kg	> 295 (high)	< 275 (low)	< 275 (low)
Urinary osmolality, mOsm/kg	Decreased (< 200)	Elevated (> 100)	Elevated (> 100)
Urinary level of sodium, mEq/L	Normal or decreased	Normal or elevated (> 25)	Elevated (> 25)
Urine output	Increased (> 250 ml/h)	Decreased	Decreased
Urine specific gravity	< 1.005	> 1.010	> 1.010
Extracellular volume	Decreased	Increased	Decreased
Serum urea nitrogen	Elevated	Normal or low	Elevated
Mental state	Normal to impaired	Confusion	Agitation, decreased, consciousness
Body weight	Decreased	Normal to increased	Decreased
Heart rate	Tachycardia	Slow to increased	Decreased
Blood pressure	Mild hypotension	Hypertension	Postural hypertension
Treatment	Fluid replacement, desmopressin or vasopressin	Fluid restriction, slow sodium replacement	No fluid restriction, slow sodium replacement

ADH – antidiuretic hormone

peripheral oedema or dehydration with no evidence of adrenal, thyroid, or renal dysfunction.[15,16,18]

Hypovolaemic hyponatraemia is marked by reductions in both total body water and sodium through renal or extrarenal sodium losses. Centrally mediated renal sodium wasting as the cause of hyponatraemia has been termed CSW syndrome.

Cerebral salt wasting syndrome

It is characterised by excessive renal sodium loss, which is suspected to be caused by a disruption of sympathetic input to the kidneys and increased production of circulating natriuretic factors.[12,15,16] Initial management includes correcting the volume contraction and serum sodium concentration with intravenous isotonic or hypertonic solutions. CSW is generally self-limiting and should be treated with continued administration of sufficient fluid to maintain euvolaemia until resolved. Fluid restriction may exacerbate the underlying neurological condition in this setting.[17]

Comparison of SIADH and CSW serum osmolality and intravascular fluid volume are the primary stimuli for ADH release. Osmoreceptors in the hypothalamus sense changes in serum osmolality and induce or depress ADH secretion from the posterior pituitary. Baroreceptors within the carotid sinuses, on the other hand, sense intravascular volume and permit the release of ADH with volume contraction (Table I). In the kidney, ADH then increases the permeability of the terminal distal tubule and medullary collecting duct to water, leading on the expansion of the ECV. A pronounced elevation of ADH, however, leads to an increase in the ECV, resulting in dilutional hyponatraemia.[2,16,18]

Additional laboratory evidence that relates to the ECV may also help distinguish SIADH from CSW (Table II).

Management of hyponatraemia

An appreciation of the time course of the change in sodium concentration is an important consideration in evaluating and treating patients. A sodium concentration of 120 mEq/L which has developed over several weeks will often be asymptomatic and can be managed conservatively. Conversely, the same sodium concentration which developed over several hours can be life-threatening and require aggressive intervention. The determination of urgency for intervention should be based on the patient's neurological status (Figure 4).[1,2,8,20]

Cerebral swelling can be prolonged and produce severe neurological symptoms that can result in permanent damage if not treated promptly. Conversely, osmotic demyelination syndrome can occur if excessive or rapid correction of serum sodium occurs. Central pontine myelinolysis, a syndrome that causes destruction of the myelin sheath that covers nerve cells was originally described in alcoholic and malnourished patients (Figure 2). The syndrome was described to occur as a result of rapid correction of chronically low serum sodium concentrations.[7,8,20]

A balanced approach to treating a symptomatic hyponatraemic patient would be to quickly raise the serum sodium concentration (0.75–1 mEq/L per h) to sodium levels between 125 and 130 mEq/L in order to reduce cerebral oedema. The rate of correction should then be dramatically reduced and should not exceed 0.5 mEq/L per h. Meticulous avoidance of overcorrection should be used.[1,2,20]

Management of asymptomatic hyponatraemia should be conservative, irrespective of the severity of sodium level. The principal treatment strategy for both euvolaemic and hypervolaemic hyponatremia involves free water restriction and removal; whereas the management approach to hypovolaemic hyponatraemia includes volume and sodium replacement. The amount of sodium required to raise the serum sodium concentration to a desired level can be estimated from the formula:

Sodium desired (mEq) = (rise in Na^+conc [mEq/L] x ECF volume)

The ECF volume can be estimated by multiplying the body weight (kg) by 0.6.

Generally, fluid restriction only raises serum osmolality by 1% to 2% per day, and many patients cannot tolerate this intensity of volume restriction. Continued administration of isotonic or hypertonic saline may then be necessary. Hypertonic saline can be used in acute symptomatic patients with serum sodium < 125 mEq/L. NaCL 3% 100 ml over 10 min. If symptoms persist, repeat up to 3 doses over 30 min. Monitor serum sodium every 1 to 2 hours to assess need for additional treatment.

Fludrocortisone acetate enhances sodium retention through its mineralocorticoid activity. This agent has shown only limited efficacy in correcting hyponatraemia and may precipitate volume overload through concurrent water retention.

Conivaptan, an intravenous V1A and V2 (vasopressin) receptor antagonist, and tolvaptan, an oral V2 receptor antagonist, promote free water excretion while sparing electrolytes, including sodium. This process, known as aquaresis, results in a rise in serum sodium and does so through reversing the underlying pathophysiology of SIADH.

Tolvaptan, an oral aquaretic, may have superior pharmacological mechanisms for the treatment of chronic SIADH; however, data supporting long-term use are limited.[1,20]

Neurosurgical conditions associated with sodium disturbances

Traumatic brain injury (TBI): Hyponatraemia is frequently seen in patients suffering from TBI. Following TBI, the acute onset of severe hyponatraemia was associated with either poor neurological outcome or death in those patients with a sudden onset of seizures, followed by coma, apnoea, and brainstem compression. Another complicating factor is the occurrence of an acute adrenal crisis within the population of head-injured patients, which may result from bilateral adrenal haemorrhage.[1,20] Although SIADH and primary adrenal insufficiency may present

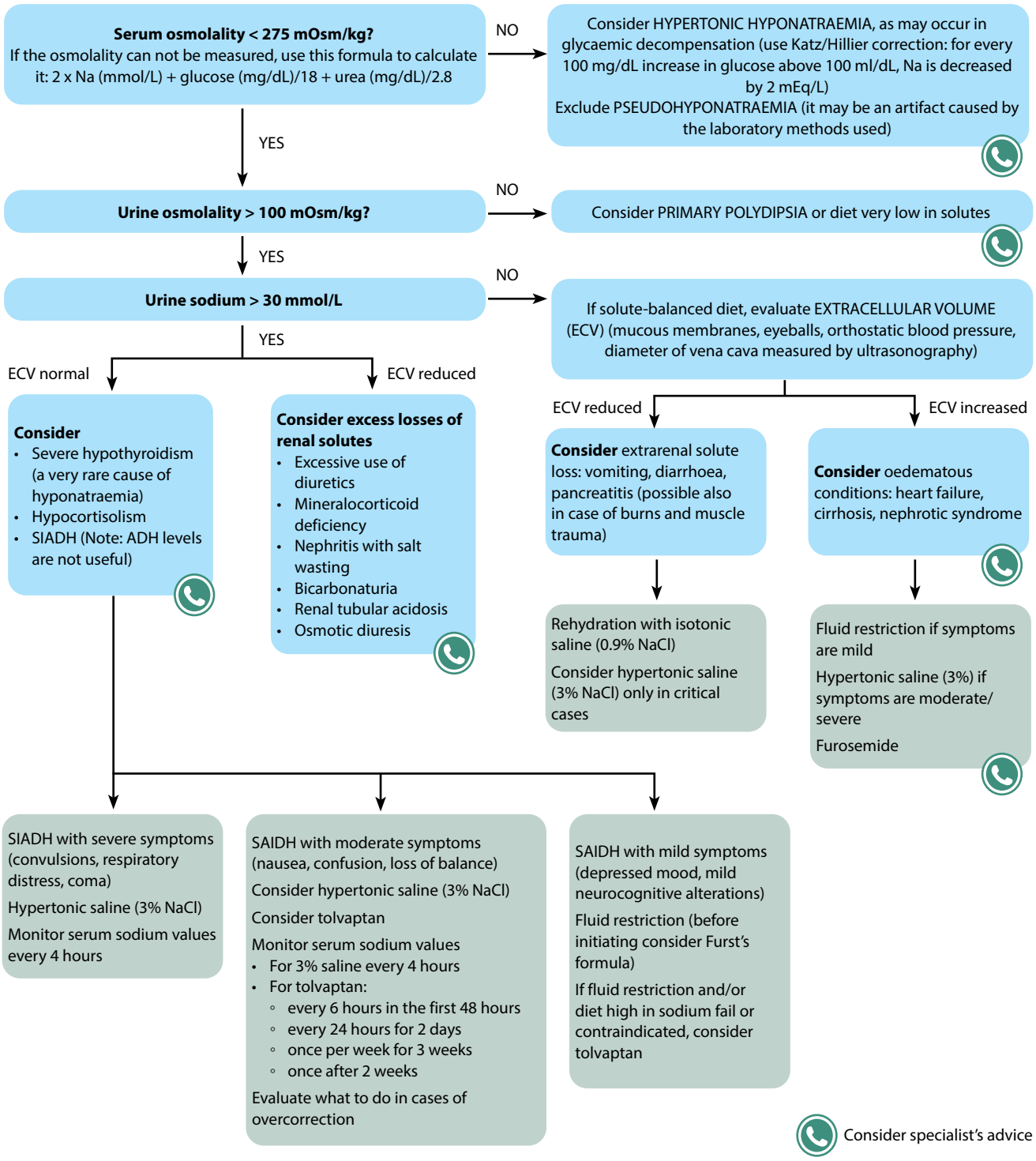

Figure 4: Treatment of hyponatraemia[21]

with similar values of osmolality and urine electrolyte levels, other causes of hyponatraemia should be considered when the patient remains unresponsive to standard treatments for SIADH. Another key to the recognition of adrenal insufficiency is the finding of relative hyperkalaemia in the context of hyponatraemia.

Aneurysmal subarachnoid haemorrhage: The presence of hyponatraemia is significant, because it is recognised as a risk factor for, as well as a predictor of, vasospasm and cerebral ischaemia. Hyponatraemia related to SAH is thought to occur secondary to the release of BNP. The low serum concentrations of sodium accentuate cerebral oedema further. The standard of care is aggressive hypervolaemic therapy for intravascular volume expansion and sodium supplementation. Aggressive hypervolaemic therapies are not always effective on their own and the use of fludrocortisone or hydrocortisone, which inhibit natriuresis, is advocated. These agents function by promoting sodium resorption in the kidney through their mineralocorticoid effects.[1,12]

Transsphenoidal surgery for pituitary tumours: Diabetes insipidus commonly occurs following transsphenoidal surgery

for pituitary tumours. Postoperatively, an ADH deficiency normally leads to polyuria (urine output 5 ml/kg/hr) with an excessive free water loss that generates a urine/plasma osmolality ratio lower than 1.5. Therapeutic intervention includes maintaining an appropriate plasma osmolality via adequate fluid replacement along with administration of desmopressin to avoid hypernatraemic hypovolaemia. Diabetes insipidus may coexist with CSW, however.[22] CSW is thought to occur secondarily to the release of BNP after transsphenoidal resection of pituitary adenomas and is possibly the cause of hyponatraemia in cases in which there are normal levels of ADH. Following pituitary surgery, DI has also been found to occur as a triple response.[22,18] This is characterised by an initial four to eight day period of DI, followed by a transient remission or an excessive release of ADH (similar to SIADH) lasting one to 14 days, which concludes with the recurrence of often permanent DI. Conversely, symptomatic delayed hyponatraemia has been reported in patients who have undergone transsphenoidal surgery for pituitary adenomas.

Cranial vault reconstruction for craniosynostosis: Hyponatraemia frequently occurs after cranial vault reconstruction for craniosynostosis in paediatric patients. Most of the patients exhibited increased urine output, normal or increased urine levels of sodium, and low serum levels of sodium, suggesting the diagnosis of CSW.[18] Daily monitoring of serum levels of sodium and maintenance of normonatraemia is important to prevent deleterious effects.

Conclusion

Sodium disturbances are a serious comorbidity in the neurosurgical population. Lack of proper assessment and management can lead to serious and permanent neurological consequences, including death. Physicians should recognise the significance of sodium dysregulation among this population and distinguish between the various therapeutic options in order to advocate safe and effective therapy.

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References

1. Murphy-Human T, Diringer MN. Sodium disturbances commonly encountered in the neurologic intensive care unit. J Pharm Pract. 2010;23(5):470-82. https://doi.org/10.1177/0897190010372323.
2. Tisdall M, Crocker M, Watkiss J, Smith M. Disturbances of sodium in critically ill adult neurologic patients: A clinical review. J Neurosurg Anesthesiol. 2006;18(1):57. https://doi.org/10.1097/01.ana.0000191280.05170.0f.
3. Andreoli TE, Abul-Ezz S. Fluid and electrolyte disorders. In: Wing E, Schiffman F, Editors. Cecil essentials of medicine. 10th ed. Elsevier; 2021.
4. Adrogué HJ, Madias NE. Hyponatremia. N Engl J Med. 2000;342(21):1581-9. https://doi.org/10.1056/NEJM200005253422107.
5. Nadel J, Couldwell W. Management of water and sodium disturbances after transsphenoidal resection of pituitary tumors. Neurol India. 2020;68(7):101-5. https://doi.org/10.4103/0028-3886.287679.
6. Up to Date [Internet]. Available from: https://www.uptodate.com/contents/image?imageKey=NEPH%2F51153&topicKey=NEURO%2F5129&source=see_link.
7. Arieff AI, Guisado R. Effects on the central nervous system of hypernatremic and hyponatremic states. Kidney Int. 1976;10(1):104-16. https://doi.org/10.1038/ki.1976.82.
8. Barrett KE, Barman SM, Boitana S, Brooks H. Ganong's review of medical physiology. 23rd ed. Lange Med Public; 2003.
9. Austin Community College [Internet]. Available from: https://www.austincc.edu/apreview/NursingPics/FluidPics/Picture7.jpg.
10. Maas AH, Siggaard-Andersen O, Weisberg HF, Zijlstra WG. Ion-selective electrodes for sodium and potassium: A new problem of what is measured and what should be reported. Clin Chem. 1985;31(3):482-5. https://doi.org/10.1093/clinchem/31.3.482.
11. Cole CD, Gottfried ON, Liu JK, Couldwell WT. Hyponatremia in the neurosurgical patient: diagnosis and management. Neurosurgical Focus FOC. 2004;16(4):1-10. https://doi.org/10.3171/foc.2004.16.4.10.
12. Moro N, Katayama Y, Kojima J, Mori T, Kawamata T. Prophylactic management of excessive natriuresis with hydrocortisone for efficient hypervolemic therapy after subarachnoid hemorrhage. Stroke. 2003;34(12):2807-11. https://doi.org/10.1161/01.STR.0000103744.05430.99.
13. Adrogue HJ, Madidas NE. Hyopnotremia. New Engl J Med. 2000;342(12):1581-9. Available from: https://www.researchgate.net/profile/HoracioAdrogue2/publication/256538321/figure/fig2/AS:601580852215810@1520439460107/Effects-of-Hyponatremia-on-the-Brain-and-Adaptive-Responses-Within-minutes-after-the.png.
14. Medscape.
15. Nelson PB, Seif SM, Maroon JC, Robinson AG. Hyponatremia in intracranial disease: Perhaps not the syndrome of inappropriate secretion of antidiuretic hormone (SIADH). J Neurosurg. 1981;55(6):938-41. https://doi.org/10.3171/jns.1981.55.6.0938.
16. Palmer BF. Hyponatremia in patients with central nervous system disease: SIADH versus CSW. Trends Endocrinol Metab. 2003;14(4):182-7. https://doi.org/10.1016/S1043-2760(03)00048-1.
17. Harrigan MR. Cerebral salt wasting syndrome. Crit Care Clin. 2001;17(1):125-38. https://doi.org/10.1016/S0749-0704(05)70155-X.
18. Webster JB, Bell KR. Primary adrenal insufficiency following traumatic brain injury: A case report and review of the literature. Arch Phys Med Rehabil. 1997;78(3):314-8. https://doi.org/10.1016/S0003-9993(97)90040-X
19. Kulkarni D. Brain injury and the kidney. J Neuroanaesthesiol Crit Care. 2016;3(4):16. Available from: https://www.researchgate.net/publication/291529017/figure/tbl1/AS:670029775384622@1536758955986/Comparison-of-central-neurogenic-diabetes-insipidus-syndrome-of-inappropriate.png.
20. Sterns RH, Emmett M. General principles of disorders of water balance (hyponatremia and hypernatremia) and sodium balance (hypovolemia and edema). Basow DS, Waltham MA; 2012.
21. Berardi R, Antonuzzo A, Blasi L, Buosi R. Practical issues for the management of hyponatremia in oncology. Endocrine. 2018;61(6). Available from: https://www.researchgate.net/publication/322997059/figure/fig1/AS:962700393861141@1606537068650/Algorithm-for-diagnosis-and-treatment-of-patients-with-hyponatremia-The-related-notes_Q640.jpg.
22. Albanese A, Hindmarsh P, Stanhope R. Management of hyponatraemia in patients with acute cerebral insults. Arch Dis Child. 2001;85(3):246-51. https://doi.org/10.1136/adc.85.3.246.