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Review Article

Hypernatremia: A Concise Practical Review

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Abstract

Hypernatremia is defined as a serum sodium concentration exceeding 145 mmol/L. It is a hyperosmolar state and arises because of a mismatch between total body sodium and total body water. The causes of hypernatremia include osmoreceptor or thirst dysfunction, excessive water or hypotonic fluid losses, and, rarely, sodium gain. Considering the normal physiologic response to hyperosmolality is useful in assessing and treating hypernatremic patients. Treatment of hypernatremia involves replacing the lost hypotonic fluid and treating the underlying etiology. Calculating the free water deficit or estimating the effect of one liter of intravenous fluid on a patient's sodium level are useful guidelines for initial treatment, but they do not replace strict sodium monitoring.

Background

Water accounts for 45–60% of an adult's body weight [1]. Cell membranes separate total body water (TBW) into Extracellular Fluid (ECF) and Intracellular Fluid (ICF) compartments; each contains different electrolytes. Sodium and potassium are the major cations in the ECF and ICF, respectively. The compartmentalization of electrolytes is essential for cell functioning and is achieved via Na^+- K^+ pump and selective cell membrane permeability [2]. Water diffuses through aquaporin channels impeded in the cell membrane between the ECF and the ICF according to osmotic gradient. As a result, osmolality (i.e., the number of dissolved particles in a kilogram of water) in both compartments is equal [3].

Changes in effective plasma osmolality (i.e., tonicity) affect cell volume and function [4]. Small changes in the composition and size of neurons and other central nervous system (CNS) cells have a significant impact on their functioning. The CNS, therefore, evolved a complex mechanism to defend against osmolar stress. Cells in the CNS accumulate electrolytes when ECF osmolality acutely rises and organic osmolytes after prolonged exposure to hyperosmolality [5].

Plasma osmolality is regulated by a complex interaction involving osmoreceptors, thirst, Arginine Vasopressin (AVP), and the kidneys [6]. In short, the hypothalamus, specifically the subfornical organ and the organum vasculosum of the lamina terminalis, senses an increase in ECF tonicity [7]. In response, the hypothalamus releases AVP from the supraoptic and paraventricular nuclei [8]. AVP in turn acts on the kidneys' collecting ducts and increases water reabsorption [8]. Hypertonicity above the threshold that triggers AVP secretion also stimulates thirst, leading to increased water intake [9]. Once normal osmolality is achieved, both the release of AVP and thirst sensation are inhibited [10].

Sodium is the most abundant electrolytes in the ECF and the primary determinant of its osmolality. Plasma sodium concentration is a function of total exchangeable sodium (Na^+_e) and total exchangeable potassium (K^+_e), as well as TBW [11].

$$\text{plasma } [Na^+] = 1.11\,\frac{Na^+_e + K^+_e}{TBW} - 25.6$$

Hypernatremia can accordingly result from either sodium gain or TBW loss. The toxicity of potassium accumulation prevents it from influencing the body's sodium concentration.

Epidemiology and Clinical Manifestation

Community-acquired hypernatremia is uncommon among healthy adults [12-14]. Hypernatremia is more frequent in older and hospitalized patients [15,16]. In hospitalized patients, hypernatremia is associated with increased mortality, longer hospital stays and discharge to long term care facility [17-19]. Patients with multiple comorbidities or admitted to the intensive care are particularly at increased risk of developing hypernatremia [19,20].

Thirst is one of the first symptoms of hypernatremia, and it intensifies as the hypernatremia worsens. Elderly individuals, however, have decreased thirst sensation, and patients with primary adipsia do not get thirsty at all [21]. Furthermore, critically ill patients may lose thirst perception due to intubation, sedation or altered mental status [22].

Polyuria can be observed in AVP disorders or other causes of kidney water wasting (e.g., the use of diuretics, osmotic diuresis, post-urinary obstruction and recovery phases of acute tubular injury). Additional manifestations include symptoms of hypovolemia and the underlying disease.

Symptoms of generalized CNS dysfunction (e.g., lethargy, irritability, tremor and confusion) may ensue. In addition, seizures and coma may develop in cases of severe or acute hypernatremia [23]. Severe acute hypernatremia can also cause considerable brain shrinkage, leading to vascular injury and intracranial hemorrhage [24].

Clinical Evaluation

Hypernatremia is commonly caused by water or hypotonic fluid loss. Less frequently, it is due to net sodium gain or impaired thirst. Common causes of hypernatremia are listed in Table 1.

	Impaired thirst	**Impaired access to water**	**Urinary loss**	**GIT and skin loss**
TBW loss	• Stroke • Aneurysm • Tumors • Granulomatous disease • Trauma	• Coma • Confusion • Paralysis • Deficient water supply	• AVP disorders • Hypercalcemia • Hypokalemia • Loop diuretics • Osmotic diuresis • Recovery phase of ATI • Post-obstruction	• Osmotic diarrhea • Profuse sweating
Fluid sequestration	• Seizures • Rhabdomyolysis • Intense exercise			
Sodium gain	• Isotonic IVF with net increased water loss • Hypertonic IVF • TPN • Sodium chloride intoxication			
ATI: Acute Tubular Injury; AVP: Arginine Vasopressin; IVF: Intravenous Fluid; GIT: Gastrointestinal Tract; TPN: Total Parenteral Nutrition				

Table 1: Common Causes of Hypernatremia.

When assessing a patient with hypernatremia, it is useful to repeat measurements of plasma sodium and osmolality. Symptoms of thirst, altered sensorium, and access to water are helpful for determining the cause. History of CNS trauma or surgery, lithium treatment, and polyuria are also helpful. Other important diagnostics include the presence diabetes mellitus, diuretic use, diarrhea, and fever.

Typical initial laboratory investigations include plasma osmolality, sodium, potassium, calcium, glucose, urea and creatinine. Urine osmolality and urine electrolytes should also be requested. Dilute urine in the presence of hypernatremia is an indicative of an AVP disorder. Hypercalcemia and hypokalemia can also cause AVP resistance. A low urinary sodium concentration and appropriately concentrated urine point to a non-renal cause of hypernatremia and volume contraction. Selected causes of hypernatremia are discussed below.

Impaired Thirst

Thirst refers to the strong desire to drink. There are several thirst stimuli, including hypertonicity (ICF contraction), mediated by CNS osmoreceptors, and hypovolemia (ECF contraction), mediated by angiotensin II [25]. Osmoreceptor dysfunction typically occurs due to the presence of destructive lesions that affect the hypothalamus. Common causes of osmoreceptor dysfunction include vascular diseases such as hemorrhage and anterior communication artery aneurysms, malignant tumors such as craniopharyngioma, meningiomas and metastases, and granulomatous diseases such as sarcoidosis and histiocytosis, as well as traumatic injuries [26].

Impaired Access to Water

Hypernatremia can result from inadequate water intake due to a lack of response to thirst stimulus. Impaired access to water can result from altered consciousness (e.g., coma, confusion), motor dysfunction (e.g., aphasia, paralysis), and a lack of access to water (e.g., a location in the desert or on the open ocean). In some cases—such as a stroke affecting motor function and interfering with thirst perception—it is difficult to distinguish the cause of hypernatremia.

Arginine Vasopressin Disorder

Arginine vasopressin disorders (formerly known as diabetes insipidus) are caused by an AVP deficiency or a reduction in its effects on the kidneys [27]. The

hallmarks of AVP disorders are polyuria of dilute urine and a lack of urine concentration upon fluid deprivation [28]. Hypernatremia is unusual in adults with AVP disorder who have a free access to water. Arginine vasopressin deficiency (AVP-D) results from a deficiency of AVP; AVP resistance (AVP-R) is a consequence of a diminished AVP effect on the kidneys. Both AVP-D and AVP-R are often acquired, but genetic factors should be considered when the disease occurs in early childhood [29]. Desmopressin administration can distinguish between AVP-D and AVP-R based on changes in urine osmolality; osmolality increases significantly in the former, but not in the latter [30]. Copeptin is a polypeptide released during normal AVP secretion. It is stable and can be used as a surrogate for AVP level [31]. A high copeptin level indicates AVP-R; a low copeptin level indicates AVP-D [32].

Gastrointestinal and Urinary Fluid Loss

For hypernatremia to occur due to fluid loss, the lost fluid must have a lower concentration of electrolytes than the plasma and lead to a net loss of free water. Osmotic diuretics and glucosuria can result in net urinary water loss. Loop diuretics cause an increase in urinary water loss and reduced kidneys' concentrating ability [33]. Hypernatremia may also result from diarrhea caused by malabsorption or osmotic laxative. In contrast, secretory diarrhea causes isosmotic fluid loss and can lead to hypovolemia without causing hypernatremia [34].

Fluid Sequestration

Intense physical exertion can lead to hypernatremia [35]. Anaerobic metabolism during intense exertion can lead to intracellular accumulation of lactate, an increase in intracellular osmolality, and water shift to ICF. Intense exertion also causes increased hypotonic fluid losses. A similar effect has been observed in patients suffering from generalized tonic clonic seizures and rhabdomyolysis. [36].

Sodium Gain

Although hypernatremia is typically caused by a net water deficit, a significant proportion of cases of hypernatremia in critically-ill patients can be attributed to sodium gain [37]. Along with a positive sodium balance, decreased kidney function and reduced sodium excretion are risk factors for hypernatremia in critically-ill patients [38]. Furthermore, critically-ill patients commonly have increased insensible water loss and impaired thirst [39]. In rare cases, hypernatremia can result from the ingestion of large amounts of sodium chloride (sodium chloride intoxication) [40].

Management

Patients with hypernatremia often have a deficit in both water and electrolytes. The initial treatment goal is to achieve hemodynamic stability. Once hemodynamic stability is achieved with isotonic fluid, water and electrolyte deficits can be replaced at a slower pace. Apart from achieving hemodynamic stability, the use of isotonic fluid in the treatment of hypernatremia is inappropriate. The sodium concentrations of commonly used intravenous fluids (IVFs) and their distribution to the ECF are listed in Table 2 [41].

Fluid	$[Na^+]$ (mmol/L)	ECF distribution (%)
0.9% sodium chloride	154	100
Ringer's lactate	130	97
0.45% sodium chloride	77	73
0.2% sodium chloride	34	55
Dextrose 5%	0	40

Table 2: Sodium concentration of commonly used IVFs and their ECF distribution

The enteral route is preferred for fluid replacement. The free water deficit can be estimated as follows: Free water deficit=TBW×(Patient^' s$[Na^+]$-140)/140. The TBW is 0.5 per kg body weight, or even lower in severely dehydrated patients.

Due to the CNS's adaptation to chronic hyperosmolality, the duration of hypernatremia should be considered [23]. Hypernatremia lasting more than 48 hours or of unknown duration is considered chronic and corrected slowly to avoid brain edema. However, hypernatremia undercorrection is common and found to be associated with an increased risk of death [18,42,43] and correcting hypernatremia at a rate above 12 mmol per 24 hours appears to be safe and associated with better survival [44]. In addition, brain edema was not reported in adults with a correction rate exceeding 0.5 mmol/L/hour [45]. Acute hypernatremia, on the other hand, should be corrected at a faster pace. The target correction rate is probably 0.5 mmol/L/hour for chronic hypernatremia and 1 mmol/L/hour for acute hypernatremia; a faster correction rate should be achieved for acute hypernatremia with severe CNS complications.

When managing hypernatremia, insensible and ongoing fluid losses should also be considered. Insensible water loss (IWL) is evaporative water loss from the skin and respiratory tract. It does not contain electrolytes. Under normal conditions, IWL is roughly 10 ml/kg/day, and it is matched by the water content of the solid food being ingested [46]. Insensible water loss increases during fever, tachypnea, hot weather and in the case of burns [41].

For example, a 60-year-old male patient weighing 80 kg is admitted due to intestinal obstruction and has had diuretic use. His admission BP is 95 / 60 mmHg, his pulse is 110 beats per minute, and his serum sodium concentration is 160 mmol/L. After receiving 1.5 liters of isotonic fluid, his hemodynamics improved. The management plan involves correcting hypovolemia

and lowering sodium concentration by 12 mmol/24 hours using 0.2% sodium chloride (0.2%NaCl), inserting a nasogastric tube, and keeping the patient Null Per Orris (NPO) while waiting for definitive treatment.

The estimated free water deficit of the above patient is 40×(160-140)/140=5.7 L. The water volume required for the first 24 hours is 5.7×12/20 = 3.4 L. Given that the patient is NPO, he will require 800 ml to replace the IWL. The total water required is therefore 3.4 + 0.8 = 4.2 L. To convert to 0.2% NaCl: 4.2/(1-0.2)=5.2L/24 hours, or 215 ml/hour. Alternatively, the effect of one liter of IVF on the patient's sodium can be calculated [23]. The effect of one liter of IVF=(Infusate $[Na^+]$-patient' s$[Na^+]$)/(TBW+1) = (34-160)/(40+1)= -3, i.e., each liter of 0.2% NaCl will decrease the sodium concentration by 3 mmol. Consequently, the patient will require 4 L/24 hours to lower sodium concentration by 12 mmol. The patient will need another liter of 0.2% NaCl to replace IWL, which leads to an IVF rate of 210 ml/hour. Frequent clinical evaluation, sodium level monitoring every 4 to 6 hours and assessing the ongoing fluid losses, should guide subsequent IVF rate.

Desmopressin, an AVP analogue, is the treatment of choice for patients with AVP-D [47]. Patients with AVP-R can be treated with variable interventions to reduce polyuria and enhance urine concentration. Interventions such as stopping the offending medication, if possible, salt and protein restrictions, using NSAIDs, thiazides, amiloride, and acetazolamide might be beneficial [48-51].

Treatment of hypernatremia caused by excess sodium (i.e., hypervolemic hypernatremia) aims to achieve a negative sodium and water balance. This can be achieved by restricting sodium intake, loop diuretics, and free water replacement [52]. Finally, dialysis therapy may be indicated in cases of sodium chloride intoxication or if the kidney function is inadequate to excrete the sodium and water loads [53-55].

Conclusion

Hypernatremia exposes the CNS to hypertonic stress and primarily leads to neurological manifestations that are more pronounced with acute sodium increases. Chronic hypernatremia leads to an adaptive increase in osmolality of CNS cells. Therefore, it should be corrected slowly to avoid brain edema. However, there is a lack of reports on this side effect in adults [9,44]. Furthermore, there is a lack of evidence from randomized studies to recommend the optimal rate of hypernatremia correction [56,57].

Reference

1. Watson PE, Watson ID, Batt RD (1980) Total body water volumes for adult males and females estimated from simple anthropometric measurements. Am J Clin Nutr 33: 27–39.
2. Clausen MJV, Poulsen H (2013) Sodium/potassium homeostasis in the cell. Met Ions Life Sci 12: 41–67.
3. Bhave G, Neilson EG (2011) Body Fluid Dynamics: Back to the Future. Journal of the American Society of Nephrology 22: 2166-81.
4. Burg MB, Ferraris JD, Dmitrieva NI (2007) Cellular response to hyperosmotic stresses. Physiol Rev 87: 1441–1474.
5. Verbalis JG (2010) Brain volume regulation in response to changes in osmolality. Neuroscience 168: 862–870.
6. Danziger J, Zeidel ML (2015) Osmotic homeostasis. Clinical Journal of the American Society of Nephrology 10: 852–862.
7. Bourque CW (2008) Central mechanisms of osmosensation and systemic osmoregulation. Nat Rev Neurosci 9: 519–531.
8. Rotondo F, et al. (2016) Arginine vasopressin (AVP): a review of its historical perspectives, current research and multifunctional role in the hypothalamo-hypophysial system. Pituitary 19: 345–355.
9. Sterns RH (2015) Disorders of Plasma Sodium — Causes, Consequences, and Correction. New England Journal of Medicine 372: 55–65.
10. Baylis PH, Thompson CJ (1988) Osmoregulation of Vasopressin Secretion and Thirst in Health and Disease. Clin Endocrinol (Oxf) 29: 549–576.
11. Edelman IS, Leibman J, O'meara MP, Birkenfeld L (1958) Interrelations between serum sodium concentration, serum osmolarity and total exchangeable sodium, total exchangeable potassium and total body water. J Clin Invest 37: 1236–1256.
12. Hawkins RC (2003) Age and gender as risk factors for hyponatremia and hypernatremia. Clinica Chimica Acta 337: 169–172.
13. Liamis G, et al. (2013) Electrolyte Disorders in Community Subjects: Prevalence and Risk Factors. Am J Med 126: 256–263.
14. Ravioli S, Rohn V, Lindner G (2022) Hypernatremia at presentation to the emergency department: a case series. Intern Emerg Med 17: 2323–2328.
15. Snyder NA, Feigal DW, Arieff AI (1987) Hypernatremia in elderly patients. A heterogeneous, morbid, and iatrogenic entity. Ann Intern Med 107: 309–319.
16. Lopes IF, Dezelée S, Brault D, Steichen O (2015) Prevalence, risk factors and prognosis of hypernatraemia during hospitalisation in internal medicine. Neth J Med 73: 448–454.
17. Jung WJ, et al. (2017) Severity of community acquired hypernatremia is an independent predictor of mortality. Intern Emerg Med 12: 935–940.
18. Arzhan S, et al. (2022) Hypernatremia in Hospitalized Patients: A Large Population-Based Study. Kidney360 3: 1144–1157.
19. Tsipotis E, Price LL, Jaber BL, Madias NE (2018) Hospital-Associated Hypernatremia Spectrum and Clinical Outcomes in an Unselected Cohort. Am J Med 131: 72-82.e1.
20. Oude Lansink-Hartgring A, et al. (2016) Long-term changes in dysnatremia incidence in the ICU: a shift from hyponatremia to hypernatremia. Ann Intensive Care 6: 22.
21. Begg DP (2017) Disturbances of thirst and fluid balance associated with aging. Physiol Behav 178: 28–34.
22. Arora SK (2011) Hypernatremic Disorders in the Intensive Care Unit. J Intensive Care Med 28: 37–45.

23. Adrogué HJ, Madias NE (2000) Hypernatremia. New England Journal of Medicine 342: 1493–1499.
24. Goshima T, et al. (2022) Treatment of acute hypernatremia caused by sodium overload in adults: A systematic review. Medicine (United States) 101: E28945.
25. Thornton SN (2010) Thirst and hydration: Physiology and consequences of dysfunction. Physiol Behav 100: 15–21.
26. Robertson GL, Aycinena P, Zerbe robert L (1982) Neurogenic disorders of osmoregulation. Am J Med 72: 339–353.
27. Arima H, et al. (2022) Changing the Name of Diabetes Insipidus: A Position Statement of the Working Group for Renaming Diabetes Insipidus. J Clin Endocrinol Metab 108: 1–3.
28. Fenske W, Allolio B (2012) Current state and future perspectives in the diagnosis of diabetes insipidus: a clinical review. J Clin Endocrinol Metab 97: 3426–3437.
29. Christ-Crain M, et al. (2019) Diabetes insipidus. Nat Rev Dis Primers 5: 54.
30. Miller M, Dalakos T, Moses AM, Fellerman H, Streeten DHP (1970) Recognition of Partial Defects in Antidiuretic Hormone Secretion. Ann Intern Med 73: 721–729.
31. Morgenthaler NG, Struck J, Alonso C, Bergmann A (2006) Assay for the measurement of copeptin, a stable peptide derived from the precursor of vasopressin. Clin Chem 52: 112–119.
32. Szinnai G, et al. (2007) Changes in plasma copeptin, the c-terminal portion of arginine vasopressin during water deprivation and excess in healthy subjects. J Clin Endocrinol Metab 92: 3973–3978.
33. Liamis G, Milionis HJ, Elisaf M (2009) A review of drug-induced hypernatraemia. NDT Plus 2: 339–346.
34. Do C, et al. (2022) Dysnatremia in gastrointestinal disorders. Front Med (Lausanne) 9: 892265.
35. Krabak BJ, Lipman GS, Waite BL, Rundell SD (2017) Exercise-Associated Hyponatremia, Hypernatremia, and Hydration Status in Multistage Ultramarathons. Wilderness Environ Med 28: 291–298.
36. Castilla-Guerra L, Fernández-Moreno M, del C, López-Chozas JM, Fernández-Bolaños R (2006) Electrolytes disturbances and seizures. Epilepsia 47: 1990–1998.
37. Hoorn EJ, Betjes MGH, Weigel J, Zietse R (2008) Hypernatraemia in critically ill patients: Too little water and too much salt. Nephrology Dialysis Transplantation 23: 1562–1568.
38. Mestrom EHJ, et al. (2021) Increased sodium intake and decreased sodium excretion in ICU-acquired hypernatremia: A prospective cohort study. J Crit Care 63: 68–75.
39. Lindner G, Funk GC (2013) Hypernatremia in critically ill patients. J Crit Care 28: 216.e11-216.e20.
40. Metheny NA, Krieger MM (2020) Salt Toxicity: A Systematic Review and Case Reports. J Emerg Nurs 46: 428–439.
41. Rose B, Post T (2001) Clinical physiology of acid-base and electrolyte disorders (clinical physiology of acid base & electrolyte disorders). 5th Edition: McGraw-Hill Education.
42. Ranjan R, Lo SC Y, Ly S, Lim AKH, Krishnananthan V (2020) Progression to severe hypernatremia in hospitalized general medicine inpatients: An observational study of hospital-acquired hypernatremia. Medicina (Lithuania) 56: 1–10.
43. Bataille S, et al. (2014) Undercorrection of hypernatremia is frequent and associated with mortality. BMC Nephrol 15: 37.
44. Feigin E, Feigin L, Ingbir M, Ben-Bassat OK, Shepshelovich D (2023) Rate of Correction and All-Cause Mortality in Patients With Severe Hypernatremia. JAMA Netw Open 6: e2335415–e2335415.
45. Chauhan K, et al. (2019) Rate of Correction of Hypernatremia and Health Outcomes in Critically Ill Patients. Clinical Journal of the American Society of Nephrology 14: 656-663.
46. Cox P (1987) Insensible Water Loss and Its Assessment in Adult Patients: A Review. Acta Anaesthesiol Scand 31: 771-776.
47. Qureshi S, Galiveeti S, Bichet DG, Roth J (2014) Diabetes insipidus: celebrating a century of vasopressin therapy. Endocrinology 155: 4605–4621.
48. Libber S, Harrison H, Spector D (1986) Treatment of nephrogenic diabetes insipidus with prostaglandin synthesis inhibitors. J Pediatr 108: 305–311.
49. Kim GH, et al. (2004) Antidiuretic Effect of Hydrochlorothiazide in Lithium-Induced Nephrogenic Diabetes Insipidus Is Associated with Upregulation of Aquaporin-2, Na-Cl Co-transporter, and Epithelial Sodium Channel. Journal of the American Society of Nephrology 15: 2836-43.
50. Bedford JJ, et al. (2008) Lithium-induced Nephrogenic Diabetes Insipidus: Renal Effects of Amiloride. Clinical Journal of the American Society of Nephrology 3: 1324-31.
51. Gordon CE, Vantzelfde S, Francis JM (2016) Acetazolamide in Lithium-Induced Nephrogenic Diabetes Insipidus. New England Journal of Medicine 375: 2008–2009.
52. Al-Absi A, Gosmanova EO, Wall BM (2012) A clinical approach to the treatment of chronic hypernatremia. American Journal of Kidney Diseases 60: 1032–1038.
53. Sakai Y, et al. (2004) Treatment of salt poisoning due to soy sauce ingestion with hemodialysis. Chudoku Kenkyu 17: 61–63.
54. Pazmiño PA, Pazmiño P (2008) Treatment of Acute Hypernatremia with Hemodialysis. Am J Nephrol 13: 260–265.
55. Huang C, et al. (2013) Treatment of acute hypernatremia in severely burned patients using continuous veno–venous hemofiltration with gradient sodium replacement fluid: a report of nine cases. Intensive Care Med 39: 1495–1496.
56. Ryu JY, et al. (2022) Efficacy and safety of rapid intermittent bolus compared with slow continuous infusion in patients with severe hypernatremia (SALSA II trial): a study protocol for a randomized controlled trial. Kidney Res Clin Pract 41: 508–520.
57. Pokhriyal SC, et al. (2024) Hypernatremia and Its Rate of Correction: The Evidence So Far. Cureus 16: e54699.