

About Salt, Sodium and Natremic Disorders

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ABSTRACT

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The factors affecting sodium metabolism are discussed clearly. The clinical features and causes of hyponatremia are discussed. The clinical approach needed for managing a case of hyponatremia is evolved. The common questions likely to be raised while managing a case of hyponatremia is discussed. Hyponatremia is also discussed.

Keywords: Sodium metabolism, Hyponatremia, Evaluation and management

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INTRODUCTION

Salt has a major role in human life. Common salt has been used to add taste and flavor and to preserve food. It is also used to preserve hides and leather, manufacture soap and keep highways clear of ice during winter. Even as late as last century, salt was used for trade by "Barter system" in exchange for forest produce from the Tribals in the hills. It has been used as a weapon against the British by Mahatma Gandhi during independence struggle. Common salt (Sodium chloride) is obtained by evaporation of sea water. Rock salt (Halite) is an impure form of sodium chloride and the source is from rocks. There are some misconcepts regarding the salt and salt substitutes. The "Induppu" as it is called in vernacular languages in south India is an impure form of sodium chloride and is not potassium chloride as it is widely believed to be.

Salt is a very important constituent of living organisms. It helps to maintain the extra cellular volume and osmolality of body fluids. The salient characteristic of living cell is high level of intracellular potassium and high level of sodium in the extra cellular compartment. When life originated as a unicellular organism in the sea, the cell wall acquired a mechanism to push the sodium out and pump the potassium into the cells so as to maintain high intracellular potassium. The sodium potassium ATPase pump in the cell wall of all animal cells achieves this. The unicellular organism was bathed in a salty external environment. When multi cellular cellular compartment containing sodium so as to maintain the homeostasis. Sodium is important in maintaining the osmolality of extra cellular fluid compartment and changes in serum sodium reflects

changes in the ECF sodium. The body homeostasis maintains the level of sodium in the ECF and plasma in the narrow range of 135-145 meq/L (m mol/L). Any alteration can be potentially harmful and the problem has to be approached systematically and carefully.

In an average adult, 66% the body weight is composed of water. The percentage of body weight contributed by water is higher in infants, males and thin individuals (upto 80%) compared to old obese females (45%) This water is distributed mainly in the intra and extra cellular fluid compartments inproportion of 2/3 and 1/3. The extra cellular fluid is further subdivided as interstitial $\frac{3}{4}$ and intravascular $\frac{1}{4}$. In the intravascular compartment, 10 % is in the arterial system, 35 % in the capillary system and 55% in the venous system.

Sodium handling in the body

The main source for salt intake is from the diet. The approximate daily intake varies from area to area. The average dietary intake of salt is approximately 10 Gms (150 meq). The organisms developed there was a need to have extrasodium level in blood is 135-145 meq/L. Sodium is filtered by the glomerulus and hence the glomerular filtrate contains around 140 meq/L of sodium. During the passage of fluid through the proximal tubule about 65-75% of filtered sodium is reabsorbed together with 65-70% of the filtered water. (isoosmotic reabsorption). No significant sodium absorption goes on in the thin limbs of loop of Henle. The thick ascending limb of the loop of Henle (TAL) is not permeable to water. There is an active Na-K-2Cl pump in the TAL accounting for reabsorption of 25% filtered sodium. The remaining

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salt absorption occurs in the distal tubule where Na reabsorption is linked to K excretion and is controlled by aldosterone. Measurement of urinary sodium helps to assess the integrity of tubular cells. When the individual is dehydrated, the urinary loss of sodium should be negligible. When the hydration is adequate and salt intake high, the urinary sodium should be high. Assessment of urinary sodium is reliable only when the patient has not been given a diuretic. When a patient develops oliguria, if the urinary sodium is less than 20 meq/L, it suggests the tubules are functioning well where as urinary sodium more than 40 meq/L indicates tubular damage.

$$\text{Fe Na (Fractional excretion of sodium)} = \frac{\text{Urinary Sodium} / \text{Urinary Creatinine}}{\text{Serum Sodium} / \text{Serum creatinine}} = \frac{\text{Urinary Sodium} \times \text{Seum creatinine}}{\text{Serum Sodium} \times \text{Urinary Creatinine}}$$

Normally in volume depleted states FENa is less than 1%. In renal tubular injury or dysfunction FENa is more than 2%.

Hormones regulating renal sodium excretion

Vasoconstrictors- (*Na retention*)

Angiotensin II
 Vasopressin
 Catecholamines
 Aldosterone
 Renal sympathetic stimulation

Vasodialtors - (*Natriuresis*)

Atrial natriuretic peptide (ANP)
 Brain natriuretic peptide (BNP)
 C type natriuretic peptide
 Urodilatin I Nitric oxide I Endothelin I
 Prostaglandins PGE₂ I PGI₂
 Bradykinin I Na-KATPase inhibitors.

The concept of Osmolar clearance and free water clearance

The urine volume consists of two components, Osmolar clearance (C_{osm}) and Free water clearance (CH₂O). C_{osm} is the volume of water required to excrete the solutes in a concentration equal to the solutes in the plasma. Free water clearance can be positive or negative. Positive free water clearance means that there is more water than C_{osm}, which in turn means that the urine is dilute and has low

osmolality. In this case, the free water clearance is the volume of solute free water that is present over and above C_{osm}. In negative free water clearance, the urine is concentrated and C_{osm} can be achieved only if water is added to the urine. The amount of water required to make the urine solute concentration same as in plasma is the negative free water clearance. In hypotonic urine, Urinary osmolality is less than plasma osmolality and CH₂O is positive. In hypertonic urine, the urinary osmolality is more than plasma osmolality and CH₂O is negative. Failure to excrete free water in settings of increased water intake causes hyponatremia. If increased excretion of free water in polyuric states is not accompanied by adequate water intake, it may cause hypernatremia.

Hyponatremia

Hyponatremia is defined as serum sodium of less than 135 meq/L and is a common problem in the hospitalized patients. It can be acute or chronic, mild or severe and symptomatic or asymptomatic. The serum contains 93% of water and 7% lipids and proteins. If the lipids or proteins are increased the water content is lesser and the flame photometer estimates lower level of sodium. This is pseudo hyponatremia and occurs in conditions associated with hyperlipidemia and hyperproteinemia. In hyperglycemia, there is more water content associated with high glucose and gives low sodium levels due to translocation of water from the intracellular to extracellular compartment. This is translocational hyponatremia

Common causes of hyponatremia

1. Due to excessive loss
 Renal & non renal salt losing states
 Addison's disease
 Diuretic abuse
2. Due to retention of water
 Cardiac
 Hepatic
 Renal
3. Inability to excrete water
 SIADH
 ARF
 Water intoxication

Hyponatremia can be classified into 3 types

1. Hypovolemic Hyponatremia- ECF volume decreased
 Eg- gastroenteritis, burns, diuretic therapy, renal loss

2. Hypervolemic Hyponatremia - ECF volume increased
Eg - CCF, cirrhosis, Nephrotic syndrome, advanced chronic renal failure
3. Isovolemic Hyponatremia- ECF volume normal
Eg - early stages of CRF, SIADH

Low level of sodium occurring acutely (acute hyponatremia) results in lowering of the extra cellular fluid osmolality. At this point there is an imbalance between the osmolality of intracellular and extra cellular fluid compartments. By the principle of osmosis, when two substances of different osmolality are separated by a semi permeable membrane, (in this case the cell wall) the water moves from the area of lower to higher osmolality (in this case ECF to ICF) resulting in cell swelling. Acute cell swelling inside the skull leads to neurological manifestations since the swollen brain cannot be accommodated within the rigid skull. As time goes on due to the removal of osmotically active substances called “idiogenic” osmoles from the intra cellular compartment, the osmolar difference is minimized or normalized. This compensation may occur in about 48 hours. Thus, any hyponatremia particularly if asymptomatic and remaining stable for 48 hours is considered “chronic”

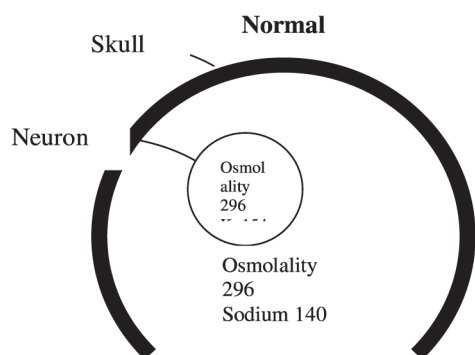


Figure 1. Showing normal osmolality of neuronal cell and ECF

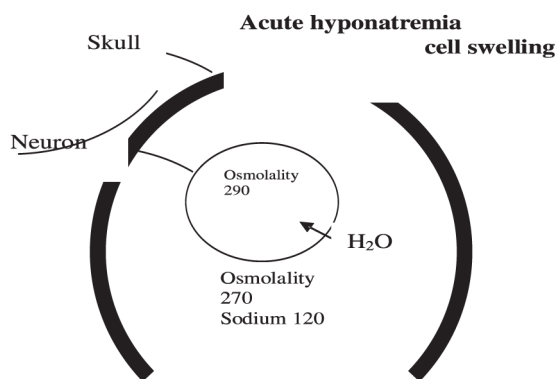


Figure 2. Showing osmolar difference between neuronal cell and ECF resulting in brain odema

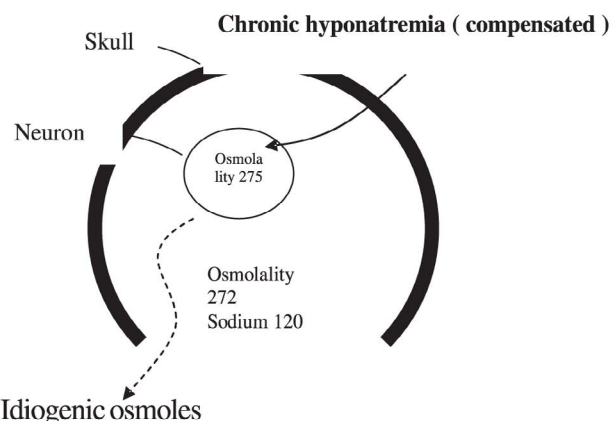


Figure 3. Showing removal of osmotically active intracellular substances and normalization of osmolar differences between neuronal cell and ECF

Hyponatremia is common and may occur in 10 -25% of all inpatients at some time during their hospitalization for serious illness. Acute Hyponatremia suggests <48 hours duration and chronic, >48 hours. Although the serum level of <135meq/ Lis considered as hyponatremia, symptoms often develop only when the levels are <125meq/ L Classification of hyponatremia based on osmolality and ECF volume status.

A. True hyponatremia¹ (HYPOTONIC HYPONATREMIA)

(serum osmolality low <280 mOsm/kg)

1. Associated with low ECF volume (dehydration due to loss of sodium and water)
 - a. Extrarenal-diarrhea, vomiting, ‘third space’ loss.
 - b. Renal loss - diabetic ketoacidosis, salt losing nephropathy, diuretic abuse
2. Associated with high ECF volume (Odematous states- accumulation of more water than sodium-dilutional hyponatremia)
 - a. Cardiac failure,
 - b. cirrhosis liver,
 - c. Nephrotic syndrome and
 - d. Renal failure.
3. Associated with euvoemia (Mild increase in total body water but no odema)
 - a. SIADH
 - b. Post-operative pain
 - c. Hypothyroidism
 - d. Glucocorticoid deficiency
 - e. Psychogenic polydipsia
 - f. Drug induced

- B. Pseudohyponatremia (Isotonic or Hypertonic Hyponatremia)
- Isotonic hyponatremia - associated with hyperlipidemia or hyperproteinemias
 - Hypertonic hyponatremia - associated with hyperglycemia or infusion of mannitol.

Approach to Hyponatremia

As in many other clinical situations, the overall clinical picture together with the laboratory reports are considered before starting aggressive treatment measures. This is particularly true in the management of hyponatremia. The tendency to institute the treatment based on results from the lab without considering the clinical circumstances or condition of the patient should be curbed. When confronted with a blood report of low serum sodium, the following 5 questions are considered in serial order to take appropriate decisions.

Question 1. Is the collection / report correct?

The method of collection should be flawless and standardized. Pseudo hyponatremia should not be overlooked and hyperglycemia, hyperlipidemia or hypoproteinemia must be ruled out. The quality control measures and the credentials of the laboratory must also be considered.

Question 2. Is there an appropriate setting for the development of hyponatremia?

Sometimes it is noted that active healthy individuals who have come for “routine health check ups” are labeled as hyponatremic because serum sodium is less than 135meq/L. The blood report gains importance only if one of the appropriate settings is also present. The usual appropriate settings are old age, post operative state, associated salt losing diseases, diuretic therapy, cardiac failure, cirrhosis, nephrotic syndrome, dehydration, neurological disorders and inappropriate fluid therapy. If the patient has the appropriate setting for the development of hyponatremia, the next question is

Question 3. Is the patient symptomatic?

As explained earlier the presence or absence of symptoms depends on the rapidity of onset, severity, and age of the patient. Some patients with associated neurological diseases may have worsening of neurological parameters or the clinical “scores” like the Glasgow coma scale score.

The symptoms may be mild or severe. Lethargy, apathy, muscle cramps, anorexia, nausea, disorientation are the symptoms. The clinical signs include abnormal sensorium, depressed deep tendon jerks, Cheyne-Stokes breathing, hypothermia and even seizures

Question 4. Are there factors that increase the risk of neurological complications?

Children, elderly women, those on thiazide diuretics post operative, menstruant women, psychiatric: polydipsic and hypoxemic patients are particularly vulnerable to neurological complications. Such patients with acute hyponatremia must be managed carefully in an ICU

The last question one must consider before aggressive correction is attempted is

Question 5. Whether correction of hyponatremia will lead to complications?

It is necessary to remember that chronic hyponatremia is a compensated state and the body has by itself normalized the osmolar differences between the intracellular and extracellular fluid compartments. Aggressive correction of hyponatremia will lead to an acute shift in the ECF osmolality to normal level. This leaves an osmotic gradient between intracellular and extracellular fluid compartments resulting in cellular dehydration. Neuronal cells subjected to osmotic damage undergo demyelination. The central pontine area is particularly vulnerable to such injury. Aggressive correction of compensated chronic hyponatremia may therefore lead to osmotic demyelination syndrome. (Central pontine myelinolysis). This is usually an irreversible and potentially fatal condition. (Figure 4).

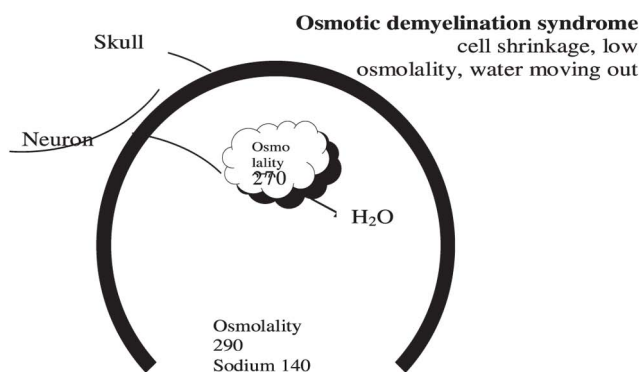


Figure 4. Representing Central Pontine Myelinolysis (Osmotic Demyelination Syndrome)

APPROACH TO MANAGEMENT OF HYPONATREMIA

Patients with asymptomatic chronic hyponatremia do not need aggressive correction. They are advised fluid restriction and oral salt supplements. Pharmacologic treatment if required includes use of Lithium carbonate (900 - 1200 mg) of demeclocycline (300-600 mg) daily. Both drugs act by inhibiting kidney's response to vasopressin and increase free water clearance. Oral salt supplementation combined with frusemide administration also helps to increase serum sodium level. Rarely, salt retaining steroids like fludrocortisone (50 - 200 microgram), Urea or V2 receptor antagonists can be used, may be used. Even if symptomatic, chronic hyponatremia is corrected very gradually by water restriction, oral frusemide, salt supplementation and rarely using normal saline infusions. Hypertonic sodium chloride should be avoided in such cases.

Patients with symptomatic and acute hyponatremia require prompt correction. However, the rate of correction should not exceed 1 mEq/Uhour or 10 mEq/L in 24 hours. Only in patients with seizures due to hyponatremia, correction@ 2-3 mEq/Uhr is advised and is continued till convulsions are controlled. For correction of acute hyponatremia in a symptomatic patient with serum sodium of 106mEq/L, the correction may be planned in 3-4 days as follows.

Day 1. Correct from 106 to 116 @ 1 mEq/L over first 6 hours followed by 0.5 mEq/L over the next 18 hours and recheck values.

Day 2. Correct from 116 to 126 @ 0.5 mEq/L over 24 hours and recheck values.

Day 3 & 4. Correct to about 135 mEq/L. Often, the body corrects minor deviations in the sodium level.

The selection of fluid depends on whether the condition is associated with hypo/iso /hypervolemia. Hypovolemic hyponatremia as in dehydration or diabetic ketoacidosis is corrected with normal saline infusions. Potassium supplementation is often necessary. Patients with hypervolemia and hyponatremia (edematous patients) are treated with water restriction, salt restriction, loop diuretics and potassium supplements. If these measures fail, 3% sodium chloride infusions are considered. Sodium requirement may be calculated from the following formula

Sodium requirement = (Desired Na- actual Na) x 0.6 x body weight in Kg.

Example-1. To increase sodium from 106 to 116

mEq/L in 1 day, the sodium requirement for a 58 kg adult will be

Sodium requirement = (116-106) x 0.6 x 58 = 348 mEq. Say (350)

100 ml of 3% sodium chloride provides 51 mEq sodium. So, 3% sodium chloride can be started at 7drops /min for 24 hours (700 mL providing about 350 mEq).

Example-2. Severely symptomatic child weighing 10 kg with sodium 100 mEq/L - initial target for correction 125 mEq/L.

Sodium deficit = (125-100) x 0.6 x 10 = 150mEq

For 10 mEq correction in 24 hours 110-100 x 0.6 x 10 = 60 mEq Na.

Maximum of 120 ml 3 % NaCl (60 meq) over 24 hrs = 5ml/ hr for 24 hrs (just about 1 drop /min for 24 hours). (Note: Rate of infusion of 3% NaCl should not exceed 20 ml /hr except under exceptional circumstances like hyponatremic convulsions.) Euvolemic hyponatremia is common in SIADH. In addition to the management of primary cause, hyponatremia is corrected with fluid restriction, IV frusemide and hypertonic sodium chloride. Isotonic saline and other hypotonic fluids are avoided.

Thiazide diuretics are associated with more salt loss than water loss (salt diuresis) and loop diuretics like Frusemide are associated with more water loss than salt loss (water diuresis). That is why thiazides are included in the 'etiology' and frusemide in the 'treatment' of hyponatremic syndromes !

Appendix 1. Sodium concentration of common IV fluids

Fluid	Sodium concentration	Remarks
7.5% Na HCO ₃	900 mEq/L	Available as 10 ml amp 90 mEq amp
3% NaCl	512 mEq/L	Available as 100 ml bottle 0.5 mEq/ml
0.9% NaCl Normal saline	154 mEq/L	
Ringer Lactate	130 mEq/L	Also contains Potassium And Lactate
0.45% NaCl Half NS	77 mEq/L	
Isolyte G	65 mEq/L	Gastric replacement fluid
Isolyte M	40 mEq/L	
5 % Dextrose	Nil	

Hypernatremia

Hypernatremia is defined as serum sodium >145 mEq/L and reflects high serum osmolality. It indicates lack of water or sodium gain. It is more often due to lack of water or loss of water than sodium gain.

Sodium gain occurs in hospitalised patients due to inappropriate hypertonic sodium chloride or bicarbonate administration. Normal thirst mechanism effectively prevents development of hypernatremia. Those with impaired thirst mechanism, patients in coma deprived of water and non availability of water are the common causes. Hospitalised patients (Hypertonic infusions, tube feedings, osmotic diuretics, mechanical ventilation), Elderly patients, those with altered mental status and infants are particularly vulnerable. Uncontrolled diabetes or polyuria due to defective concentrating mechanism contribute to hyponatremia.

Causes of hypematremia

- a. Excess water loss
Renal loss - Central diabetes insipidus
Nephrogenic diabetes insipidus
Loss from skin Severe burns
severe exercise/ sweating
From GIT Osmotic diarrhea
- b. Water deficit due to impaired thirst
Comatose patient
Confused I bedridden patient'
Non availability
Primary hypodipsia
- c. Excessive administration of Hypertonic fluids

As with hyponatremia, three broad types of hypernatremia may occur based on the volume status.

- a. Associated with hypovolemia: (low total body sodium)
Such patients sustain relatively greater loss of water compared to sodium. Signs of dehydration, hypotension, tachycardia and mental changes may occur. Such patients need administration of normal saline to correct the dehydration and prevent rapid fall in sodium level. Once dehydration and hypotension are corrected, water by oral or nasogastric tube, IV 0.45% sodium chloride or 5% dextrose should be used. The rate of correction should not exceed 10 mEq/L in 24 hours and 1 mEq/L per hour.

- b. Associated with hypervolemia: (increased total body sodium)

This is rare and occurs when hypertonic solutions (3% sodium chloride, sodium bicarbonate or excessive salt is consumed. Hypoalbuminemia, azotemia and oedematous patients who also have defective concentrating mechanism are vulnerable for the development of this type of hypernatremia. Hypernatremia with volume overload needs administration of loop diuretic along with water. (Thiazides are not preferred because long duration of action. Rarely, dialysis may be necessary in this type of hypematremia.

- c. Associated with euvolemia: (normal total body sodium)
Water loss when associated with defective intake or impaired thirst mechanism may lead to hypematremia. In such patients, water deficit is calculated and replaced. Appropriate treatment for diabetes insipidus should be instituted

END NOTE

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REFERENCES

1. Reynolds RM, Padfield PL, Seckl JR. Disorders of sodium balance. *BMJ*. 2006 Mar 25;332(7543):702-5.
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 Jan;18(1):57-63.
3. Schrier RW. Body fluid volume regulation in health and disease: a unifying hypothesis. *Ann Intern Med*. 1990 Jul 15;113(2):155-9.
4. Adrogue HJ, Madias NE. Hyponatremia. *N Engl J Med*. 2000 May 25;342(21):1581-9.
5. Gross P, Reimann D, Neidel J, Döke C, Prospert F, Decaux G, et al. The treatment of severe hyponatremia. *Kidney Int Suppl*. 1998 Feb;64:S6-11.