Hyponatremia - Stepwise Approach for Diagnosis and Management

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ABSTRACT

The human body is a complex creation with a well balance of various physicochemical and hormonal entities that help to run efficiently the various body functions. Disturbances in any of these components invite a variety of clinical problems. Among the various balances that are maintained, regulation of electrolyte balance is most essential. In clinical practice, electrolytes play a very important role. Disturbance in sodium balance is common in clinical practice. Hyponatremia i.e. depletion in serum sodium values leads to a variety of clinical problems.

Needless to say the astute clinician is sensitive to a variety of clinical syndromes that develop as a result of hyponatremia. Recognition and correction of hyponatremia is very essential. As a word of caution corrective measures should be gradual and in a scientific manner. This article attempts to highlight a stepwise approach towards diagnosis and correction of hyponatremia.

INTRODUCTION

The human body is endowed with a unique balance of water and electrolytes, which ensures effective discharge of various functions of the human body. Disturbances in this natural homeostasis predisposes towards a myriad of clinical presentations. Recognition of these disturbances and corrective measures form an important facet in the management of patients. Among the various electrolyte imbalances that are discussed, hyponatremia forms an important enigma to a clinician in routine practice.

Normal serum sodium values are 134-145 mmol/Litre. Drop in serum values below 134 mmol/litre amounts to hyponatremia. Abnormality can occur due to a variety of etiological factors and are usually associated with a change in serum osmolality and extracellular volume (ECV). It must be understood that hyponatremia has no relation whatsoever with how the kidneys handle sodium, but how it handles free water. Despite large water intake, hyponatremia is prevented by formation of a dilute filtrate in the loop of Henle and the inhibition of the antidiuretic hormone, causing excretion of the dilute urine. Impairment of these two steps predisposes to hyponatremia.

To understand approach towards management of Hyponatremia, it is essential to know the causes of Hyponatremia.

CAUSES OF HYPONATREMIA

A. Iso-osmolar Hyponatremia

a. Pseudo-hyponatremia/ Spurious hyponatremia.
   Hyperlipidemia,
   Severe hyperproteinemia (multiple myeloma or macroglobinemia).
b. Infusion of isotonic mannitol, glucose, sorbitol, glycerol, glycine.
c. Presence of non-sodium cation: immunoglobulin G myeloma, lithium, tromethamine infusion.

B. Hyper-osmolar Hyponatremia

a. Hyperglycemia.
b. Infusion of hypertonic mannitol, glycerol, sorbitol, glycine.

C. Hypo-osmolar Hyponatremia

1. Hypervolemic hypo-osmolar hyponatremia (edematous and increased ECF).
   a. Urine sodium concentration lower than 10 mmol/L.
      1. CCF
      2. Cirrhosis
      3. Nephrotic syndrome
      4. Hypothyroidism
      5. Hypoalbuminemia due to malnutrition
      6. Pregnancy
      7. Idiopathic
   b. Urinary sodium concentration greater than20mmol/L.
      1. Acute renal failure.
      2. Chronic renal failure.
2. Hypovolemic hypo-osmolar hyponatremia. (non-oedematous but ECF depleted).

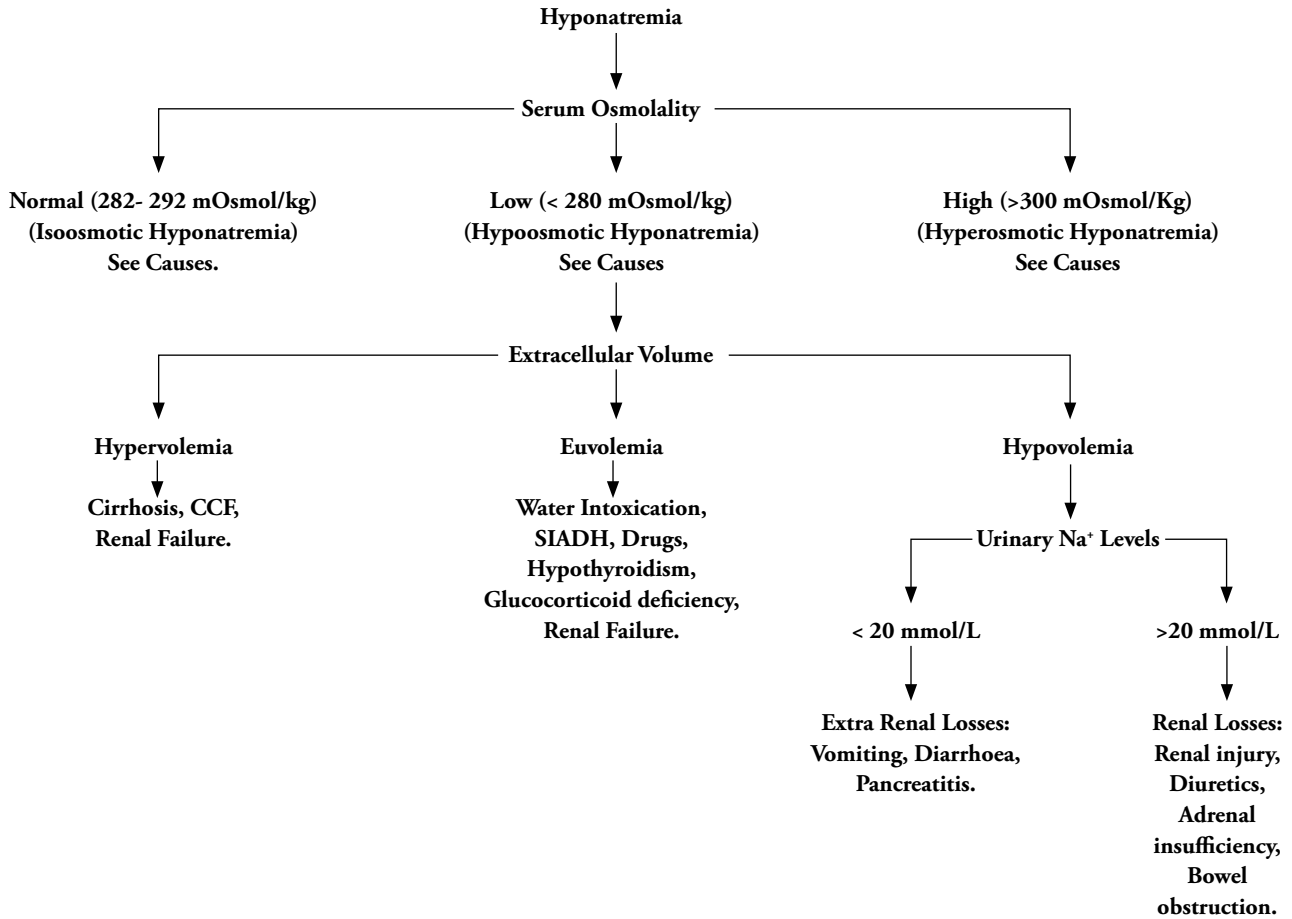

Fig 1 : Algorithm for evaluation of hyponatremia.

a. Urinary sodium concentration less than 20 mmol/L.
   1. Gastrointestinal (GI).
      e.g. Vomiting, nasogastric suction, diarrhoea, pancreatitis, GI fistula, fluid loss.
   2. Cutaneous water loss (urinary sodium concentration lower than 10 mmol/L).
      e.g. Burn injury, excessive sweating.

b. Urinary sodium concentration greater than 20mmol/L
   1. Renal disease
      e.g. Non-oliguric failure, partial urinary tract obstruction, renal tubular acidosis, tubulointerstitial nephritis and other salt-wasting nephropathies.
   2. Diuretics
   3. Cerebral salt wasting caused by disorders of central nervous system.
   4. Mineralocorticoid deficiency.

c. Third space fluid sequestration
   1. Peritonitis
   2. Pancreatitis
   3. Bowel obstruction
   4. Rhabdomyolysis

3. Isovolemic, hypo-osmolar hyponatremia (normal ECF and no edema).
   a. Water itoxication
      1. Psychogenic polydipsia
      2. Dipsogenic polydipsia. (dipsogenic diabetes insipidus)
      3. Iatrogenic. (e.g. excessive hypotonic saline iv fluid administration, excessive water administration.)
   b. Renal failure
   c. SIADH
   d. Glucocorticoid deficiency,
   e. Hypothyroidism.

APPROACH FOR CORRECTION OF HYPONATREMIA (FIG. 1)

a. Assess patient's volume status, e.g. neck veins, orthostatic hypotension, cardiac signs of fluid overload, skin turgor. This will help in establishing the etiology and the subsequent treatment.

b. Measure Serum osmolality.

$$\text{Serum osmolality} = [2 \times (Na + K) + \frac{BUN}{2{\cdot}8} + \frac{Glucose}{18}]$$

Normal Range: 282- 292 mosm/kg H_2O.

c. Measure urine osmolality.

d. Determine urinary Na^+ levels and serum Na^+ levels.

e. Estimate sodium deficit.

Na^+ deficit = Normal TBW x (140 – current S Na^+)

= 60% Body weight (Male) OR 70% Body weight (Female) } x(140 - current S Na^+)

This will help to establish whether hyponatremia is iso-osmolar, hypoosmolar or hyper-osmolar.

MANAGEMENT

Certain general principles need to be followed while tackling hyponatremia.

a. Mild asymptomatic hyponatremia (i.e. > 120 mmol/L, but < 134 mmol/L) may not require corrective measures except treatment of the underlying factors.

b. Correction of hyponatremia should be gradual to avoid risk of both fluid overload and osmotic demyelination syndrome (ODS) characterized by flaccid paralysis, dysarthria and dysphagia.

c. Avoid overcorrection of serum sodium concentration.

Iso-osmolar Hyponatremia

- Pseudohyponatremia: No treatment required. Serum sodium is actually normal.
- If isotonic mannitol or other osmotic infusates : Discontinue infusion.

Hyper-osmolar Hyponatremia

- If due to hypertonic mannitol or other osmotic agent : Discontinue infusion.
- Hyperglycemia: Stop or decrease glucose administration.

  Administer insulin and iv fluids.

  Target a drop in glucose concentration of 75 to 100 gms/dl per hour.

Hypo-osmolar Hyponatremia

A. General measures

a. Closely monitor vital signs.

b. Monitor serum sodium levels at regular intervals to assess the progress of the therapy

c. Periodically recalculate fluid requirements.

d. Monitor fluid intake and output closely.

e. Obtain urine osmolality and urine electrolyte measurements.

f. Order routine tests.

g. Obtain adequate iv access.

h. Stop drugs that lead to SIADH.

i. Calculate patients total body water (TBW).

j. Saline infusion should be as follows,

- Estimate the volume (ml) of the selected infusate to achieve the targeted increment in serum sodium concentration over the next 1 hour as follows,

Volume = (1000 X Δ Na **s** X TBW) ÷ (Na **inf**).

Where Δ Na **s** represents change in serum sodium concentration i.e. Δ Na **s** = (Na inf − Na s) ÷ (TBW + 1).

- Recalculate and adjust infusion rates at regular intervals based on serum sodium values.
- Avoid an overly rapid rise in serum sodium concentration (more than 8 mmol/L per day).

i. Treat underlying causes.

j. Correct hyypokalemia if present.

k. Provide supportive care.

B. If ECF space is contracted.

a. Ensure adequate perfusion with isotonic (9%) saline iv, if hypotension or signs of hypoperfusion is present.

b. In the absence of hypovolemia or after its correction titrate saline infusions to raise serum sodium values to no more than 8 mmol/L per day or 0.3 mmol/L per hour.

C. If ECF space is expanded.(Chronic >12 hours)

Patient Asymptomatic	**Patient Symptomatic**.
# Restrict water intake (≈ 500-1000 ml per day) and sodium intake.	# Restrict fluid intake if mildly symptomatic and urine osmolality < 200 mOsmol/kg H_2O.
# Target serum sodium increase of less than 8 mmol/L per day (approx 0·3 mmol/L per hour).	# Symptoms severe/ urine osmolality > 200 mOsmol/kg give hypertonic saline to raise serum Na^+ by ≈0·3mmol/L/hr upto not more than 8 mmol/L/day.
# Treat CCF if present.	# Treat convulsions if present with routine anticonvulsant therapy.
	# Diuretics if ECF expanded.
	# Treat endocrine deficiency if present.

In the management of hyponatremia an important factor that must be recognized is SIADH.

Syndrome of Inappropriate Antidiuretic Hormone (SIADH)

Predisposing Factors

1. Neoplasms (ectopic production of ADH or ADH-like factor).

   e.g., Mesothelioma, pancreatic cancer, mediastinal tumours, prostatic cancer, sarcoma, lymphoma etc..

2. Non-neoplastic pulmonary causes,

   e.g., Pneumonia, lung abscess, pulmonary embolism, COPD etc.

3. Neurologic causes

   e.g., Meningitis, encephalitis, brain abscess, brain rumours, head injury, CVA etc.

4. Drugs

   e.g., ADH and ADH analogues, opiates, barbiturates, carbamazepine, cyclic antidepressant, MAO inhibitors,

chlorpropamide, theophyline, vincristine, loop and thiazide diuretics etc.

5. Miscellanous

   Atrial tachydysrythmias, post-mitral commisurotomy, trauma, alcohol withdrawal, etc.

Diagnosis

Salient features in diagnosis of SIADH.

- Hypo-osmolar hyponatremia.
- Clinically isovolemic.
- Urine osmolality > 300 mOsmol/kg H2O.
- Urinary sodium conc. > 40 mmol/L.
- Normal renal, hepatic, adrenal and thyroid function.
- Serum osmolality < 280 mOsm/kg H_2O.
- Serum sodium < 134 mmol/L.

Management of SIADH

- Restrict total fluid intake approximately to 600 to 1000 ml/ day, depending on the severity of hyponatremia.
- Orally addition of salt to diet.
- Controlled hypertonic (3%) saline infusion.
- Stop all drugs that may be affecting ADH secretion.
- Stop all unnecessary hypotonic fluid administration.
- Drug therapy.

  Demeclocycline:

  150 - 300 mg orally three to four times a day.

  Fludrocortisone

  0·05 to 0·2 mg orally three to four times a day.

CONCLUSION

Hyponatremia as seen is caused by a myriad of clinical conditions, identification of which is essential. Equally important is a stepwise approach towards correction of this imbalance. However caution should be exercised to ensure that the correction should be gradual to avoid hypernatremia or to rapid correction to avoid development of osmotic demyelination syndrome.

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