Hyponatraemia (HoN) is a serum sodium concentration ($s[Na] < 135\text{mmol/l}$). It is due to an excess of body water in relation to existing Na stores. HoN is the commonest disorder of body fluid and electrolyte balance and is usually an incidental finding on routine blood tests. It is often multifactorial. The classification according to Extracellular Volume (ECV) status is most useful for its diagnostic and therapeutic value. Management of HoN depends on comprehensive history, thorough physical examination and selective investigations$^{[1–8]}$.

**TYPES OF HYPONATRAEMIA$^{[1–8]}$**

1. Hypotonic (dilutional) HoN: is the commonest type. *It is the type associated with a hypotonic state (hypotonicity and IC oedema), responsible for the Symptoms and Signs (S/S).* Its causes and management are discussed in the flow charts below and the section ‘Treatment – further’.
ABC of Intravenous Fluids

- **Low measured Serum Osmolality (sOsm):** in most cases, see flow chart below.
- **Normal measured sOsm:** secondary to flushing with iso-osmotic solutions during Transurethral Resection of the Prostate (TURP) – using glycine or sorbitol; both are ineffective (permeable) osmole.
- **High measured sOsm:** secondary to alcohols and advanced Chronic Kidney Disease (CKD). It is hypotonic despite the high sOsm as both alcohol and urea are ineffective osmoles.

2. Non-hypotonic (measured sOsm normal or high) HoN:
   - Isotonic: **normal measured sOsm** (pseudo-hyponatraemia) HoN: due to high protein or lipids.
   - Hypertonic: **high measured sOsm** (translocational, re-distributive) HoN: due to hyperglycaemia or hypertonic mannitol – both are effective (impermeable) osmoles.

Non-hypotonic hyponatraemia is not associated with the hypotonic state; hence no S/S of HoN

### Hypotonic HoN: Clinical Management Flow Chart[^1-8]

<table>
<thead>
<tr>
<th>Symptoms and Signs (S/S):</th>
<th>Asymptomatic in most patients; often non-specific; <strong>moderate</strong>: nausea, headache and confusion; severe: drowsiness, seizures and coma – death from Brain herniation* in acute cases. Unless s[Na] is falling rapidly, levels of 125–135mmol/l are usually asymptomatic</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>S/S are prominent when the decrease in s[Na] occurs rapidly or is large</strong></td>
<td></td>
</tr>
<tr>
<td>O/E: assess ECV</td>
<td>Mucous Membranes, Skin Turgor, Blood Pressure (BP), Pulse – aided by biochemical tests</td>
</tr>
</tbody>
</table>
| Investigations: (s[Na] in mmol/l) | Paired Serum & Urine (spot sample): U&E, Osmolality; Glucose (serum)  
Degree of HoN, if s[Na]: **mild**: 130–135; **Moderate**: 125–129; **Severe**: <125 |
Management of Hyponatraemia

### Hypotonic HoN: Clinical Management Flow

<table>
<thead>
<tr>
<th>Mechanism</th>
<th>ECV</th>
<th>Hypovolaemic HoN</th>
<th>Euvolaemic HoN</th>
<th>Hypervolaemic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Relative depletion of salt to water</td>
<td></td>
<td>Excess of water to salt</td>
<td>Retention of water</td>
<td></td>
</tr>
<tr>
<td>Exclude the error of sample taken from the drip arm</td>
<td></td>
<td>+ ADH, and salt</td>
<td>+ (RAAS)</td>
<td></td>
</tr>
</tbody>
</table>

### Expected Results

<table>
<thead>
<tr>
<th>Mechanism</th>
<th>ECV</th>
<th>Hypovolaemic HoN</th>
<th>Euvolaemic HoN</th>
<th>Hypervolaemic</th>
</tr>
</thead>
<tbody>
<tr>
<td>uOsm≤100(^\circ)</td>
<td>sUrea&gt;7 (UA normal/high)</td>
<td>uOsm≤100(^\circ)</td>
<td>sUrea variable</td>
<td></td>
</tr>
<tr>
<td>u[Na]&gt;30</td>
<td>uOsm≤100(^\circ)</td>
<td>u[Na]=30 (if not on diuretics)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Cause:

<table>
<thead>
<tr>
<th>Rate of onset:</th>
<th>1. Renal losses: Diuretics – especially HCZ, renal tubular disease, Addison’s, Cerebral salt wasting syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute&lt;48h</td>
<td>2. Extra-renal losses: GI (diarrhoea/vomiting)/ Skin (sweat) (NB: u[Na]≤30)</td>
</tr>
<tr>
<td>Chronic≥48h</td>
<td>1. SIAD, [Drugs – CMZ, TCA, SSRI, PPI, Pulmonary, Cerebral diseases, Secondary adrenal insufficiency, Hypothyroidism (rare)]</td>
</tr>
<tr>
<td></td>
<td>2. Psychogenic Polydipsia; low salt intake (rare) Excess iv fluids – 5% D (the commonest cause) (NB. uOsm&lt;100)</td>
</tr>
</tbody>
</table>

### Treatment

<table>
<thead>
<tr>
<th>ECV</th>
<th>Hypovolaemic HoN</th>
<th>Euvolaemic HoN</th>
<th>Hypervolaemic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Restore euvolaemia (the 5 Rs – see IVF therapy, P ---): e.g. 0.9% NS 1–2L in 3 h then sodium chloride 0.45% 1–2L in 12hr.</td>
<td>SIAD: Treat underlying cause Fluid Res traction (FR) (to&lt; UOP volume) usually to &lt;800ml/d (first line treatment)</td>
<td>1. Advanced Cardiac failure</td>
<td></td>
</tr>
<tr>
<td>Recheck U&amp;E at 3 and 12hrs, monitor UOP</td>
<td>Osmotic solutes PO, Urea (second line treatment) or</td>
<td>2. Advanced Hepatic failure</td>
<td></td>
</tr>
<tr>
<td></td>
<td>NaCl + Low dose furosemide 20mg am/ MD</td>
<td>3. Nephrotic syndrome</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Monitor the response</td>
<td>4. Renal failure (NB. sOsm≥295, u[Na]&gt;30)</td>
<td></td>
</tr>
</tbody>
</table>

### Abbreviations:

- ADH = Anti-Diuretic Hormone
- RAAS = Renin-Angiotensin-Aldosterone System
- sOsm = Serum Osmolality
- uOsm = Urine Osmolality
- UA = Uric Acid
- HCZ = Hydrochlorothiazide
- SIAD = Syndrome of Inappropriate Anti-Diuresis
- CMZ = Carbamazepine
- TCA = Tricyclic Antidepressant
- SSRI = Selective Serotonin Reuptake inhibitor
- PPI = Proton Pump Inhibitors
- D = Dextrose
- UOP = Urine Output
- PO = Orally
- MD = Mid-Day

*Brain Herniation is reported almost exclusively in acute hypotonic HoN (short time for brain adaptation): post-operative in women and children, massive water ingestion in psychosis and marathon runners; intracranial pathology e.g. SAH.

*uOsm=100 indicates an inappropriately concentrated urine, usually substantially higher: uOsm typically>sOsm.
ABC of Intravenous Fluids

Treatment for all Patients (continuation)

a. Swift determination and treatment of the underlying cause. Monitor $s[Na]$ and UOP;
b. Stop non-essential parenteral fluids and medications that can provoke hyponatraemia;
c. Correct any concomitant hypokalaemia, this raises $s[K]$ and $s[Na]$ simultaneously;
d. Rate of correction of HoN depends on the duration, symptoms and severity;
e. Hypertonic saline, see footnote, should be used carefully with consultant approval;
f. Failure to correct or recurrence of hyponatraemia merits referral to the appropriate team, e.g. renal, endocrine and psychiatric.

Treatment (further)

1. Prompt fluid resuscitation in volume-deplete patients to restore Euvolaemia:
   The type, strength, volume and rate of administration of the IV fluid should be clearly written and explained to the nurses. See chart above and note below.

   Restoring EC volume stops the non-osmotic stimulation of ADH release and promotes water diuresis that speeds correction – can cause overly rapid correction. Hence, sudden increase in UOP to (>100ml/h) suggests that a rapid correct of hyponatraemia is imminent and necessitates optimising the fluid type, e.g. ½ NS instead of NS and closer monitoring of $s[Na]$ levels.

2. Emergency therapy, using 3% Hypertonic Saline Solution (HSS) (513mmol/l):
   Hyponatraemia with SEVERE symptoms such as seizures or coma, see footnote.

   On achieving the $s[Na]$ correction target – do not expect patients with symptoms to completely recover immediately

3. Non-emergency, in-patient therapy:
   a. Hyponatraemia with moderate symptoms, including self-induced water intoxication and post-operative cases, admit.
      
      Apply the steps in b. below as appropriate.
      Close monitoring. Consider HSS at a lower dose and slower infusion rate.

   b. Severe Hyponatraemia with no or mild symptoms, admit:
      
      • Fluid restriction ($<800ml/d$) to introduce negative fluid balance: in patients with oedema (HF/ Cirrhosis), advanced CKD, SIADH, and PP.
      
      • Loop Diuretics (LD) in HF/SIADH. This also guards against volume overload if HSS is used.
Osmotic solutes orally in SIADH with s[Na] >120: Urea (20–120g powder in, e.g. orange juice), it induces osmotic diuresis, increasing the excretion of electrolyte-free water. NaCl + LD are an alternative.

Avoid Demeclocycline/Lithium because of their side effects profile, the unpredictability of N DI, and the difficulty of titrating the effect when it happens.

4. Community Treatment:

Chronic Moderate Hyponatraemia: (SIAD, heart failure, or cirrhosis) is typically Asymptomatic. It can be associated with subclinical or subtle neurological symptoms, e.g. gait instability, falls and cognitive deficit. Thus selective treatment, in the community, as outlined in 3/b above is worthwhile.

CONCLUSION

Prevention of hyponatraemia is of paramount importance since most initial therapies, such as fluid restriction, are relatively ineffective in correcting euvolemic and hypervolemic hyponatremia.[16]

3% Hypertonic Saline Solution (HSS):
Suggested 3% HSS boluses: 100ml bolus over 10–15 minutes; increases s[Na] by 2–3mmol/l; check s[Na] after 20 minutes. If severe neurologic symptoms persist, or if the s[Na] is not improving, a 100ml bolus of HSS can be repeated 1–2 more times at 10-minute intervals. Rapidly increase s[Na] by 4–6mmol/l over several hours; this alleviates symptoms and prevents Brain Herniation. If no symptomatic improvement, other possibilities should be explored. The increase in s[Na] should not exceed 8mmol/l in any given 24hr period to avoid the rare, serious Osmotic Demyelination Syndrome (ODS), in chronic hyponatraemia when s[Na] increases too rapidly. The risk of ODS through overly rapid correction is less of a concern in acute hyponatraemia because the brain has not had time to adapt to its hypotonic environment. However, this would make them more prone to develop brain herniation and necessitates prompt therapy.[1–5,7,9,10–12]

Patients at highest risk of ODS are those with: s[Na]<105mmol/l; Hypokalaemia; Thiazide therapy; Alcoholism; Malnutrition; Liver disease.

Close monitoring of treatment in ‘ICU’ to avoid s[Na] overcorrection and possible ODS:
Beware: the correction can be much more than the expected or calculated. Apply conservative therapeutic goals for correction, 8mmol/l in 24hrs, 14mmol/l in 48hrs and 16mmol/l in 72hrs. Monitor s[Na] and UOP to prevent overcorrection, every 2hr in emergency cases. Reduced ADH secretion and Brisk Diuresis is the commonest cause of overcorrection. Sudden increase in UOP to (>100ml/h) suggests a rapid correction of hyponatraemia is imminent, and necessitates closer monitoring of s[Na] levels. If overcorrection occurs, stop HSS; consider Desmopressin 2mcg IV with 5%D 10ml/kg over 1hr to re-lower s[Na]. Hypokalaemia correction can contribute to s[Na] overcorrection.[3,9–14]

HSS: the experience and evidence to guide its use is very limited. A global clinical trial or at least a prospective, standardized registry to collect data on its use is worthwhile. Chronic HoN: the administration of HSS will only be required in exceptional circumstances.

HHS: prepare if not available, arrange with the pharmacist.
ABC of Intravenous Fluids

Practical Exercises 1–4

All results are in mmol/L unless stated otherwise

Practical Exercise 1:

A 60 year old healthy chronic smoker presented to his doctor with general malaise. He was euvaemic, weight 70kg, early clubbing, systemic examination was unrevealing. Lab results: s[Na] 110, s[K] 4, urea 2, s[Cr] 54μmol/L, sOsm 226mOsm/Kg, uOsm 618mOsm/Kg, u[Na] 46. Other biochemical tests and Full Blood Count (FBC) indices were within the normal range. Chest X-ray (CXR) revealed a suspicious shadow left mid-zone. He was admitted under the respiratory physicians for further investigations.

Q1. The cause of hyponatraemia is:
   a. SIADH  
   b. Addison’s disease  
   c. Psychogenic polydipsia  
   d. Pseudo-hyponatraemia  
   e. Central diabetes insipidus

A1. The cause is SIADH, statement (a), resulting in euvaemic hypotonic hyponatraemia. The SIADH is likely due to bronchogenic carcinoma.

Q2. Treatment included:
   a. 0.9% Normal saline, 24hr infusion, at 100mL/h  
   b. 750mL oral fluid restriction  
   c. 3% HSS at 100ml infusion over 20 minutes  
   d. Intravenous furosemide and sodium chloride  
   e. Demeclocycline

A2. Treatment included fluid restriction, statement (b); oral furosemide and sodium chloride.

Practical Exercise 2:

A 21 year old athlete developed a grand mal seizure after completing the marathon. Observations were unremarkable, weight was 62kg. He was in post-ictal state; Glasgow Coma Scale (GCS) was 6/15, needed intubation. Other systems examination was unrevealing. s[Na] 114, it was normal a week earlier at a routine medical,
s[K] 4.2, urea 1, s[Cr] 46μmol/L, sOsm 232mOsm/Kg, uOsm 98mOsm/Kg, and u[Na] 32. Other complete biochemical screening, FBC, and C-Reactive Protein (CRP) tests were normal.

Q1. The cause of hyponatraemia is:
   a. Cerebral salt wasting syndrome
   b. Hypothyroidism
   c. Excessive water intake
   d. Diabetic ketoacidosis
   e. SIADH

A1. The cause is excessive water intake, statement (c), causing euvolaemic hypotonic hyponatraemia.

Q2. What is the immediate treatment?
   a. 0.9% Normal saline at 250mL/h
   b. 750mL oral fluid restriction
   c. Intravenous anti-convulsant infusion
   d. Tolvaptan
   e. 3% HSS at 100ml infusion over 20 minutes

A2. The immediate treatment is 3% HSS at 100ml infusion over 20 minutes, statement (e). Tolvaptan is contraindicated in hyponatraemic urgencies, hypovolaemia, and liver disease.

Practical Exercise 3:
A 70 year old male was admitted with diarrhoea, vomiting for four days, lethargy, and inability to stand because of dizziness for two days. He continued to take Indapamide for essential hypertension. The skin turgor was reduced, weight 64kg, BP 90/50, pulse rate 108 per minute. Systemic examination was unrevealing. Serum urea 16.4, s[Cr] 125μmol/L, s[Na] 108, s[K] 2.7, serum bicarbonate 28, sOsm 236 mOsm/Kg water and uOsm 655 mOsm/Kg water, u[K] 28.

Q1. The cause of hyponatraemia/ hypokalaemia is:
   a. Gastrointestinal and renal loss
   b. Mainly gastrointestinal loss
   c. Pseudo-hyponatraemia
d. SIADH
e. Lab error

A1. The cause is gastrointestinal and renal loss, statements (a), resulting in hypovolaemic hypotonic hyponatremia and hypokalaemia.

Q2. Treatment included:

- Admission to High Dependency Unit (HDU).
- Prompt fluid resuscitation with 5% dextrose
- Increase Indapamide dose
- A trial of Demeclocycline
- Slow sodium tablets

A2. He needed High Dependency Unit (HDU) admission, statement (a), and prompt fluid resuscitation with 2 litres (L) of (0.9% normal saline + 20mmol KCl/L) over four hours. Euvolaemia restored, BP 115/70 mmHg, no postural drop. Repeat s[Na] 112, K 3. Intravenous fluid switched to hypotonic 0.45% saline + 20mmol KCl/L, 1L over next eight hours. This is because volume repletion stops the non-osmotic stimulation of ADH release and promotes water diuresis that speeds correction, can cause overly rapid correction. Further, s[Na] was 114, s[K] 3.1. Next 12 hours, additional infusion of 1L of 0.45% saline + 20mmol KCl, plus increased oral intake to match the increasing hourly UOP, this is to guard against overly rapid correction rate. Repeat s[Na] 116, s[K] 3.4. Over the next 24 hours patient was encouraged to drink to match the high UOP and given oral KCl, s[Na] and s[K] monitored closely. Indapamide was discontinued on admission.

Practical Exercise 4:

A 76 year old male, chronic smoker, known case of hypertension admitted with increasing ankle swelling and shortness of breath. He felt unwell two months prior with intermittent central chest pains that lasted for a week; sought no medical advice. BP was 125/75mmHg, pulse rate 108/minute irregular. Jugular Venous Pressure (JVP) was high, lower limb oedema to the thigh, weight 78kg – 66kg three weeks earlier. Bi-basal chest crackles, systemic examination was unremarkable otherwise. Investigations included ECG, CXR, Echocardiogram, s[Na] 121, s[K] 4.3, sOsm 244mOsm/Kg, uOsm 554mOsm/Kg. Other biochemical screening, FBC and CRP tests
were normal. A diagnosis of heart failure secondary to Ischaemic cardiomyopathy was made.

Q1. The cause of hyponatraemia is:

a. SIADH  

b. Psychogenic polydipsia  

c. Renal loss of sodium  

d. Pseudo-hyponatraemia  

e. Congestive heart failure  

A1. The cause is congestive cardiac failure, statement (e), resulting in hypervolaemic hypotonic hyponatremia.

Q2. Treatment included all except:

a. Avoidance of loop diuretics as they will worsen hyponatraemia  

b. Scrupulous monitoring of weight and renal function  

c. Restrict Na⁺ intake <100mmol/day  

d. Fluid restriction to 750ml/day  

e. Gradual introduction of beta blockers and RAAS blockade  

A2. Treatment included all except (a). Loop diuretics are essential for diuresis, and correction of hyponatraemia.

REFERENCES


+49 351 458 2645. 

