Guidelines for the Management of Hyponatraemia

Note

These guidelines are based on the European[1] and UK consensus[2] guidelines for the management of hyponatraemia. The main difference is that these guidelines describe the use of 3.0% saline as hypertonic saline for use in the emergency setting. Within the health board this is not routinely available and therefore 2.7% saline has replaced this. This is available as a 500ml polyfusor.

There is a summary poster/algorithm to accompany this guideline.

Background

Hyponatraemia is defined as a serum sodium concentration <135mmol/L. It is the commonest electrolyte disorder in hospitalised patients and is associated with increased morbidity, mortality and length of hospital stay.[3]

It can be subdivided by:

1) *Length of onset*
    - Acute (<48hours),
    - Chronic (>48 hours).

2) *Severity*
    - Mild (130-135mmol/L),
    - Moderate (125-129mmol/L),
    - Profound (<125mmol/L).

The majority of cases of hyponatraemia are hypotonic in nature; however isotonic or hypertonic cases can also occur (for example, in the case of raised glucose).

Clinical Features

Presentation can be asymptomatic, nonspecific or life-threatening:

Mild features:

- Nausea.
- Confusion.
- Headache.

Severe features (usually acute hyponatraemia):

- Vomiting.
- Cardiorespiratory distress.
- Abnormal and deep sleep.
- Seizures.
- Coma.

Chronic hyponatraemia can present with subtle features including:

- Gait abnormalities.
- Falls.
- Reduced concentration.
- Cognitive deficits.
- Increased osteoporosis and fractures (no causal relationship established).

Causes

Causes of hypotonic hyponatraemia can be classified according to extracellular fluid volume (ECF).

1) **Decreased** ECF volume:
   - GI loss (diarrhoea, vomiting)
   - Transdermal loss (heavy sweating)
   - Diuretics (especially thiazides)
   - Primary adrenal insufficiency
   - Cerebral salt wasting (e.g., subarachnoid haemorrhage)
   - Kidney disease (salt-losing nephropathies)
   - 'Third spacing' (bowel obstruction, pancreatitis, sepsis, muscle trauma)

2) **Normal** ECF volume:
   - SIADH (see Appendix below)
   - Secondary adrenal insufficiency
   - Hypothyroidism
   - High water and low solute intake (e.g., primary polydipsia) with inappropriate low urine osmolality <100mOsm/kg

3) **High** ECF volume:
   - Renal failure
   - Heart failure
   - Liver failure
   - Nephrotic syndrome

Note: Key medication classes that can cause hyponatraemia include antipsychotics, antiepileptic medications, SSRIs, ACE inhibitors, ARBs, PPIs and diuretics.

Management

The below guidance is based on the European Clinical Practice Guideline[1] on hyponatraemia.

Classifying hyponatraemia:

- Undertake a clinical examination of the patient to determine whether the patient is euvolaemic, hypovolaemic or hypervolaemic.
- Measure **serum glucose** to exclude pseudohyponatraemia. If serum glucose is elevated, correct for the serum glucose by using the formula in the Appendix below.
- Measure **serum osmolality**. If <275mOsm/kg then diagnose as hypotonic hyponatraemia. If above this, then diagnose as isotonic or hypertonic hyponatraemia.
- Measure the **urine osmolality, sodium, and potassium** of a spot urine sample:
    - If urine osmolality ≤100mOsm/kg, there is a relative excess water intake
    - If urine osmolality >100mOsm/kg, look at the urinary sodium
    - If urinary sodium is <30mmol/L the cause is low effective arterial volume
    - If urinary sodium is >30mmol/l, assess extracellular fluid status and use of diuretics to determine the likely cause.
    - If the patient has SIADH, consider the urinary potassium in addition to osmolality and sodium to guide fluid restriction using the Furst formula (see below).

Note: Assume hypotonic hyponatraemia unless there is evidence of another cause, such as presence of osmoles that raise serum osmolality, e.g., glucose, urea. Non-hypotonic hyponatraemia is uncommon and does not cause cerebral oedema. It is managed differently to the guidance below.

1) Management of hyponatraemia with *severe* symptoms:

First hour:

- Give 150ml IV 2.7% hypertonic saline over 20 minutes, then measure the serum sodium. The bolus should be administered via a large-bore peripheral cannula[4].
- Repeat the infusion if no clinical improvement after 20 minutes whilst awaiting the result.
- Repeat the infusion up to two times, or until an increase in sodium of 5mmol/L is achieved.
- Contact ITU for advice regarding management and potential admission.

Follow-up management if improvement after first hour:

- Stop the hypertonic saline infusion.
- Slow 0.9% saline infusion at a rate of 20ml/h until cause-specific treatment started.
- Increase sodium concentration by no more than 10mmol/L during first 24 hours and no more than 8mmol/L every subsequent 24 hours.
- Check serum sodium after 6 hours, then 12 hours, and then daily until stabilised.
- Investigate and address cause (see below).

If no improvement with the first hour of treatment:

- Continue IV 2.7% hypertonic saline, checking sodium every 4 hours, aiming for a maximum serum sodium increase 1mmol/L/hr.
- Stop when either the symptoms improve, sodium increases by 10mmol/L or serum sodium of 130mmol/L is attained.
- Consider alternative diagnoses if no improvement < 1 hour and a sodium rise of >5mmol/L.

2) Management of hyponatraemia with *moderately severe* symptoms:

- Single IV infusion of 150mls 2.7% hypertonic saline over 20 minutes via a large-bore peripheral cannula.
- Stop any contributing medications.
- Re-check serum sodium after 1, 6 and 12 hours.
- Aim for a 5mmol/L increase in sodium concentration in 24 hours, with a maximum increase of 10mmol/L in first 24 hours, and 8mmol/L in each subsequent 24 hours.
- Investigate and address cause (see below).

3) Management of *acute* hyponatraemia (<48hrs) without severe symptoms:

- Stop any fluids or medications that may be contributing.
- If the acute drop in serum sodium is >10mmol/L, consider giving a single IV infusion of 150mls 2.7% hypertonic saline over 20 minutes.
- Repeat serum sodium measurement after 4 hours.
- Investigate and treat the cause (see below).

4) Management of *chronic* hyponatraemia (>48hrs/ unknown) without severe symptoms

General management

- Stop any non-essential medications or fluids that may be contributing.
- Investigate and address cause. This includes assessment of ECF status.
- If mild, treat underlying cause (e.g., fluid volume status).
- If moderate or profound, check serum sodium daily until stabilised and increase sodium by no more than 10mmol/L in first 24 hours, subsequently <8mmol/L every 24 hours.
- If there is no improvement in serum sodium, reconsider the causes and investigations.

Patients with **increased ECF or SIADH**:

- Fluid restriction.
- To calculate the degree of fluid restriction, use the Furst formula to calculate the electrolyte free water clearance (EFWC)[2]:
  - $EFWC = \frac{\text{Urine sodium + urine potassium}}{\text{Serum sodium}}$
  - If EFWC <0.5 commence 1.0L fluid restriction; if EFWC 0.5-1.0 commence 0.5L fluid restriction; if EFWC >1/0 fluid restriction is not advised.
- If no improvement in moderate/profound hyponatraemia, consider using a combination of low dose loop diuretics and oral sodium chloride. Seek specialist advice.
- Consider causes of SIADH (see Appendix)

Patients with **reduced circulating volume**:

- IV 0.9% saline or balanced crystalloid solution at a rate of 0.5-1.0ml/kg/hr

Note: If haemodynamically unstable, fluid resuscitation should override the risks of rapidly increasing serum sodium. Please see European Guidelines in reference list for further details.

Rapid Correction of Serum Sodium

Increasing serum sodium too rapidly can cause osmotic demyelination syndrome, with serious long term neurological sequelae, hence the limitations in speed of correction included in the guidelines.[1,2]

Management of over-rapid serum sodium correction

- Stop treatment of hyponatraemia if there is an increase of 10mmol/L in first 24 hours or >8mmol/L in each subsequent 24 hours.
- Seek expert advice on whether to begin an infusion of 10ml/kg of electrolyte free solutions (e.g., glucose solutions) over 1 hour under strict fluid balance and urine output monitoring.
- Seek expert opinion on use of desmopressin.

Appendix

Causes of SIADH

Once a diagnosis of SIADH is established, it is important to consider the need for further investigation to elucidate the cause. The table summarises commonly observed causes.

Malignant Disorders	Pulmonary Disorder	CNS Disorders	Medications
Carcinoma ➢ **Lung** ➢ **Oropharynx** ➢ **GI Tract** ➢ **GU Tract** **Lymphoma** **Sarcoma**	Infections ➢ Bacterial/Viral Pneumonia ➢ TB ➢ Abscess Asthma Cystic Fibrosis	Infection ➢ Meningitis ➢ Encephalitis ➢ Abscess Vascular ➢ Subdural ➢ Subarachnoid haemorrhage ➢ Stroke Other ➢ Brain Tumour ➢ Trauma ➢ Hydrocephalus ➢ Multiple Sclerosis ➢ Guillain-Barré Syndrome	Antidepressants ➢ SSRIs ➢ Tricyclic's ➢ MAOI ➢ Venlafaxine Anticonvulsants ➢ Carbamazepine ➢ Sodium Valproate ➢ Lamotrigine Antipsychotics ➢ Phenothiazides ➢ Butyrophenones Miscellaneous ➢ Opiates ➢ NSAIDs ➢ Amiodarone ➢ PPIs

Investigating the cause of hyponatraemia

As described above, the causes of hyponatraemia can be classified by the associated fluid volume status. In practice, undertaking a serum and urine panel to support making the diagnosis is important. We suggest considering the following investigations in patients with clinically significant hyponatraemia to establish the cause:

- **Serum:** Urea & electrolytes, plasma osmolality, glucose, lipids, liver function tests, cortisol (preferably 9am) and thyroid function tests. Consider testing inflammatory markers
- **Urine:** Osmolality, sodium, and potassium
- **Other: I**nvestigate the cause of SIADH (see Table above)

Pseudohyponatraemia

Pseudohyponatraemia is a spuriously low serum sodium concentration, typically associated with hyperglycaemia or hypertriglyceridaemia which affect laboratory testing of serum electrolytes as a result of fluid shifts and resultant erroneous serum sodium concentration. For each 5.5mmol/L rise in the serum glucose above 5.5mmol/L, there is typically a reduction in the reported serum sodium level of approximately 2.4mmol/L. Therefore, one estimates the true serum sodium concentration in people with hyperglycaemia using the formula[5]:

$$\textbf{Corrected serum sodium} = \text{Measured serum sodium} + \frac{2.4 \times [\text{serum glucose (mmol/L)} - 5.5\text{mmol/L}]}{5.5\text{mmol/L}}$$

If pseudohyponatraemia is suspected, seek specialist advice.

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4. Madieh J, Hasan B, Khamayseh I, et al. The safety of intravenous peripheral administration of 3% hypertonic saline: A systematic review and meta-analysis. Am J Med Sci. 2023:S0002-9629(23)01181-3.

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