Emergency management of severe and moderately severely symptomatic hyponatraemia in adult patients

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Introduction

Hyponatraemia (serum sodium <135mmol/L) is common. Clinical presentation can include a broad spectrum of symptoms and signs. Severe hyponatraemia can be life threatening, requiring emergency assessment and treatment. This guidance covers emergency management of patients presenting with hyponatraemia associated with severe and moderately severe symptoms. The document builds on previous guidance published in 2016 (1). It incorporates new data that support the approach outlined in the original, while adding additional guidance on specific elements of implementation and patient safety. In addition, recommendations within the revised guidance have been graded (reflecting the level of evidence supporting them) using a modified GRADE system (Table 1).

Recognition of the patient presenting with severe and moderately severe, symptomatic hyponatraemia

Biochemical assessment

The degree of biochemical hyponatraemia is classified in three groups.

1. Mild: Na⁺ 130–135mmol/L
2. Moderate: Na⁺ 125–129mmol/L
3. Profound: Na⁺ <125mmol/L
Clinical assessment
Severity of clinical presentation may not match the degree of biochemical hyponatraemia: profound biochemical hyponatraemia may be symptom-free, while some patients with moderate biochemical hyponatraemia may have significant neurological symptoms and signs. For the purposes of this guidance, symptoms have been classified as follows.
1. Severe symptoms: persistent vomiting, cardiorespiratory arrest, seizures, reduced consciousness/coma (Glasgow Coma Scale ≤8).
2. Moderately severe symptoms: nausea without vomiting, confusion, headache.
3. Mild or absent symptoms.

The clinical status of the patient presenting with hyponatraemia reflects the balance of several factors.
1. The degree of biochemical hyponatraemia.
2. The rate of development of hyponatraemia.
3. The intrinsic ability of the individual patient’s central nervous system to adapt to changing osmolar stress resulting from hyponatraemia.
4. The range and severity of the individual patient’s co-morbidities.

The underlying pathophysiology driving presentation with hyponatraemia may change during assessment and treatment. The situation is therefore dynamic, one that requires careful monitoring and a care plan that can be adapted over time rather than one that is fixed.

Severe symptoms are unlikely with serum sodium >130mmol/L and alternative causes of neurological dysfunction should be considered in this context.

Recommendations
1. We recommend that in patients presenting with hyponatraemia, management decisions should be based on presenting clinical symptoms and signs rather than the degree of biochemical hyponatraemia (2, 3). ☀️☀️
Treatment of the patient presenting with severe or moderately severely symptomatic hyponatraemia

**Treatment recommendations**

1. We recommend patients presenting with hyponatraemia and with severe or moderately severe symptoms receive immediate treatment with intravenous hypertonic sodium chloride, irrespective of the cause of the hyponatraemia. ☑️
   a. We recommend a 5 mmol/L rise in serum Na⁺ within the first hour to reduce immediate danger from cerebral oedema while minimising the risk of over-rapid correction and osmotic demyelination. ☑️
   b. We recommend the rise in serum Na⁺ within the first 24 hours after presentation does not exceed 10 mmol/L or 8 mmol/L per 24 hours thereafter. If these limits are exceeded, we recommend active management to limit further increases in serum Na⁺ (see Management of over-correction). ☑️
   c. We recommend that hypertonic fluid is administered in the form of intermittent boluses rather than as a continuous infusion over 24 hours. Bolus therapy is associated with more rapid improvement in serum Na⁺ within the first hour, more rapid improvement in symptoms and reduced risk of over-correction (4, 5). ☑️
   d. We recommend that if the clinical status of the patient does not improve after a 5mmol/L rise in serum Na⁺ in the first hour, an additional bolus of hypertonic sodium chloride is given to achieve a further rise of 1 mmol/L in serum Na⁺ (Fig. 2). ☑️

**Follow up management after 5 mmol/L rise Na⁺**

- Stop infusion hypertonic saline
- Keep iv line open minimum volume 0.9% saline
- Start diagnosis-specific treatment
- Limit increase Na⁺ to 10 mmol/L first 24 hours
- Limit increase Na⁺ to additional 6 mmol/L every 24 hours thereafter until Na⁺ 130 mmol/L
- Check Na⁺ 6 hours, 12 hours & daily until stable under stable treatment

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**Figure 1. Recommended approach to the use of hypertonic sodium chloride in patients with hyponatraemia and severe or moderately severe symptoms**

See text for additional recommendations
e. We recommend increased monitoring of serum Na\(^+\) over the first 24 hours following initiation of treatment in specific circumstances recognised as predisposing to over-correction (4, 6, 7). ☒☒
   1. Patients in whom serum Na\(^+\) increases by more than 5 mmol/L after the first or second bolus of hypertonic fluid.
   2. Patients who receive 3 or more boluses of hypertonic fluid.
2. We recommend against the use of Vaptan aquaretics in the treatment of patients with hyponatraemia who present with severe or moderately severe symptoms. There is both absence of evidence of efficacy of aquaretics and evidence of increased risk of over-correction of hyponatraemia in this context (3). ☒☒
3. We recommend against the use of the Androge-Madias formula to calculate the amount and rate of hypertonic fluid treatment in patients presenting with hyponatraemia associated with severe of moderately severe symptoms. Use of the formula lacks precision in this (dynamic) context and is associated with increased risk of over-correction of hyponatraemia (8). ☒☒

![Diagram](image)

**Figure 2. Recommended approach to patients treated with hypertonic sodium chloride if no improvement following 5 mmol/L rise in Na\(^+\) in the first hour after initiation of treatment**

See text for additional recommendations

**General recommendations**

4. We recommend that both the decision to treat and the supervision of treatment with hypertonic fluid should the responsibility of a senior clinician with appropriate training and experience. (Not graded)
5. We recommend that the analytical platform used to measure serum Na\(^+\) (point of care direct potentiometry vs. standard dilution-based venous blood analysis) remains consistent during treatment with hypertonic fluid, minimising potential impact of inter-platform variation in analyte measurement on management decisions. (Not graded)
6. We recommend that patients with hyponatraemia associated with severe or moderately severe symptoms who require treatment with hypertonic fluid are managed in a clinical environment that can deliver, monitor, and assess efficacy of treatment safely; and with facilities and processes to support appropriate escalation of care. (Not graded)
7. We recommend that a clinical data set are collected for all patients treated with hypertonic fluid and that these data are used in local prospective quality improvement/audit processes to inform and refine practice over time. (Not graded)

Managing over-correction of serum Na⁺
Over-correction of serum Na⁺ (a rise of > 10 mmol/L in the first 24 hours or 8 mmol/L per 24 hours thereafter) risks precipitating osmotic demyelination. Over-correction requires active management. It is important to recognise that over-correction can occur in the absence of treatment with hypertonic fluid (e.g., self-correction after ingestion or administration of high volumes of hypotonic fluid, recovery from adrenal crisis).

Recommendations
1. We recommend that urine output is monitored carefully during treatment. An increase in urine output can be an early indicator of aquaresis: a prelude to rapid rise in serum Na⁺. ⊕⊕
2. We recommend that if the rise in serum Na⁺ exceeds 10mmol/L in the first 24 hours or 8mmol/L per 24 hours thereafter, hypertonic fluid should be stopped. ⊕⊕
3. We recommend consulting a clinician with experience in managing over-correction. Clinicians may wish to consider introducing hypotonic fluid to limit the rise or re-lower serum Na⁺, with or without co-administration of parenteral Desmopressin (DDAVP) to limit renal water loss and support controlled changes in serum Na⁺ over time (9). ⊕
4. We recommend that a clinical data set are collected for all patients treated for over-correction of serum Na⁺ following hypertonic fluid and that these data are used in a local prospective quality improvement/audit process to inform and refine practice over time. (Not graded)
Differential diagnosis and aetiology-dependent treatment of hyponatraemia

A management strategy based on specific aetiology should follow the emergency (aetiology-independent) treatment of hyponatraemia associated with severe and moderately severe symptoms outlined in this guidance. An algorithm to support establishing the cause of hyponatraemia is outlined in Fig. 3 (1, 3, 10).

Recommendations

1. We recommend an algorithm-based approach to the differential diagnosis of hyponatraemia (11).
2. We recommend urine osmolality and urine Na⁺ concentration form part of the portfolio of diagnostics available ‘round the clock’ to support urgent and emergency care. (Not graded)

Table 1. Modified GRADE system demonstrating level of evidence to support recommendations (12)

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References


