Scarborough, Hull and York Pathology Service

Hyponatraemia in Primary Care – Investigation and Management (Adults)

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Aims of the guideline

This guideline is intended to support primary care clinicians to safely investigate and manage low blood sodium results. Secondary care clinicians should refer to the advice that is available on Staff Room (Hyponatraemia and SIADH Diagnosis and Management).

The purpose of ***this*** guidance is to support decision making. It cannot replace the need for sound clinical judgement.

Relevant clinical information and a drug history should be included on the request form when requesting renal function and electrolytes (see Table A.). This information will assist laboratory staff in providing the most appropriate advice.

Definitions

Normal serum sodium: 133 to 146 mmol/L

Hyponatraemia: serum sodium less than 133 mmol/L

Laboratory Responsibility

The lab will normally telephone new serum sodium results below 125mmol/L during normal working hours. This is at the discretion of the Duty Biochemist and may depend on clinical information provided and other results. A new finding of serum sodium below 120mmol/L will be telephoned to the out of hours GP service.

Symptoms

Symptoms of hyponatraemia are primarily neurological and reflect changes in brain volume. There is no specific concentration at which symptoms start to appear and hyponatraemia developing over days to weeks may be relatively asymptomatic, even at very low sodium levels.

Even mild levels of hyponatraemia may predispose to falls and cognitive deficits. Chronic hyponatraemia is also a risk factor for osteoporosis and fragility fractures.

Symptoms range in severity and include:

- Lethargy (excessive)
- Headache
- Nausea
- Vomiting
- Irritability
- Confusion
- Seizures
- Reduced conscious level, loss of consciousness, coma
- Cardiorespiratory distress

Worsening symptoms suggest cerebral oedema, which is a life-threatening medical emergency.

Principles for managing a low serum sodium

1. Severe hyponatraemia can be a medical emergency.
2. You should try and establish the likely cause of hyponatraemia AND the speed of onset of hyponatraemia as this will help guide management. This requires clinical assessment and blood and urine samples for laboratory testing.
3. If possible you should obtain laboratory samples PRIOR to initiating any treatment (otherwise the results will be difficult or impossible to interpret).
4. Medications are often involved in causing hyponatraemia – review every medication that the patient is taking (prescribed, over the counter, illicit and in a drip) (see Table A)

<u>When is hyponatraemia a medical emergency?</u>

Hyponatraemia of rapid onset (fall of >10mmol/L within 48h) and/or symptoms of cerebral oedema should be treated as a medical emergency – the patient should be admitted to hospital.

If the patient is well, which may be the case with quite low serum sodium levels (especially if this has fallen slowly), then it may be reasonable to investigate for the underlying cause through primary care. Whether or not the patient needs admitting to hospital or referral to secondary care may then depend on the underlying cause.

Making a diagnosis

Causes of hyponatraemia according to volume status		
Hypervolaemia (Elevated JVP, oedema)	**Euvolaemia**	**Hypovolaemia** (Low BP, Postural BP drop, JVP not visible)
Heart failure Liver failure / ascites Nephrotic syndrome / hypoalbuminaemia	SIADH Primary Polydipsia	Renal salt wasting syndromes (including diuretics) Primary hypoaldosteronism (Addison) GI or extra-renal fluid losses partially replaced with water

What samples do I need?

- **Blood:**
  - **U&E (includes eGFR), random glucose, 9am cortisol, osmolality**
  - **TSH – *if no recent result available***
- **Early Morning Urine:**
  - **Sodium and osmolality**

Step 1: Is the hyponatraemia real?

*Rule out **hyperglycaemia** and **pseudohyponatraemia.***

Hyperglycaemia (uncontrolled diabetes) can also cause low serum sodium levels due to movement of water from the intracellular to extra cellular space. **Pseudohyponatraemia** is an artifactually (falsely) low sodium due to presence of high protein levels (e.g. myeloma), or hypertriglyceridaemia.

A normal (275-295 mOsm/kg) or high serum osmolality in the presence of hyponatraemia is suggestive of pseudohyponatramia, but other causes exist, e.g. raised blood urea. Please check report for interpretative comments appended by the lab. Serum osmolality measurement is not required if patient has a normal or well controlled blood glucose and a normal total protein. If present, significant hypertriglyceridaemia is always reported on all U&E requests.

Step 2 – Is ADH acting (i.e. what is the **urine osmolality**)?

- If the urine is dilute (<100 mOsm/kg), then ADH is NOT acting.

  This indicates free water overload due to polydipsia, a low solute intake or high beer intake (potomania).
- If the urine is concentrated (>100 mOsm/kg), then ADH is acting.

Step 3 – Check **urine sodium**.

- Urine Sodium <30mmol/L – Low effective circulating blood volume
  - With oedema: Heart failure, Nephrotic syndrome, Cirrhosis with portal hypertension
  - Without oedema: GI fluid loss, third space loss, previous diuretic use
- Urine Sodium >30mmol/L – Inappropriate renal losses of sodium

  If **clinical signs and symptoms of hypovolaemia**, consider:
  - Salt wasting (diuretics, kidney disease, cerebral salt wasting)

- Adrenal insufficiency – check 9 am cortisol. Note that glucocorticoid use, stress, and oestrogenic states, e.g. pregnancy, COCP use, can increase cortisol levels and mask adrenal insufficiency.
- GI or extra-renal losses (vomiting, diarrhoea, fistula, stoma, etc)

If **no clinical signs of hypovolaemia (euvolaemic)**, consider:

- Syndrome of Inappropriate ADH (SIADH)

SIADH

SIADH is a fairly common cause for hyponatraemia, but there is no specific test for it and the diagnosis is based on the exclusion of other causes AND the following criteria:

- Euvolaemia
- Normal renal (eGFR), adrenal (9am cortisol) and thyroid (TFTs) function
- Urine osmolality >100mOsm/kg
- Urine sodium >30mmol/L

Causes:

- Pulmonary disease – pulmonary embolus, pneumonia, trauma, TB, infection
- Malignancy (ectopic ADH secretion) – small cell lung carcinoma
- Central nervous system disease – tumour, infection, CVA, trauma
- Medication (see Table A)

Management of hyponatraemia

Patients with severe hyponatraemia (i.e. those with evidence of cerebral oedema) should be admitted to hospital as an emergency.

Management of other patients depends on the underlying cause and volume status.

Primary polydipsia requires fluid restriction, which may be challenging depending on the underlying drivers to fluid consumption.

Hypovolaemic hyponatraemia: The majority of patients with hypovolaemic hyponatraemia will require hospital admission for intravenous fluids.

SIADH requires management of both the low serum sodium (which ranges from simple fluid restriction in mild cases to the use of tolvaptan or demeclocycline under the supervision of a consultant endocrinologist in more complex cases; demeclocycline is a tetracycline and can cause photosensitivity) and the underlying cause. Drug withdrawal and treatment of infection may be straightforward. Management of malignant disease will require appropriate specialist referral.

A fluid restriction should only be imposed if you are confident of the diagnosis of SIADH. Please discuss with an Endocrinologist or Duty Nephrologist (via switchboard), or send an Advice and Guidance request, if you are unsure.

Hypervolaemic hyponatraemia: Most patients with hypervolaemic hyponatraemia have complex and advanced underlying pathology that will require specialist support (e.g. liver cirrhosis, nephrotic syndrome, advanced kidney disease, or severe heart failure). An opinion should be obtained from the appropriate specialist.

Table A. Drugs associated with hyponatraemia		
Class	**Examples**	**Mechanism**
Diuretics - Thiazides	Indapamide, Bendroflumethiazide, Chlorthalidone.	Renal losses
Diuretics – Loop Particularly in combination with ACE-I or spironolactone	Furosemide, Bumetanide	Renal losses
Anticonvulsants	Carbamazepine, Oxcarbazepine, Phenytoin, Sodium valproate, Lamotrigine and other antiepileptics	ADH release or action stimulus (SIADH)
Opiates	Morphine, Tramadol	ADH release or action stimulus (SIADH)
Chemotherapuetic agents	Vincristine, Vinblastine, Carboplatin, Cisplatin, Cyclophosphamide	ADH release or action stimulus (SIADH)
Anti-psychotics	Aripiprazole, Clozapine, Fluphenazine, Haloperidol, Risperidone , Thioridazine	ADH release or action stimulus (SIADH)
Anti-depressants (tricyclics, SSRIs)	Sertraline, Fluoxetine, Paroxetine, Citalopram, Venlafaxine, Amitriptyline	ADH release or action stimulus (SIADH)
NSAIDs and COX-2 inhibitors Particularly in combination with thiazides or heart failure	Ibuprofen, Diclofenac, Naproxen, Celecoxib	Loss of ADH inhibition (SIADH)

Dopamine antagonists	Metoclopramide, Domperidone	ADH release or action stimulus (SIADH)
ACE-Inhibitors, ARBs	Ramipril, Perindopril, Lisinopril, Losartan, Olmesartan	ADH release or action stimulus (SIADH)
Anti-diabetic drugs	Chlorpropamide, Tolbutamine	ADH release or action stimulus (SIADH)
Proton Pump Inhibitors (PPIs)	Lanzoprazole, Omeprazole, Pantoprazole	ADH release or action stimulus (SIADH)
ADH analogues	Desmopressin DDAVP (overdose)	ADH analogue
Recreational drugs	MDMA (ecstasy)	ADH release or action stimulus (SIADH)
Hypotonic iv fluids	5% dextrose, 0.18% sodium chloride/dextrose solution	Dilution

Further Information

- GP Notebook - Hyponatraemia
- NICE Clinical Knowledge Summary – Hyponatraemia
  https://cks.nice.org.uk/hyponatraemia#!scenario
  Accessed 01/08/2022

References

- Spasovski, G, *et al*. Clinical practice guideline on diagnosis and treatment of hyponatraemia. *Ur J Endocrinol*, 2014;**170:**G1-G47.
- Jacob, P, *et al.* Hyponatraemia in primary care. *BMJ,* 2019;**365:**l1774
- Ball, S, *et al*. The Society for Endocrinology Clinical Committee. Society for endocrinology endocrine emergency guidance: Emergency management of severe symptomatic hyonatraemia in adult patients. *Endocrine Connections,* 2016;**5:**G4-G6
- Southern Derbyshire Shared Care pathology Guidelines – Hyponatraemia in Adults. https://www.uhdb.nhs.uk/download.cfm?doc=docm93jijm4n892.pdf&ver=1046
  Accessed 30/09/2024