

## **HYPONATREMIA – MANAGEMENT OF INCLUDING HYPERTONIC SALINE – ADMINISTRATION AND PRECAUTIONS**

*This LOP is developed to guide clinical practice at the Royal Hospital for Women. Individual patient circumstances may mean that practice diverges from this LOP.*

Additional background information is available in the accompanying educational notes.

### **1. AIM**

- To guide clinicians in the recognition, differential diagnosis, classification and appropriate management of patients with hyponatremia

### **2. PATIENT**

- Any patient who has serum blood sodium (Na) result <135mmol/L (<130 mmol/L in pregnancy)

Mild-moderate hyponatremia is usually defined as serum Na 121-135 mmol/L

Severe hyponatremia is defined as serum Na  $\leq$ 120mmol/L.

Symptoms range from nausea and malaise, with mild reduction in the serum Na, to lethargy, decreased level of consciousness, headache, and, if severe, seizures and coma.

**It is important to note that only acute (<48 hours), symptomatic hyponatraemia should be reversed rapidly.**

### **3. STAFF**

- Medical, midwifery and nursing staff

### **4. EQUIPMENT**

- Witches hat or indwelling catheter
- Intravenous cannula
- 3% Sodium Chloride: may be obtained from Prince of Wales Hospital ICU

### **5. CLINICAL PRACTICE**

- Take a careful clinical and medication history
- Assess the patients volume/hydration and neurological status by physical examination including GCS
- Take blood for measurement of serum osmolality
- Collect a spot urine for measurement of urine osmolality and sodium
- Identify and treat any potentially reversible underlying cause of hyponatremia: Table 1
- Identify patients with acute, symptomatic and/or severe hyponatremia who may require treatment with 3% sodium chloride (hypertonic saline). See Figure 1
- Document a detailed plan in the integrated notes for all severities of hyponatremia
- Avoid complications related to rapid correction of serum Na particularly osmotic demyelination by aiming for a maximum rate of change in the serum sodium concentration of not more than 8-10 mmol/L in the first 24 hours and an additional 4-8 mmol/24 hours thereafter
- Review and modify all existing medications
- Restrict oral and IV fluid to 500 mL to 800mL per 24 hours, or 500 mL less than daily urine output.
- Closely observe the patients neurological and fluid status until hyponatremia is corrected
- Monitor serum electrolytes, creatinine and urine output daily or twice daily until the hyponatremia has resolved.

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**CLINICAL POLICIES, PROCEDURES & GUIDELINES**

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- **Acute (<48 hours duration), symptomatic and/or severe hyponatremia is a medical emergency**
- **Initiate PACE Tier 2**
- Notify the Anaesthetic fellow, Physician on call +/- referral to POW ICU or nephrologist.
- Discuss treatment plans with the Acute Care Nurse in charge and the bed manager as transfer to ACC or POW ICU is mandatory for these patients.
- Be aware that harm often follows inappropriate or rapid treatment of hyponatraemia in asymptomatic patients.
- Refer to the following guide for rapid correction:
- Aim to acutely raise the serum sodium concentration by 4 to 6 mmol/L to prevent neurological damage secondary to brain herniation, swelling and cerebral ischaemia.
- Rapid correction of hyponatremia requires critical care monitoring ie HR, BP, RR, Oxygen saturation, neurological observations including GCS and strict fluid balance
- An estimate of the required volume of 3% sodium chloride (hypertonic saline ) may be determined using the formula and calculations in Appendix A.
- Administer 3% sodium chloride (hypertonic saline ) 150 mL IV over 20 minutes via infusion pump
- Discard remaining 3% sodium chloride and infusion line after 150mL administered.
- Recheck serum sodium every 2 to 4 hours depending on GCS and clinical status scores
- Repeat infusion as needed up to a maximum of 3 infusions
- Cease 3% sodium chloride infusion when **either** of the following three criteria are met:
  - symptoms improve
  - target increase in serum sodium has been achieved
- Fluid restrict the patient to maintain the serum sodium
- Oral sodium chloride tablets may be useful

**6. DOCUMENTATION**

- Integrated Clinical Notes
- NSW health fluid order chart
- NSW health fluid balance chart
- GCS score chart

**7. EDUCATIONAL NOTES**

**Background:**

The normal range of the serum or plasma sodium concentration is 135 to 145 mmol/L.

In pregnancy, the lower limit of normal is 130mmol/L.

Hyponatraemia, defined as a serum sodium (Na) concentration <135mmol/L [<130 mmol/L in pregnancy], is the most common disorder of body fluid and electrolyte balance encountered in clinical practice. It can lead to a wide spectrum of clinical symptoms, from subtle to severe or even life threatening, and is associated with increased mortality, morbidity and length of hospital stay in patients presenting with a range of conditions. It is usually associated with a reduction in effective plasma osmolality i.e. hypotonic hyponatremia.

Hyponatraemia is NOT primarily a disorder of SODIUM but a disorder of water balance. Whether the patient is hypovolaemic or euvolaemic there is a relative excess of body water compared to total body sodium and potassium content. True hyponatraemia is always associated with either an appropriate or inappropriate activation of the hormone vasopressin (also called antidiuretic hormone).

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**Classification**

Pseudohyponatraemia is a laboratory artefact that occurs when abnormally high concentrations of lipids or proteins in the blood interfere with the accurate measurement of sodium. Serum osmolality will be within the normal range in case of pseudohyponatraemia and direct measurement of sodium using a blood gas analyser will yield the true sodium concentration.

Isotonic hyponatraemia: In the majority of patients that present with hyponatraemia, the serum is hypotonic i.e. both the sodium concentration and the effective osmolality are low. Sometimes, the serum contains other osmoles that may effectively replace sodium to produce isotonic (isosmotic) hyponatraemia. Initially when these osmoles are added to sodium they increase osmolality, “attracting” water from the intracellular compartment: water actually moves from a higher concentration inside cells to the now relatively reduced concentration in the extracellular space. This then reduces the serum sodium concentration until the osmolalities in the two compartments are equalised. Examples of such osmoles include glucose (hyperglycaemia due to uncontrolled diabetes mellitus), mannitol and glycine (absorption of irrigation fluids during urological or gynaecological surgery).

Hypertonic hyponatraemia: In hyperglycaemia-induced hyponatraemia, hyponatraemia is similarly caused by dilution due to hyperosmolality but there is such a rapid excess of the additional osmoles that there is insufficient time for equilibration and, in any case, water is continuously lost through the osmotic diuresis caused by the hyperglycaemia.

It is important to distinguish between measured osmolality and calculated osmolality which is all that is provided unless *measured osmolality* is specifically requested.

When SIADH persists long term (often when it is due to cerebral or pulmonary abnormalities or malignancy), first-line therapy is chronic fluid restriction, usually restricting intake to 1 litre daily. Sodium chloride 600mg tablets may also assist in some patients.

When this is insufficient, specialist (nephrology or endocrine) assistance should be sought.

**Clinical classification (see Table 1)**

Hyponatraemia cannot be maintained without ADH activity leading to distal tubular water reabsorption. Thus all cases of hyponatraemia have a relative or absolute excess of ADH activity.

A clinical estimation of hydration status is ESSENTIAL before the cause can be determined and guide therapy. This will determine whether the patient is hypo-, eu- or hypervolemic.

Excretion of water may be impaired in older people or by pain and nausea. It is also impaired by inadequate plasma volume eg blood loss, low cardiac output eg cardiac failure or shock and kidney impairment, as well as inadequate glucocorticoid and thyroid function. These possibilities must be excluded before diagnosing the syndrome of inappropriate secretion of antidiuretic hormone (SIADH).

**Clinical diagnosis of hyponatremia-see Figure 1.**

**The syndrome of inappropriate secretion of antidiuretic hormone (SIADH)**

SIADH has diverse causes. These most commonly relate to intrathoracic or intracranial pathology, malignancy or drugs that can impair water excretion.

**SIADH cannot be diagnosed in the presence of diuretic use, hypothyroidism or hypocortisolaemia .**

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SIADH is likely when the following results apply.

- serum sodium concentration lower than 130 mmol/L
- serum osmolality lower than 275 mmol/kg
- urine osmolality higher than 100 mmol/kg and usually higher than serum osmolality
- urine sodium concentration higher than 30 mmol/L.

The diagnosis can generally be established from the clinical context and the relationship between urine and serum osmolality, which should be assessed in concurrent samples. *Assaying plasma antidiuretic hormone (ADH) is not required.* Serum urea, uric acid and potassium concentrations are often low.

**Treating hyponatremia**

In general, treatment is dependant on the chronicity, the underlying cause, the clinical and biochemical severity and the patient's co-morbidities. Harm often follows inappropriate or rapid treatment of hyponatraemia in asymptomatic patients.

**Only acute (<48 hours), symptomatic hyponatraemia should be reversed rapidly.** If in doubt, assume the hyponatraemia is chronic.

Always identify and treat any underlying cause in addition to direct treatment for hyponatremia

In general, 0.9% sodium chloride is not helpful in euvolaemic hyponatraemia and will usually worsen hyponatraemia in SIADH. This is because the sodium will be lost in the urine whilst the water will be retained in proportion to the urine:plasma osmolality ratio.

**Recommendations for treatment by volume status**

**Hypovolaemic hyponatraemia :**

Volume depleted patients may require resuscitation. Any drugs implicated as a cause of hypovolaemic hyponatraemia should be stopped before intravenous treatment begins.

Clear-cut sodium and water depletion e.g. from diuretic drugs may respond to intravenous 0.9% sodium chloride, with potassium supplements if required. Careful observation is required.

If hyponatraemia is severe or chronic, boluses (250 mL) of sodium chloride 0.9% followed by frequent (2 to 4 hourly) assessment of sodium and water balance are safer than continuous infusion, since rapid correction can depress ADH and lead to sudden massive diuresis and an overly rapid increase in sodium.

**Hypervolaemic hyponatraemia:**

Patients who are oedematous due to heart, liver or kidney failure should be treated with fluid restriction. A loop diuretic may be added as long as the effective intravascular volume is not depleted further.

**Euvolaemic hyponatraemia:**

Treatment will depend on:

- presence of central nervous system symptoms eg unconsciousness, seizure, drowsiness, headache
- severity
- rate of development.

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Acute: severe symptomatic hyponatraemia generally needs treatment with intravenous sodium chloride 3%.

Chronic: or slowly developing hyponatraemia of the same degree should be managed by fluid restriction.

**Recommendations for treatment by severity of hyponatremia**

**Mild to moderate hyponatraemia**

- **MAY BE MANAGED ON THE WARD**

For mild to moderate hyponatraemia in euvolaemic or hypervolaemic patients (serum sodium concentration from 120 to 135 mmol/L with no cerebral symptoms):

- Fluid restrict: 500 mL to 800mL per 24 hours, or 500 mL less than daily urine output.
- Monitor serum electrolytes, creatinine and urine output daily or twice daily.

More aggressive intervention to increase the serum sodium concentration above 120 mmol/L is generally not indicated.

**Severe hyponatraemia**

- **ADMIT TO ACC or ICU**

For severe hyponatraemia (serum sodium concentration < 120 mmol/L or with cerebral symptoms), treatment is intravenous 3% sodium chloride (513 mmol/L). The initial target serum sodium concentration should not be higher than 120 mmol/L.

*Rapidly correcting hyponatraemia may produce permanent central nervous system injury, due to osmotic demyelination.*

Patients with chronic hyponatraemia (ie known duration more than 48 hours) are particularly at risk. Additional factors that increase this risk include:

- serum sodium concentration lower than or equal to 105 mmol/L
- hypokalaemia
- alcoholism
- malnutrition
- advanced liver disease.

To avoid osmotic demyelination, the maximum rate of change in the serum sodium concentration in chronic hyponatraemia should be:

- not more than 8-10 mmol/L in the first 24 hours
- and an additional 8 mmol/24 hours thereafter

To reduce the risk of overcorrection, the initial goal of therapy can be even lower: 4 to 8 mmol/L daily. For patients with the additional risk factors listed above, the goal should be 4 to 6 mmol/L daily.

This infusion should be given with critical care monitoring i.e. HR, BP, strict fluid balance and daily weighs.

More rapid initial correction can be considered in patients with:

- seizures or coma, regardless of whether the hyponatraemia is known to be chronic
- self-induced acute water intoxication (e.g. psychiatric conditions, endurance exercise)
- known hyponatraemia for less than 24 to 48 hours
- intracranial pathology or increased intracranial pressure.

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The goal of therapy in these patients is to raise the serum sodium concentration by 4 to 6 mmol/L, to prevent neurological damage secondary to brain herniation, swelling and cerebral ischaemia. Use:

- 3% sodium chloride 150 mL IV over 20 minutes.
- recheck serum sodium every 2 to 4 hours depending on GCS and clinical status scores
- repeat as needed up to a maximum of 3 infusions and cease 3% sodium chloride infusion when **either** of the following three criteria are met:
  - symptoms improve
  - target increase in serum sodium has been achieved
- fluid restrict the patient to maintain the serum sodium
- oral sodium chloride tablets may be useful

Often it is difficult to assess whether severe hyponatraemia is acute or chronic. Unless it is clearly acute, a slower rate of correction is essential. The volume of bolus sodium chloride and the patient's response must be considered when calculating the remaining volume and infusion rate in chronic hyponatraemia.

**8. RELATED POLICIES / PROCEDURES / CLINICAL PRACTICE LOP**

- Acute Care: Admission Criteria, Process and Management Guideline
- Catheterisation
- Potassium – Administration of Oral or Intravenous

**9. RISK RATING**

- High

**10. NATIONAL STANDARD**

- Medication safety

**11. REFERENCES**

- Spasovski G, Vanholder R, Allolio B, Annane D, Ball S, Bichet D, et al. Clinical practice guideline on diagnosis and treatment of hyponatraemia. *European Journal of Endocrinology*. 2014;170(3):G1-G47.
- Moulds R, Black K, Clearihan L, Ebeling P, Frauman A, Greenberg P, et al. Endocrinology Expert Group. Therapeutic Guidelines: endocrinology. Version 5. 2014.

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**Table 1:** Clinical classification of causes of hyponatremia

Volume status	Cause of low serum sodium concentration
Hypervolaemia("wet")	heart failure liver cirrhosis kidney failure nephrotic syndrome
Euvolaemia	SIADH drug induced (eg carbamazepine, SSRIs, SNRIs) cerebral or pulmonary pathology malignancy-associated (SIADH) hypothyroidism psychogenic polydipsia pain nausea surgery and anaesthesia adrenal insufficiency
Hypovolaemia ("dry")	sodium loss with free water intake vomiting and/or diarrhoea burns* thiazides and related diuretic drugs (indapamide, hydrochlorothiazide, chlorthalidone) other sodium-wasting states hypopituitarism
Others	
pseudohyponatraemia	severe hypertriglyceridaemia,
osmotic dilution	hyperglycaemia mannitol or glycine administration (gynaecological and prostatic surgery)
mechanism uncertain	HIV
SSRI = selective serotonin reuptake inhibitor; SNRI = serotonin and noradrenaline reuptake inhibitor	

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FIGURE 1

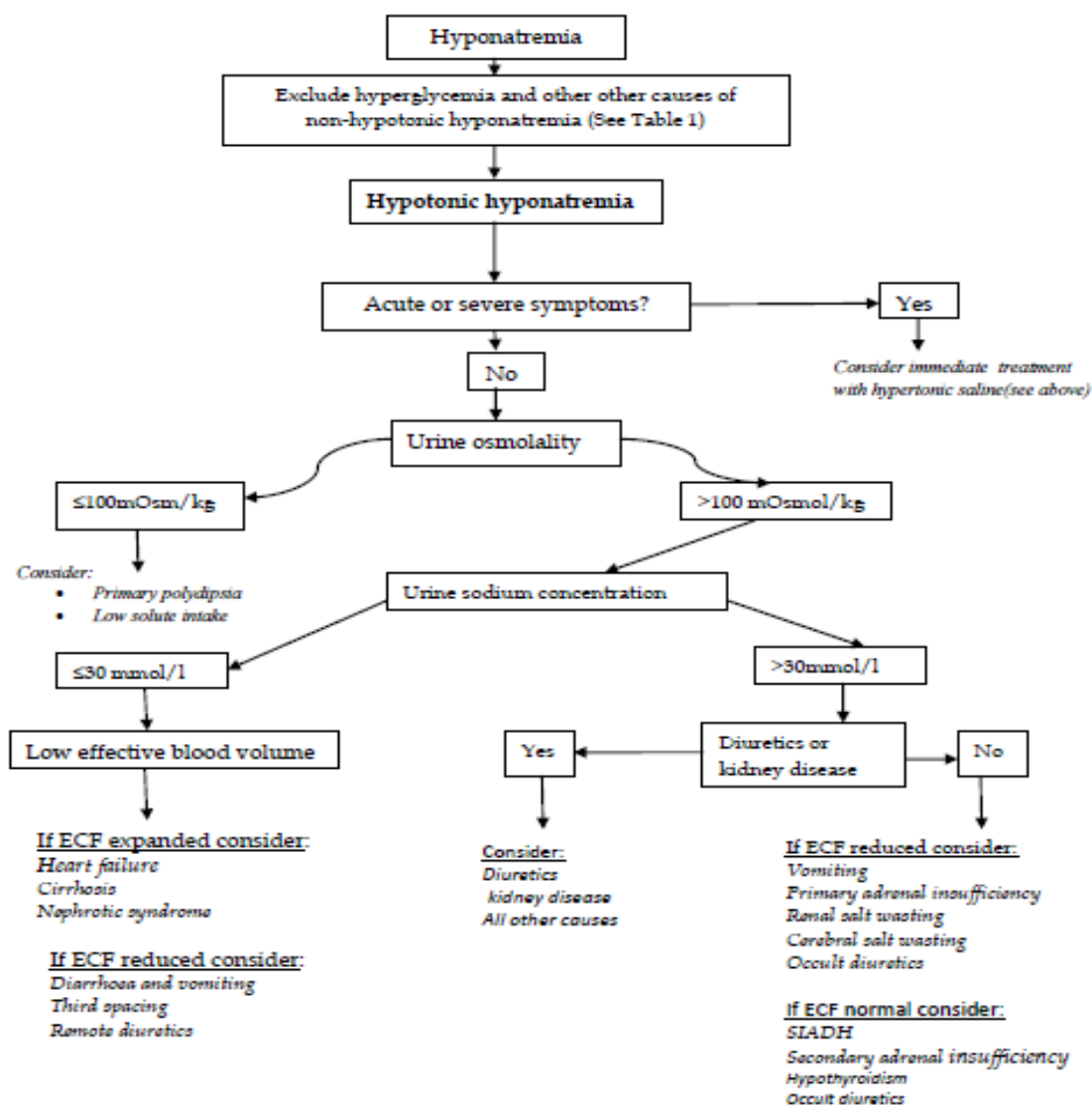


Figure1: Algorithm for the diagnosis of hyponatremia



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**Appendix A**

These calculations should be used as a guide to the total amount of 3% sodium chloride required but patients do vary in their response and the most important aspect of management is frequent assessment of sodium and water balance including urine output as well as BP, PR and GCS.

$$\text{increase in serum sodium / litre of infused sodium chloride 3\%} = \frac{[513 - \text{measured serum sodium concentration (mmol/L)}]}{[\text{total body water (kg)} + 1]}$$

To calculate total body water:

In women: Total body water (kg) = body weight x 0.5 (nonelderly) or x 0.45 (elderly).

Sample calculation:

Patient: 60 kg, 40 years, female

Serum sodium concentration: 110 mmol/L

Target serum sodium concentration at 24 hours: 118 mmol/L

$$\begin{aligned} \text{increase in serum sodium / litre of infused sodium chloride 3\%} &= \frac{[513 - \text{measured serum sodium concentration (mmol/L)}]}{[\text{total body water (kg)} + 1]} \\ &= \frac{[513 - 110]}{[(60 \times 0.5) + 1]} = \frac{403}{31} = 13 \text{ mmol/L} \end{aligned}$$

To achieve an increase of 8 mmol/L calculate the total amount of 3% sodium chloride required in mL using the equation below:

$$\left( \frac{\text{Number of mmol to be increased}}{\text{Increase in serum sodium/litre of Infused 3\% sodium chloride}} \right) \times 1000 \quad \left( \frac{8}{13} \right) \times 1000 = 615 \text{ mL of 3\% sodium chloride}$$

To achieve an increase of 8 mmol/L in 24 hours: infusion rate = 615 mL ÷ 24 hours = 26 mL/hour

If an initial rapid increase in the serum sodium concentration is needed, for example to achieve 115 mmol/L of serum sodium in 6 hours, begin the infusion at 64 mL/hour for an anticipated 6 hours (to deliver 5 mmol) and then reduce to 13 mL/hour for the following 18 hours (to deliver the remaining 3 mmol).

If two bolus doses of 100 mL have been given initially, the remaining infusion volume over 24 hours is 615 – 200 mL = 415 mL, so the infusion rate = 17 mL/hour.

As a quick check of the calculation, the following conservative formula may be used to determine the initial infusion rate (mL/hour) of 3% sodium chloride:

$$\text{infusion rate of sodium chloride 3\% (mL/hour)} = \text{body weight (kg)} \times \text{desired increase in serum sodium concentration per hour}$$