Guideline

Treatment of Severe Hyponatraemia in Children

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Author/custodian	Director Endocrinology/ Paediatric Intensive Care Unit			**Review date**	16/10/2024
Supersedes	3.0				
Applicable to	Children and young people (less than 18 years) and outside the neonatal period				
Authorisation	Executive Director Clinical Services				

Purpose

This purpose of this guideline is to provide clinical guidance for all staff involved in the care and management of severe hyponatraemia in paediatric patients at the Queensland Children's Hospital (QCH).

Mild to moderate hyponatraemia is very common in paediatric practice and can usually be reduced by avoiding intravenous (IV) hypotonic electrolyte solutions. This guideline will deal with the potentially life-threatening situation of severe hyponatraemia (serum sodium less than 120 mmol/L) where there is risk of central demyelination as a consequence of rapid correction of sodium.

Scope

This guideline applies to all clinical staff involved in the care and management of a child with severe hyponatraemia. It is not intended to be a substitute for specific professional or clinical advice, or to replace consultation with senior staff, which should always be sought if clinically relevant.

This material is published by Queensland Health with the intention of providing a guideline for use at QCH. Anyone wishing to use this guideline outside QCH should refer to their local Medicines Advisory Committee before using.

Related documents

Policy and standard(s)

- 01039 – CHQ Medication Administration Procedure
- 01001 – CHQ Medication – Prescribing

Procedures, Guidelines, Protocols

- CHQ-GDL-60016) Diabetic Ketoacidosis (DKA) and Hyperosmolar Hyperglycaemic State (HHS) – Emergency Management in Children

- CHQ-GDL-80114 Management of Severe Traumatic Brain Injury in Children
- CHQ-GDL-01025 Intravenous Fluid Guidelines – Paediatric and Neonatal

Guideline

Introduction

Hyponatraemia is the most common electrolyte abnormality encountered in children. Hyponatraemia results from an excess of water relative to sodium in the extracellular fluid compartment. Severe hyponatraemia is defined as a serum sodium level less than 120 mmol/L or as a rapid fall in serum sodium levels. It is associated with increased morbidity and mortality and can lead to a wide spectrum of clinical symptoms.

It is most common in children with pre-existing morbidities and may have delayed presentation as part of critical illness. The management of hyponatraemia can commence within any area of the hospital under care of a variety of specialist medical teams.

Causes

Hyponatraemia usually occurs in the setting of excess water intake with or without sodium losses, in the presence of impaired free water excretion.

Under normal circumstances, the human body can maintain sodium within the normal range of 135-145 mmol/L and will attempt to prevent hyponatraemia by generating dilute urine in order to excrete free water.

Water excretion is often impaired secondary to increased anti-diuretic hormone (ADH) levels. If this occurs in the absence of osmotic or hypovolaemic stimulus it is termed "Syndrome of Inappropriate Diuretic Hormone Secretion" (SIADH).

Table 1 lists some of the known causes of hyponatraemia (common causes have been highlighted in bold).

Fluid overload	Euvolaemic	Volume depletion

• **Intravenous fluid administration (in excess)**
• Oedematous states
  ○ Nephrotic syndrome
  ○ Heart failure
  ○ Cirrhosis
  ○ Hypoalbuminaemia
• Acute/chronic renal failure
• Obstructive uropathy
	• Enteral hypotonic fluid intake (dilute formula, oral rehydration solutions, excessive water intake)
	• Psychogenic polydipsia
	• **Increased ADH secretion**
	  ○ **Pulmonary (pneumonia, bronchiolitis, ventilation)**
	  ○ **CNS (infection, injury, tumour)**
	  ○ **Post-operative, trauma, pain**
	  ○ Endocrine (hypothyroid, low cortisol)
	• Medications
	  ○ Chemotherapy
	  ○ Antiepileptics
	  ○ Argipressin (Vasopressin)
	  ○ Desmopressin (DDAVP)
		• **Gastrointestinal loses with free water**
		  ○ Gastroenteritis
		  ○ Secretory/osmotic diarrhoea
		  ○ Ostomies
		• Skin losses (CF, burns)
		• Abdominal third spacing
		• Excessive fluid consumption post activity
		• Hyperglycaemia
		• Renal losses – diuretic therapy
		• Salt wasting
		• Primary renal tubular disorders
		• Hypoaldosteronism
		• Metabolic alkalosis

Table 1 – Causes of hyponatraemia

NB: Artefactual causes of hyponatraemia are also possible, including laboratory or sampling errors, administration of mannitol, severe hypertriglyceridaemia with visible lipaemia, or hyperglycaemia (see Appendix 1).

ALERT

If volume depletion is sufficient to cause shock, there may be activation of ADH secretion from carotid baroreceptor stimulation that bypasses the hypothalamic osmoreceptors, further worsening the hyponatraemia. Treatment of shock therefore turns off ADH and the resulting diuresis, causing sodium to rise rapidly.

Assessment

The presence of hyponatraemia of any degree is not normal and should prompt investigation to determine a cause and repeat testing of serum levels should occur to ensure moderate or severe hyponatraemia is not developing.

Severe hyponatraemia more commonly occurs in children with a pre-existing chronic comorbidity that may delay recognition of symptoms, or in acutely unwell patients receiving critical care (post traumatic brain injury or burns).

History

History should include specific information on:

- Fluid intake – including both intravenous and enteral intake
- Fluid losses
- Current medications
- Weight
- Fluid balance

Examination

Early symptoms of hyponatraemia may be non-specific and include:

- Headache
- Nausea/vomiting
- Weakness
- Impaired level of consciousness, agitation or irritability
- Seizures
- Encephalopathy
- Respiratory depression

ALERT

Severe hyponatraemia can result in a medical emergency if left untreated, including seizures, apnoea, cardiac arrhythmias and coma, with a high risk for cerebral herniation.

Refer to the flowchart in Appendix 2 for further information about establishing a cause of hyponatraemia and suggested interventions.

Investigations

Routine pathology should include:

- Serum sodium
- Plasma osmolarity
- Urine osmolarity
- Urine sodium

- Blood glucose (if hyperglycaemia present in addition to hyponatraemia (DKA))

Management

If there are no neurological manifestations of hyponatraemia, active correction with Sodium Chloride 3% solution is not required and potentially harmful.

Consult the QCH Endocrinology team for all cases of symptomatic hyponatraemia.

ALERT

Rapid correction of serum sodium is associated with osmotic demyelination syndrome

Rise in serum sodium should not exceed 10mmol/L in the first 24 hours and 18mmol/L in the first 48 hours.

Refer to Appendix 3 for further details

Consider insertion of an arterial line or large bore venous line to allow for frequent blood sampling during sodium correction.

Management of confirmed severe hyponatraemia (less than 120 mmol/L) with presence of symptoms:

1. Treat shock (if present) with appropriate fluid resuscitation using Sodium Chloride 0.9%. Pause and reassess. Fluid resuscitation may cause a rise in serum sodium as diuresis occurs. Monitor urine output.
2. Administer 1.5 to 2.5 mmol/kg (3 to 5 mL/kg) of Sodium Chloride 3% over 30 minutes, preferably via a central line, using Dose Error Reduction Software (DERS). Do not delay treatment in a symptomatic patient if central access is not available.
3. Check serum sodium concentration immediately following the Sodium Chloride 3% infusion. Aim to correct the sodium by 6 mmol/L.
4. If still symptomatic and serum sodium remains < 125 mmol/L, repeat administration of 1.5 to 2.5 mmol/kg (3 to 5 mL/kg) of Sodium Chloride 3% over 30 minutes.

ALERT

Sodium Chloride 3% should be administered via a central line as it is hyperosmotic. Do not delay administration if central access is not available. Careful use of a peripheral line is appropriate until central access is obtained.

Acute severe hyponatraemia does not carry the same risk of osmotic demyelination. It can be safely corrected without a limit on the rise of sodium. **If there is any likelihood that the hyponatraemia may have been present for more than 48 hours, proceed with slow correction of sodium.**

If no resolution of symptoms:

1. Commence continuous infusion of Sodium Chloride 3% aiming for an increase of serum sodium of 1mmol/L every hour
2. Consider a differential diagnosis for CNS symptoms other than hyponatraemia

Check serum sodium concentration hourly for the duration of the Sodium Chloride 3% infusion and until a sodium level of 130 mmol/L is reached.

Cease the Sodium Chloride 3% infusion when:

a. Symptoms improve
b. Serum sodium concentration has increased by a total of 10 mmol/L
c. Serum sodium concentration reaches 130 mmol/L

When symptomatic improvement occurs:

1. Cease the Sodium Chloride 3% infusion immediately
2. Commence cause-specific treatment if available, aiming to stabilise sodium concentration
3. Limit the increase of serum sodium concentration to a total of 10 mmol/L during the first 24 hours and an additional 8 mmol/L during every 24 hours thereafter until the serum sodium concentration reaches 130 mmol/L
4. Once the sodium level has reached 130 mmol/L, reduce monitoring to every four hours.

Hyperosmolar therapy in traumatic brain injury (PICU only):

Hyperosmolar therapy is effective in the management of raised intracranial pressure (ICP) post traumatic brain injury.

Goals of ICP control include maintaining a serum sodium level between 145-155 mmol/L. Electrolytes should be measured every 4 hours initially, reducing to every 8 hours once stable.

1. Administer 1 to 2.5mmol/kg (2 to 5 mL/kg) of Sodium Chloride 3% as an intravenous infusion over 20 minutes using Dose Error Reduction Software (DERS) pump

2. For persistent low sodium despite bolus dosing, commence a continuous infusion of Sodium Chloride 3% at a rate of 0.08 – 0.25 mmol/kg/hr.
NB: infusions rates > 0.35 mmol/kg/hr are associated with an increased risk of cerebral demyelination

3. Older patients requiring strict fluid restriction may be suitable for administration of a neat Sodium Chloride 23.4% (4 mmol/mL) infusion. This is considered very high risk and should be under direct advice and supervision of the Senior Medical Officer in PICU.

Mannitol 20% is an alternative option to reduce raised ICP, however its effect can be transient. With repeated doses or if the blood brain barrier is not intact, there is an increased risk of mannitol accumulation in the brain, resulting in an increased ICP due to fluid shifts in the brain parenchyma.

1. Administer 0.25 g/kg of mannitol 20% by intravenous infusion over 15 to 30 minutes using Dose Error Reduction Software (DERS)

Refer to CHQ Guideline: Management of Severe Traumatic Brain Injury in Children (CHQ-GDL-80114) for further details.

Management of mild to moderate hyponatraemia:

Consider initial enteral supplementation at a dose of 0.5 to 1 mmol/kg (maximum 40mmol) every 4 to 6 hours. Mix enteral dose with feed to minimise gastric intolerance. Occasionally sodium supplementation can cause diarrhoea. Higher doses may be required in consultation with senior medical officer.

Product available	Sodium content	Indication
Sodium Chloride 600mg tablets (dissolvable)	Each tablet contains: 10 mmol sodium 10 mmol chloride	Mild to moderate hyponatraemia Suitable for administration in the ward and outpatient setting
Sodium Chloride 6% sachets for inhalation **Can be given enterally**	Each 10 mL sachet contains: 1 mmol/mL sodium chloride	Mild to moderate hyponatraemia Suitable option where a liquid formulation is required (ie gastric tube administration)
Sodium Chloride 23.4% concentrated injection **Can be given enterally**	Each 10 mL glass vial contains: 4 mmol/mL sodium chloride	Mild to moderate hyponatraemia Suitable for patients with a high sodium requirement or those with fluid restrictions **Risk of harm if administered intravenously in error. Not recommended for home use by patients with IV access**

Consultation

Key stakeholders who reviewed this version:

- Pharmacist Senior – Critical Care
- Pharmacist Lead Critical Care
- SMO PICU
- Safety and Quality PICU
- SMO Endocrine

Definition of terms

Term	Definition	Source
Hyponatraemia	Serum sodium < 135 mmol/L • Mild: 130 – 134 mmol/L • Moderate: 120 – 129 mmol/L • Severe: < 120 mmol/L	Up to Date European and USA guidelines (see reference list)
Chronic hyponatraemia	Hyponatraemia that has been present for **more than** 48 hours	Up to Date

Acute hyponatraemia	Hyponatraemia that develops over a period of **less than** 48 hours	Up to Date
Osmotic demyelination	Neurological manifestations arising as a result of overly rapid correction of hyponatraemia	Up to Date
ADH	Anti-diuretic hormone	

References and suggested reading

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Guideline revision and approval history

Version No.	Modified by	Amendments authorised by	Approved by
1.0	Dr Jerry Wales	Director of Endocrinology	29/9/2018
2.0 16/01/2017	Gemma Burns (Pharmacist Senior – Critical Care)	Divisional and Medical Director, Division of Medicine	Executive Leadership Team
3.0 09/12/2020	Michele Cree- Pharmacist Lead- Critical Care	Director Endocrinology	Executive Director Medical Services
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Keywords	Severe hyponatraemia, sodium, SIADH, cerebral demyelination, central pontine myelinosis
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Appendix 1: Hyponatraemia as part of diabetic ketoacidosis (DKA).

Hyponatraemia developing as part of treatment of DKA is a risk factor for cerebral oedema *per se* but not cerebral demyelination as it is non-hypotonic hyponatraemia. Glucose "holds water" in the circulation, lowering the measured sodium value whilst the total amount of sodium in the circulation remains the same.

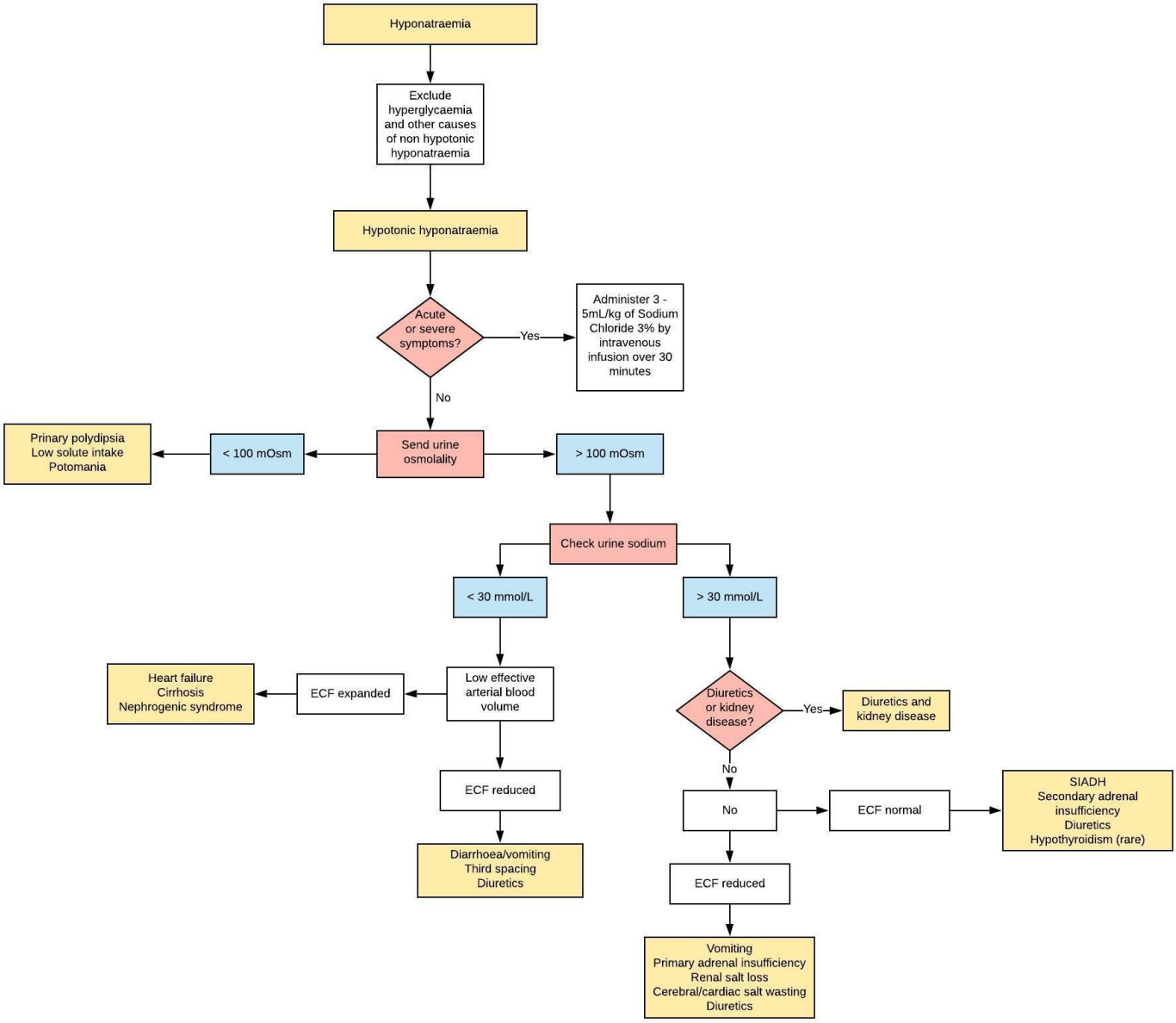
In DKA the true sodium value needs to be corrected to take into account the hyperglycaemia according to the following formula.

$$\text{Corrected sodium} = \text{Measured Sodium} + 2.4 \times \frac{\text{(Measured Glucose (mmol/L) - 5.5 mmol/L)}}{\text{5.5 mmol/L}}$$

(This is the same as adding 2.4 mmol/L to the measured serum sodium concentration for every 5.5 mmol/L incremental rise in serum glucose concentration above a normal serum glucose concentration of 5.5 mmol/L).

The sodium level should rise as glucose is removed from the circulation with treatment of DKA. A failure to do so is a worrying sign. Please see the State Guidelines for treatment of DKA 2016 edition.

Appendix 2: Establishing a cause of severe hyponatraemia



Flowchart adapted from European Journal of Endocrinology (2014) 170, G1-G47

Appendix 3: Osmotic demyelination syndrome

Rapid correction of sodium can cause permanent central nervous system injury as a result of osmotic demyelination.

Symptoms may not present for several days following the over-correction and can include:

- Dysarthria
- Dysphagia
- Paraparesis/quadriparesis
- Behavioural disturbances
- Movement disorders
- Seizures
- Lethargy
- Confusion, disorientation and/or obtundation
- Coma

ALERT

Relowering of sodium in patients at risk of cerebral demyelination should only be performed under the direction of the QCH Endocrinology team

Risk factors for developing cerebral demyelination

- Severe chronic hyponatraemia (sodium < 115mmol/L)
- Development of hypernatraemia during sodium correction
- Serum sodium increase exceeding 25mmol/L in 48 hours
- Hypoxaemia
- Severe liver disease
- Use of thiazide diuretics
- Severe burns
- Malnutrition
- Hypokalaemia
- Renal failure