GUIDELINE

Hyperammonaemia

Scope (Staff):	Nursing and Medical Staff
Scope (Area):	NICU KEMH, NICU PCH, NETS WA

Child Safe Organisation Statement of Commitment

CAHS commits to being a child safe organisation by applying the National Principles for Child Safe Organisations. This is a commitment to a strong culture supported by robust policies and procedures to reduce the likelihood of harm to children and young people.

This document should be read in conjunction with this disclaimer

Aim

Hyperammonaemia is a medical emergency this guideline provides clinicians with direction in the management of this medical emergency.

Risk

Failure to initiate prompt treatment may result in adverse neurological outcomes.

Elevated plasma ammonia is a medical emergency

- The neurological outcome of affected neonates is directly related to the duration of hyperammonaemic coma.

DO NOT delay treatment whilst awaiting results of further investigations.
Discuss early with neonatal consultant and then the Metabolic Unit team.

Definition

- Premature neonate > 150 μmol/L.
- Term neonate > 100 μmol/L.

Symptoms

- Symptoms are non-specific but include tachypnoea, seizures and encephalopathy.
- Consider hyperammonaemia in the differential diagnosis of any sick neonate.

Differential Diagnosis

- Spurious: Incorrect sampling (sample haemolysed, not collected on ice, or delayed separation).
- Hepatic: Liver failure / impairment.
- Metabolic Urea Cycle defects (UCD):
  - Organic acidaemias (OA).
  - Fatty acid oxidation defects (FAOD).
- Transient hyperammonaemia of the newborn (due to open ductus venosus).
- HIHA - Hyperinsulinism/hyperammonaemia - hypoglycaemia with raised ammonia.

Investigations

Acute Investigations	Additional Information
Ammonia (x2)	Free flowing, consider arterial sample if difficult. Place on ice, do not shake the tube. Transport urgently to laboratory.
Blood gas	Respiratory alkalosis in UCD, metabolic acidosis in OA.
Lactate	Raised in OA, FAOD & UCD with circulatory collapse.
Liver function	Deranged in liver failure, OA & FAOD.
Clotting	Deranged in liver failure, OA & FAOD.
Glucose	Low in FAOD & OA.
Ketones (urine dipstick)	Low in FAOD & UCD, raised in OA.
Amino acids (plasma)	Glucose and ketones are not necessarily reduced in OA's and UCD's.
Amino acids (urine)	
Organic acids/ Orotic acid (urine)	Obtain baseline.
Acylcarnitines (Guthrie card and plasma)	If hyperinsulinemia is a consideration with associated hypoglycaemia - then do insulin tests as well.

Acute Management

ALL measures to lower plasma ammonia must be instituted as soon as possible. Follow steps below:

1. **Stop all enteral feeds.** Promote anabolism. Start intravenous 10% glucose infusion to ensure glucose infusion rate of 6 mg/kg/minute, aiming for blood glucose levels of 4-8 mmol/L.
2. **Commence insulin infusion** 0.05 U/kg/hr if blood glucose > 10 mmol/L. DO NOT just turn down the rate of 10% glucose (remember that the aim is to stop catabolism and this can only be done by giving lots of calories).
3. If boluses of fluid are required, use 0.9% Saline. **AVOID** 4.5% human albumin solution and FFP as they contain protein. If FFP is needed to treat coagulopathy, discuss with consultants and the metabolic team prior to giving.
4. If ammonia > 100µmol/L repeat in 4 hours.
5. If ammonia > 150 µmol/L, discuss with Neonatal and Metabolic Consultant, as urgent exclusion of possible 'small molecule' metabolic disease has to be considered and managed appropriately (see step 7).
6. The decision to administer ammonia scavengers (sodium benzoate and phenylbutyrate - both at 250 mg/kg) either as a loading dose (i.e. over ~ 2 hours) or maintenance over 24 hours depends on the level of elevation of ammonia and clinical presentation (i.e. encephalopathic etc).
    - **URGENTLY** obtain a rapid review of newborn screening results as well as urine metabolic screen, plasma amino acids, and acylcarnitine profile and liaise with the metabolic team.
    - Arrange cranial ultrasound to look for cerebral oedema.
    - Sodium benzoate and phenylbutyrate are stocked in NICU (**hyperammonaemia kit**). See Neonatal Hyperammonaemia Medications.
        - **KEMH:** Hyperammonaemia kit is kept in SCN3 Medication imprest cupboard.
        - **PCH:** 'Hyperammonaemia Kit' is kept in the ADM as a virtual kit.
    - Contact the on-call pharmacist urgently if there are any problems with accessing the kit.
    - In addition, consider arginine ~ 250 mg/kg/day as a continuous infusion but depends on type of urea cycle defect etc. Get metabolic tests analysed **urgently.**
7. The ammonia level at which a decision needs to be made on haemodiafiltration (usually if >300) depends on clinical presentation, and how soon the levels drop post-loading dose of ammonia scavengers.
    - At levels of ammonia more than 300 umol/L; an urgent multidisciplinary team meeting (MDT) should be initiated. The MDT should include the on-call metabolic consultant, neonatologist and PCC consultant who will decide on the need for haemofiltration.
    - Obtain central access (appropriate access can take time and needs careful planning), and commence haemodiafiltration,

8. In the event of imminent death, obtain an ante mortem liver biopsy and skin biopsy to assist with diagnosis. Contact the biochemistry laboratory to arrange. Collect 2 mLs EDTA whole blood for potential genetic studies and state "**extracted DNA for storage"** on lab form.
9. Consider carefully whether to perform a post-mortem, even if liver and skin biopsies have been taken.

Related CAHS internal policies, procedures and guidelines
Neonatology Medication Protocols • Hyperammonaemia Medications

This document can be made available in alternative formats on request.

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