NCCU CLINICAL GUIDELINES
SECTION: 10

METABOLIC MANAGEMENT

Section: 10 Metabolic Management
Neonatal hyperammonaemia
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NEONATAL HYPERAMMONAEMIA

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.**

DEFINITION

Premature neonate >150μmol/l Term neonate >100μmol/l

SYMPTOMS

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

DIFFERENTIAL DIAGNOSIS

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

ACUTE INVESTIGATIONS	
Ammonia (x2)	Free flowing, consider arterial if difficult. Place on ice and 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 Hiawatha's is a consideration with associated hypoglycemia- then insulin tests should be done additionally.

ACUTE MANAGEMENT

1. **Stop all enteral feeds**. Promote anabolism. Start intravenous glucose to ensure glucose infusion of 8-10mg/kg/minute, aiming for glucose 4-8 mmol/L.

2. Add insulin infusion 0.05U/kg/hr if blood glucose >10mmol/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. Remember that 4.5% human albumin solution and FFP contain protein.

4. If ammonia >150µmol/L, discuss with Metabolic Consultant, as urgent exclusion of possible 'small molecule' metabolic disease has to be considered and managed appropriately (see step 6.).

5. The decision to administer ammonia scavengers (sodium benzoate and phenylbutyrate - both at 250mg/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**). Contact the on-call pharmacist urgently if there are any problems with accessing the kit. In addition, consider arginine ~250mg/kg/day as a continuous infusion but depends on type of urea cycle defect etc. Hence, important to get metabolic tests analyzed urgently.

6. The ammonia level at which a decision needs to be made on haemodiafiltration depends on clinical presentation, and how soon the levels drop post-loading dose of ammonia scavengers. If there is a need to prepare for probable haemodiafiltration. Contact PICU Consultant to discuss. Remember that it can take some time to get appropriate central access and commence haemodiafiltration so ALL other measures to lower plasma ammonia (i.e. steps 1, 2, 3 and 4) must be instituted as soon as possible.

7. In the event of imminent death, an ante mortem liver biopsy and skin biopsy should be obtained, to assist with diagnosis. Contact the biochemistry laboratory to arrange. 2mls EDTA whole blood should also be collected for potential genetic studies and state "**extracted DNA for storage"** on lab form.

8. Finally, consider carefully whether to perform a post-mortem, even if liver and skin biopsies have been taken.