Management of Hypoglycaemia on the Neonatal Unit

The definition of hypoglycaemia is controversial, however, <2.6mmol/L is generally accepted as correct in a term or preterm infant. Symptomatic hypoglycaemia may cause long term neurological injury in up to 50% of cases, but the duration of hypoglycaemia required for this to occur is unclear. Occipital brain injury associated with hypoglycaemia can result in long term disability, epilepsy and visual impairment.

Causes of hypoglycaemia

<table>
<thead>
<tr>
<th>Endocrine</th>
<th>Metabolic</th>
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</thead>
<tbody>
<tr>
<td>Hyperinsulinoma</td>
<td>Disorders of fatty acid</td>
</tr>
<tr>
<td>Adrenal insufficiency</td>
<td>metabolism</td>
</tr>
<tr>
<td>Hypopituitarism</td>
<td>Disorders of carbohydrate</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>metabolism</td>
</tr>
<tr>
<td></td>
<td>Disorders of Organic Acid</td>
</tr>
<tr>
<td></td>
<td>Metabolism</td>
</tr>
<tr>
<td></td>
<td>Disorders of gluconeogenesis</td>
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At Risk infants

<table>
<thead>
<tr>
<th>Maternal conditions</th>
<th>Neonatal problems</th>
</tr>
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<tbody>
<tr>
<td>Diabetes</td>
<td>Preterm</td>
</tr>
<tr>
<td>Medications - beta-blockers/ oral hypoglycaemics</td>
<td>IUGR</td>
</tr>
<tr>
<td>Intrapartum IV glucose administration</td>
<td>Perinatal hypoxia-ischaemia</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>Hypothermia</td>
</tr>
<tr>
<td>Infection</td>
<td>Polycythaemia</td>
</tr>
<tr>
<td>Infants on parenteral nutrition</td>
<td>Obvious syndromes eg. midline defects</td>
</tr>
</tbody>
</table>

Obtain a full history and examine carefully.
Any at-risk infants and/or unwell infants should be monitored for hypoglycaemia.
Symptoms of hypoglycaemia include jitteriness, irritability, poor feeding, hypothermia, lethargy, hypotonia, apnoea and seizures.
Most babies have transient hypoglycaemia either due to substrate deficiency (IUGR, Prematurity and stress) or transient hyperinsulinism.
Occasionally, some babies will require further investigations due to persistent hypoglycaemia in order to exclude rare metabolic/endocrine disorders.
Have a low threshold to consider infection, and perform a septic screen in all babies with persistent hypoglycaemia.

Consider Metabolic/ endocrine disorders in the following situations:
- Family history of sudden infant death, Reye’s syndrome or developmental delay.
- Hypoglycaemia in an otherwise healthy, well-grown infant with no obvious risk factors.
- Persistent or recurrent hypoglycaemia despite adequate treatment.
- Hypoglycaemia with seizures or abnormalities of consciousness.
- Hypoglycaemia in association with other abnormalities eg midline defects, micropenis, undescended testis, poor scrotal development, exomphalos, erratic temperature control.

Most patients with hypoglycaemia improve quickly with appropriate management (optimum feeding and IV fluids). However, occasionally such as in the above situations a hypoglycaemia screen (HOG screen) may be indicated. Please discuss with the Registrar before doing a HOG screen.

Investigations:

**Blood tests to be taken at time of persistent hypoglycaemia**

<table>
<thead>
<tr>
<th>Glucose</th>
<th>Cortisol</th>
<th>Ammonia (on ice)</th>
<th>Amino acids</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lactate, blood gas</td>
<td>Acylcarnitines</td>
<td>Non esterified fatty acids</td>
<td>3-OH butyrate (ketone body)</td>
</tr>
<tr>
<td>Insulin</td>
<td>C-Peptide</td>
<td>Non esterified fatty acids</td>
<td>3-OH butyrate (ketone body)</td>
</tr>
</tbody>
</table>

**Urine tests** (first urine void after hypoglycaemic episode)

- Organic acids

**5mls of blood and 5mls of urine total** 3x lithium heparin bottles (green), 1x EDTA bottle (purple), 1x Fluoride Oxalate bottle (grey), 1x Guthrie card for Acylcarnitines, 1x white top urine bottle, 1x capillary gas tube

The investigations below are also required however; they can be done once glucose has been administered.

<table>
<thead>
<tr>
<th>U&amp;E</th>
<th>LFT</th>
<th>Blood Culture</th>
<th>CRP</th>
</tr>
</thead>
<tbody>
<tr>
<td>TFT</td>
<td>17-OHP</td>
<td>Galactosaemia Screen</td>
<td>Growth Hormone</td>
</tr>
</tbody>
</table>

1 x culture bottle, 1x white top bottle for TFT, 4x lithium heparin,
Other investigations to consider depending on the clinical picture include: Cranial Ultrasound scan, ophthalmology examination and MRI of the head.

Hypoglycaemia kits are available on the unit in the fridge in the store room, they include a form stating which tests to send and the blood bottles required. Please call biochemistry to restock if only a few remain.

**GIR Calculation**: 0.167 x Rate of fluid in (ml/hr) x concentration of Dextrose administered (%) / weight (kg)

**Management Thresholds for hypoglycaemia:**
- Healthy term infants: No need to measure blood sugar unless symptomatic
- In all other babies blood sugar levels < 2.6 mmol/L requires treatment.

**Management of Hypoglycaemia when blood sugar < treatment threshold:**
- Increase feed volumes to one day ahead, and consider decreasing feed intervals from three hourly to two, or one hourly if necessary. Repeat blood glucose in 1 hour.
  - If repeat blood glucose is 2.0 - 2.5mmol/L, further intervention is needed and IV dextrose should be considered. Start IV dextrose 10% at 50% of total daily fluid volume and give 50% feeds and recheck blood glucose in 1 hour.
  - If the blood glucose is <2.0mmol/L, start IV dextrose at 100% of daily total fluid volume until a glucose above 2.6mmol/L is achieved.
- Reintroduce milk feeds as soon as blood sugars allow. Initially, with hourly or two hourly feeds. Breast milk is preferable as it is more ketogenic. As milk intake increases decrease IV fluids accordingly.
- If having difficulty titrating feeds up quickly due to persistent hypoglycaemia, see regime below.

**Management of Symptomatic Hypoglycaemia**
- If neurological signs are present, give a minibolus of Dextrose 200mg/kg (2ml/kg 10% dextrose).
- Otherwise, start Dextrose with a glucose infusion rate (GIR) of at least 5-6 mg/kg/min and check blood sugar 20-30 minutes later.
  - If blood glucose <2.6mmol/l, increase the GIR by 1mg/kg/min by increasing the total fluids (increase up to one day ahead). Recheck blood sugar after a further 20-30 minutes.
  - If blood glucose remains <2.6mmol/l increase the concentration of Dextrose in 2.5% intervals (ie up to 12.5% and then 15% and further if necessary). After each change check blood sugar after 20-30 minutes. Continue until the blood sugar is >2.5mmol/l.
- Reintroduce feeds as soon as tolerated. Remember that breast milk is preferable as it is more ketogenic. Monitor blood glucose 4 hourly.
- After 2 consecutive blood glucose levels >3mmol/l are achieved, start reducing the IV Dextrose by decreasing the GIR by 1mg/kg/min. Repeat this process of decreasing the IV intake and increasing the feeds until the patient is on full feeds and IV fluids have discontinued. Remember that decreasing the fluid rate will lead to variable GIR changes; for the same change the GIR will drop more in a smaller baby. Please look at GIR calculation above.
  - If blood glucose is between 2.6mmol/L and 3mmol/L, continue on current management regime until 2 blood glucose measurements greater than 3mmol/L.
  - If blood glucose is <2.6mmol/L, increase the GIR by 1mg/kg/min and recheck in 1 hour.
- Whilst weaning IV Dextrose remember to decrease concentration back to 10% dextrose prior to final discontinuation.
- Have a low threshold for inserting central access (UVC, LL) especially in cases where fluid restriction is needed: this is essential if hypoglycemia requiring IV correction persists. A central line is needed once the concentration of glucose is greater than 12.5%.

**Note: Minibolus (2ml/kg 10% dextrose) should only be given in symptomatic infants.**

**Remember that boluses can induce an insulin response which can provoke secondary hypoglycaemia.**

If the above measures have failed, consider persistent hypoglycaemia due to endocrine causes. This is a consultant to consultant referral.

Features of hyperinsulinism that may require further endocrine investigations include: a GIR >10mg/kg/min, detectable insulin and high C-peptide during the hypoglycaemic episode and absence of ketonuria.

Medications which may be considered by the Endocrine team include: Diazoxide: 5-20mg/kg/day 8hrly PO, Chlorthiazide: 7-10mg/kg/day 12 hrly PO, Glucagon: bolus of 200microgram/kg followed by 1-18mcg/kg/hr infusion, Octreotide: 5-20mcg/kg/day infusion.

**References:**