HYPOGLYCAEMIA IN A NEONATE – MONITORING AND MANAGEMENT OF AT RISK NEONATES

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

This LOP has been developed in partnership with obstetric physician, and Endocrine and Metabolic Teams Sydney Children’s Hospital

1. AIM
   • Early identification of at risk neonates, timely investigations and interventions for hypoglycaemia among neonates

2. PATIENT
   • Neonates

3. STAFF
   • Registered Midwives
   • Student Midwives
   • Registered Nurses
   • Medical Staff

4. EQUIPMENT
   • Glucometer
   • Blood gas and electrolyte analyser with incorporated electrochemical glucose biosensors

5. CLINICAL PRACTICE
   • Identify the at-risk neonates: Neonates of diabetic mothers, late preterm (34⁰-36⁶ weeks), small for gestational age (SGA- birth weight less than 10th percentile), large for gestational age (LGA – birth weight greater than 97th percentile – or 4500 g at term)
   • Determine if diabetes in mother is poorly controlled (as assessed by the obstetric team, physician/endocrinologist or by elevated fructosamine or HbA₁C ≥6.5%, or elevated maternal BGL>8mmol/L at delivery). Refer to maternal diabetes care plan
   • At delivery:
     • Commence skin-to-skin contact between the mother and her baby as soon as possible after birth
     • Commence breast feeding within half an hour of birth.
     • Check if the neonate fits the admission criteria to NICU: Poorly controlled diabetes in mother (as defined above) and/or symptomatic hypoglycaemia
     • Monitor the neonate for any clinical symptoms of hypoglycaemia (examples: jitteriness, lethargy, floppiness, central cyanosis, apnoea, poor feeding and seizures):
       • If no symptoms/signs, perform the first blood glucose level (BGL) (heel prick using the glucometer) around 2 hours of age and follow the clinical pathway (Appendix A)
       • If symptomatic, perform the first BGL (heel prick using the glucometer) immediately and if confirmed (BGL<2.6mmol/L), admit to Newborn care centre (NCC) and follow the clinical pathway (Appendix B)
HYPOGLYCAEMIA IN A NEONATE – MONITORING AND MANAGEMENT OF AT RISK NEONATES  cont’d

Ongoing monitoring:
• Monitor at-risk neonates for at least the first 24 hours of life as per clinical pathway (Appendix A)
• Continue monitoring until the neonate’s BGLs remain at safe levels (≥2.6mmol/L) for at least 24 hours after the last episode of hypoglycaemia, as per clinical pathway (Appendix A)
• Determine if the neonate has resistant, recurrent or unexplained hypoglycaemia:
  o Resistant Hypoglycaemia: hypoglycaemia requiring infusions of large amounts of glucose (>12 mg/kg/min) to maintain normal BGLs
  o Recurrent hypoglycaemia: recurrent hypoglycaemia (if persisting beyond the first few days of life)
  o Unexplained hypoglycaemia: hypoglycaemia without recognised predisposing factors such as neonates of diabetic mothers, small or large for gestational age
• Consult endocrine team at Sydney Children’s Hospital urgently and consider the clinical pathway (Appendix C) for the management. However, remember that clinical pathway (Appendix C) is only a suggested pathway and may vary based on the underlying aetiology and the response of the neonate
• Refer to Appendices D and E for a quick guide on the glucose infusion rates and the list of investigations and relevant sampling for resistant or persistent hypoglycaemia

6. DOCUMENTATION
• Integrated Clinical Notes
• Neonatal Medication chart
• Standard Neonatal Observation Chart.
• Maternal Diabetes Care Plan

7. EDUCATIONAL NOTES
• Blood glucose concentrations reach a nadir in healthy neonates around 1 to 2 hours after birth; and stabilise by 3 to 4 hours. Healthy neonates compensate for “physiologic” hypoglycaemia by producing and using alternative fuels including ketone bodies, lactate and free fatty acids
• Preterm and small for gestation neonates have limited metabolic capacity for production of these alternative fuels
• Neonates of diabetic mothers (IDM) are hyperinsulinaemic which prevents production of alternative fuels
• A widely used cut-off for neonatal hypoglycaemia is <2.6mmol/L
• Abnormal brain stem and somato-sensory evoked potentials, and abnormalities in MRI and brain ultrasounds may be demonstrated in some neonates with BGLs below this level. Furthermore, preterm neonates with recurrent BGL readings less than this level were found to have adverse neurodevelopmental outcomes at 18 months of age. These differences in developmental outcomes were no longer discernible when the children were assessed at 8 years of age
• Portable glucometer test-strip results demonstrate a reasonable correlation with actual plasma glucose concentrations, but the variation from the actual level may be as much as 0.5 to 1.1mmol/L (or 15-20%). This variation is greatest at low glucose concentrations.
HYPOGLYCAEMIA IN A NEONATE – MONITORING AND MANAGEMENT OF AT RISK NEONATES  cont’d

8. RELATED POLICIES / PROCEDURES / CLINICAL PRACTICE LOP
   • Diabetes in pregnancy service LOP
   • Obesity in pregnancy, labour and postpartum guideline

9. REFERENCES
   **Current AAP neonatal hypoglycaemia management guideline
   **First population meta-analysis of low plasma glucose thresholds in full term normal newborn neonates.
   **This study indicates that most of neonates of diabetic mothers except pre-existing diabetes type 1 can largely be managed with breast and supplementary feeding.
   **First detailed account making pragmatic recommendations for operational threshold for treatment of hypoglycaemia in different subgroups of newborn neonates.
HYPOGLYCAEMIA IN A NEONATE – MONITORING AND MANAGEMENT OF AT RISK NEONATES  cont’d


**A cross sectional study was performed of 156 term neonates and 62 preterm neonates to establish the normal ranges and interrelationships of blood glucose and intermediary metabolites in the first postnatal week, and to compare these with those of 52 older children.


*Study assessing sensory evoked potentials in relation to glucose level to establish glucose level causing neural dysfunction.


*A study describing effect of glucose minibolus prior to continuous intravenous glucose infusion.


**First description defining a glucose level in relation to adverse neurodevelopmental outcome of moderate neonatal hypoglycaemia in newborn neonates.


**Comprehensive neonatal hypoglycaemia management protocol with available evidence.


**First prospective study attempting to establish normal blood sugar level in healthy full term newborn neonates.


REVISION & APPROVAL HISTORY

Endorsed Therapeutic & Drug Utilisation Committee 19/2/13 and Maternity Services LOPs Feb 2013
Replacing 'Postnatal Ward Management of Term Infants at risk of Hypoglycaemia'
Endorsed Neonatal Clinical Committee 8/2/05, Approved Quality Council 21/2/05

…../Appendix A - E
APPENDIX ‘A’

Asymptomatic neonates at risk of Hypoglycaemia
(Maternal diabetes, late preterm 34 – 36+6/40, Term SGA and LGA infants)

- Skin-to-skin contact
- Breastfeed within half an hour of birth

- **BGL < 2.6 mmol/L**
  - Notify Paed RMO. Perform formal BGL. Administer 40% Dextrose*, Refeed with breast or EBM or formula (10-20 ml) and recheck glucometer BGL in 30 – 60 minutes

- **BGL 2.6 mmol/L or more**
  - **BGL less than 1.5**
    - Admin to NCC
    - Formal BGL check
    - 10% Dextrose IV bolus 2 ml/kg and infusion at 60 – 80 ml/kg/day. If IV access is delayed, give tube feeds (60 ml/kg/ 3 hourly quota) and consider IM Glucagon 200 mcg/kg, maximum dose 1 mg. Recheck BGL after 30 minutes
  - **BGL 1.5 – 2.5 mmol/L**
    - 40% Dextrose* Refeed with either breast or EBM or formula
    - Recheck BGL in 30 – 60 min
  - **BGL 2.6 mmol/L or more**
    - Continue 3 hourly feeds
    - Pre feed BGL up to 24 Hrs of age. Anytime, BGL readings are <2.6mmol/L, follow the respective pathway

- **BGL ≥2.6 mmol/L**
  - Continue IV fluids (IVF)
  - Continue 3 hourly BF
  - Continue 3 hourly pre-feed BGLs
  - If BGL remains ≥2.6 mmol/L (preferably 3.3 mmol/L) x 3, consider weaning IVF

- **BGL < 2.6 mmol/L**
  - Increase Total fluid requirement to 100 ml/kg/day#
  - Check BGL in 30 minutes

- **BGL ≥2.6 mmol/L**
  - Change to 12% dextrose
  - Repeat BGL in 30 mins. If BGL <2.6mmol/L, increase fluid rate or glucose concentration and follow refractory hypoglycaemia pathway

**Notes:**
- Beware of contraindications for excess fluids
- * Orally 0.5 ml/kg 40% Dextrose

# Beware of contraindications for excess fluids
APPENDIX ‘B’

Symptomatic Hypoglycaemia*

* Symptomatic hypoglycaemia: Defined as symptoms including irritability, tremors, exaggerated Moro reflex, high-pitch cry, seizures, lethargy, floppiness cyanosis, apnea and poor feeding with a corresponding BGL of <2.6mmol/L

Urgently check formal BGL
Administer 40% dextrose if oral solution allowed
Insert cannula, give 10% Dextrose IV bolus at 2ml/kg and commence IV Dextrose infusion at age appropriate fluid rate
Repeat BGL after 30 minutes
**APPENDIX ‘C’**

Refractory Hypoglycaemia*

**Required glucose infusion >12mg/kg/min**
Consult endocrine team
Perform critical bloods and metabolic work-up

**Give glucagon bolus at 200 mcg/kg (Max 1mg) IV/IM/SC, followed by Glucagon infusion (5 mcg/kg/hr)**
Repeat BGL after 30 minutes
If BGL < 2.6MMOL increase glucagon in steps up to maximum of 20mcg/kg/hr
Repeat BGL after 30 minutes

**If BGL < 2.6mmol/L,**
Start Hydrocortisone at 1 – 2.5 mg/kg/dose 6 hourly IV/IM
Continue monitoring BGL

**Consider Diazoxide 15 mg/kg/day in 3 divided doses with Hydrochlorothiazide 1 – 2 mg/kg/dose bd if refractory hypoglycaemia is due to hyperinsulinism.**
Monitor for adverse effects
If required, other drugs to consider with expert advice are octreotide and nifedipine

**If BGL stable (preferable >3.3 mmol/L) for at least 24 hours, weaning can be commenced but always discuss with Neonatologist / endocrine team before weaning**

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* Refractory Hypoglycaemia is defined as Hypoglycaemia requiring infusions of a large amount of glucose (>12 mg/kg/min) to maintain normoglycaemia
APPENDIX ‘D’

Values of different dextrose concentrations and infusion rates for glucose infusion

Table 1: Preparation of higher dextrose concentration fluid for 100ml burette

<table>
<thead>
<tr>
<th>Desired Dextrose Conc.</th>
<th>Volume of 10% Dextrose</th>
<th>Volume of 50% Dextrose</th>
</tr>
</thead>
<tbody>
<tr>
<td>12%</td>
<td>95 ml</td>
<td>5 ml</td>
</tr>
<tr>
<td>14%</td>
<td>90 ml</td>
<td>10 ml</td>
</tr>
<tr>
<td>16%</td>
<td>85 ml</td>
<td>15 ml</td>
</tr>
<tr>
<td>18%</td>
<td>80 ml</td>
<td>20 ml</td>
</tr>
<tr>
<td>20%</td>
<td>75 ml</td>
<td>25 ml</td>
</tr>
</tbody>
</table>

ADD THE VOLUME OF 50% DEXTROSE TO THE VOLUME OF 10% DEXTROSE TO MAKE UP A TOTAL OF 100 ML

Table 2: Glucose infusion rate in mg/kg/min by dextrose infusion rate in ml/kg/day with different dextrose strengths

<table>
<thead>
<tr>
<th>Glucose Infusion</th>
<th>Dextrose Strength with Infusion Rate in ml/kg/day</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>10%</td>
</tr>
<tr>
<td>5</td>
<td>72</td>
</tr>
<tr>
<td>6</td>
<td>86</td>
</tr>
<tr>
<td>7</td>
<td>101</td>
</tr>
<tr>
<td>8</td>
<td>115</td>
</tr>
<tr>
<td>9</td>
<td>130</td>
</tr>
<tr>
<td>10</td>
<td>144</td>
</tr>
<tr>
<td>11</td>
<td>158</td>
</tr>
<tr>
<td>12</td>
<td>173</td>
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<td>230</td>
</tr>
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<td>17</td>
<td>245</td>
</tr>
<tr>
<td>18</td>
<td>259</td>
</tr>
<tr>
<td>19</td>
<td>274</td>
</tr>
<tr>
<td>20</td>
<td>292</td>
</tr>
</tbody>
</table>

Formula for calculating glucose infusion rate in mg/kg/min

Glucose infusion rate (mg/kg/min) = \[
\text{Dextrose concentration} \times \frac{\text{Vol. infused in ml/kg/day}}{144}
\]
APPENDIX ‘E’

List of investigations and relevant sampling for resistant or persistent hypoglycaemia

<table>
<thead>
<tr>
<th>No</th>
<th>Test</th>
<th>Amount</th>
<th>Container</th>
<th>Sample</th>
</tr>
</thead>
<tbody>
<tr>
<td>A.</td>
<td>INVESTIGATIONS THAT ARE MORE RELIABLE WHEN THE FORMAL BLOOD GLUCOSE &lt;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Insulin, Cortisol, and Growth Hormone</td>
<td>1300 uL</td>
<td>Gold</td>
<td>Serum</td>
</tr>
<tr>
<td>2</td>
<td>Plasma Ketones #</td>
<td>200 uL</td>
<td>Grey</td>
<td>Plasma</td>
</tr>
<tr>
<td>3</td>
<td>Blood Lactate #</td>
<td>300 uL</td>
<td>Grey</td>
<td>Plasma</td>
</tr>
<tr>
<td>4</td>
<td>Urine for a metabolic screen to include ketones, amino acids, organic acids and acylcarnitine</td>
<td>10 ml</td>
<td>Sterile Yellow</td>
<td>Urine</td>
</tr>
<tr>
<td>5</td>
<td>Urine Ketones</td>
<td></td>
<td>Clinistix</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Urine for reducing substances*</td>
<td>5 ml</td>
<td>Yellow Urine Jar</td>
<td>Urine</td>
</tr>
<tr>
<td>B.</td>
<td>CONSIDER FURTHER INVESTIGATIONS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Capillary gas</td>
<td></td>
<td>Capillary tube</td>
<td>Blood</td>
</tr>
<tr>
<td>2</td>
<td>Carnitine#</td>
<td>250 uL</td>
<td>Dark Green</td>
<td>Plasma</td>
</tr>
<tr>
<td>3</td>
<td>Aspirate aminotransferase (AST)</td>
<td>100 uL</td>
<td>Gold</td>
<td>Serum</td>
</tr>
<tr>
<td>4</td>
<td>Alanine aminotransferase (ALT)</td>
<td>100 uL</td>
<td>Gold</td>
<td>Serum</td>
</tr>
<tr>
<td>5</td>
<td>Uric acid</td>
<td>200 uL</td>
<td>Gold</td>
<td>Serum</td>
</tr>
<tr>
<td>6</td>
<td>Lactic acid#</td>
<td>300 uL</td>
<td>Grey</td>
<td>Plasma</td>
</tr>
<tr>
<td>7</td>
<td>Plasma amino acids #</td>
<td>250 uL</td>
<td>Dark Green</td>
<td>Plasma</td>
</tr>
<tr>
<td>8</td>
<td>Creatine kinase (CK)</td>
<td>100 uL</td>
<td>Gold</td>
<td>Serum</td>
</tr>
<tr>
<td>9</td>
<td>Ammonia#</td>
<td>500 uL</td>
<td>Purple</td>
<td>Plasma</td>
</tr>
<tr>
<td>10</td>
<td>Acylcarnitine profile#</td>
<td>250 uL</td>
<td>Dark Green</td>
<td>Blood</td>
</tr>
<tr>
<td>11</td>
<td>DNA for MCAD mutation</td>
<td>3 ml</td>
<td>Purple</td>
<td>Blood</td>
</tr>
</tbody>
</table>

The last two investigations can be done from the neonatal screening blood spots.

C. OTHERS

1. Ophthalmic examination
2. Cranial ultrasound scan and/or MRI (specifically requesting pituitary views)

# Specimens that need to go on ICE
* Specimen needs to send to laboratory within 30 minutes