HYPOGLYCAEMIA – MONITORING AND MANAGEMENT OF HIGH RISK NEONATES

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

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

2. PATIENT
   - Newborns

3. STAFF
   - Midwifery, nursing and medical staff

4. CLINICAL PRACTICE
   Identification of high risk neonates
   - Neonates of diabetic mothers; late preterm (34+0 to 36+6 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 blood glucose level (BGL) >8 mmol/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 breastfeeding within half an hour of birth.
   - Check if the neonate fits the admission criteria to NCC – Poorly controlled diabetes in mother (as defined above) and/or symptomatic hypoglycaemia.
   - Monitor the neonate for any clinical symptoms of hypoglycaemia (eg. jitteriness, lethargy, floppiness, central cyanosis, apnoea, poor feeding, seizures):
     o If no symptoms/signs, perform the first BGL (heel prick using the glucometer) around 2 hours of age and follow the clinical pathway in Appendix A
     o If symptomatic, perform the first BGL (heel prick using the glucometer) immediately and if confirmed (BGL<2.6mmol/L), admit to NCC and follow the clinical pathway in Appendix B

Ongoing Monitoring
   - Monitor high 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 in 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
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- In these cases, consult endocrine team at Sydney Children's Hospital urgently and consider the clinical pathway in Appendix C for management. NB. The clinical pathway in 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.

5. DOCUMENTATION
- eMR
- Medication chart
- Neonatal Observation Chart
- Maternal Diabetes Care Plan

6. 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 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.

7. RELATED POLICIES/PROCEDURES/CLINICAL PRACTICE LOP
- SESLHD Gestational Diabetes Mellitus Management (GDM) Policy (August 2018)
- RHW Obesity and Weight Gain in Pregnancy, Labour and Postpartum LOP (December 2014)

8. RISK RATING
- Medium

9. NATIONAL STANDARD
- Standard 1 Governance for Safety and quality in Health Service Organisation
- Standard 9 Recognising and Responding to Clinical Deterioration in Acute Health Care

10. ABBREVIATIONS AND DEFINITIONS OF TERMS

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
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<tbody>
<tr>
<td>NCC</td>
<td>Newborn Care Centre</td>
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<tr>
<td>SGA</td>
<td>Small for Gestational Age</td>
</tr>
<tr>
<td>LGA</td>
<td>Large for Gestational Age</td>
</tr>
<tr>
<td>BGL</td>
<td>Blood Glucose Level</td>
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</tbody>
</table>
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11. 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.
  *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.
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  *Study assessing sensory evoked potentials in relation to glucose level to establish glucose level causing neural dysfunction.
  *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.

12. AUTHORS

| Primary | Feb 2013 | P Patel (Fellow), S Bolisetty (Staff Specialist), Obstetric Physicians Royal Hospital for Women, Endocrinology Team Sydney Children’s Hospital, Metabolic Team Sydney Children’s Hospital |

REVISION & APPROVAL HISTORY

August 2018 reviewed and endorsed RHW NCC LOPs Committee
July 2013 Minor amendment
Endorsed Therapeutic & Drug Utilisation Committee 19/2/13 and Maternity Services LOPs February 2013 – replacing ‘Postnatal Wad Management of Term Infants at risk of Hypoglycaemia’
Approved Quality Council 21/2/05
Endorsed Neonatal Clinical Committee 8/2/05

FOR REVIEW: 2021
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

BGL ≥2.6 mmol/L or more

Notify Paed RMO
Perform formal BGL (Gas machine in the NICU)

BGL less than 1.5

Admit 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

Oral 40% Dextrose Gel* to be massaged into buccal mucosa
Refeed with either breast or EBM or formula (10-20 ml) and recheck BGL in 30 – 60

BGL <2.6 mmol/L

BGL ≥2.6 mmol/L or

Continue 3 hourly feeds
Pre feed BGL up to 24 hr of age
Anytime, BGL readings are <2.6mmol/L, follow the respective pathway

BGL <2.6 mmol/L

Increase Total fluid requirement to 100 ml/kg/day#
Check BL in 30 minutes

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

Change to 12% dextrose
Repeat BGL in 30 minutes
If BGL <2.6mmol/L increase fluid rate or glucose concentration and follow refractory hypoglycaemia pathway

BGL ≥2.6 mmol/L

# Beware of contraindications for excess fluids
* Orally 0.5 ml/kg 40% Dextrose (maximum 3 times)
NB. Oral glucose gel, on average, raises blood glucose by 0.4 mmol/L and should not be used for moderate to severe hypoglycaemia
Symptomatic Hypoglycaemia*

*Symptomatic hypoglycaemia: Defined as symptoms including irritability, tremors, exaggerated Moro reflex, high-pitch cry, seizures, lethargy, floppiness cyanosis, apnoea 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

* Refractory Hypoglycaemia is defined as Hypoglycaemia requiring infusions of a large amount of glucose (>12 mg/kg/min) to maintain normoglycaemia
### 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 Rate (mg/kg/min)</th>
<th>10%</th>
<th>12.5%</th>
<th>15%</th>
<th>20%</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>72</td>
<td>58</td>
<td>48</td>
<td>36</td>
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<tr>
<td>20</td>
<td>292</td>
<td>230</td>
<td>192</td>
<td>146</td>
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</table>

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

\[
\text{Glucose infusion rate (mg/kg/min)} = \frac{\text{Dextrose concentration} \times \text{Vol. infused in ml/kg/day}}{144}
\]
**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><strong>INVESTIGATIONS THAT ARE MORE RELIABLE WHEN THE FORMAL BLOOD GLUCOSE &lt;</strong></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>
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<tr>
<td>4</td>
<td>Urine for a metabolic screen to include ketones, amino acids, organic acids and</td>
<td>10 ml</td>
<td>Sterile Yellow Urine Jar</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>
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<tr>
<td>B.</td>
<td><strong>CONSIDER FURTHER INVESTIGATIONS</strong></td>
<td></td>
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</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