Guideline

Women and Babies: Neonatal Hypoglycaemia - Prevention and Management

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Functional Sub-Group: Clinical Governance
Corporate Governance
Summary: Describes the prevention and management of hypoglycaemia in newborn infants
National Standard: Standard 1: Governance for Safety and Quality in Health Service Organisations
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Neonatal Hypoglycaemia- Prevention and Management

1. INTRODUCTION

The risks addressed by this guideline:

Risk of neonatal hypoglycaemia

The aims / expected outcome of this guideline:

Detection and prevention of neonatal hypoglycaemia

2. STATEMENT

This guideline outlines the indications for screening for neonatal hypoglycaemia with a view to prevention and the management of babies with diagnosed hypoglycaemia.

3. GUIDELINES

BACKGROUND:

Glucose is an essential nutrient for the brain. Abnormally low levels can cause an encephalopathy and have the potential to produce long term neurological injury.\textsuperscript{1,2} Definitions of hypoglycaemia were originally set by the studies of Cornblath et al\textsuperscript{3} as <1.1mmol/l in growth restricted and preterm babies and <1.7mmol/l in term babies.

Term Babies: There is still considerable uncertainty as to the level of blood glucose (BGL) below which there is a risk of brain injury in a term baby.\textsuperscript{4} The situation is confused by the normal postnatal fall in BGL in healthy term infants – the lower range of the 95% confidence intervals of this nadir at 1-2 hours was a BGL 1.4 mmol, a level that could be defined as pathological. By 24 hours, the lower 95% CI were 2.4mmol/L.\textsuperscript{5} The controversy was fuelled by the study of Koh et al\textsuperscript{6} who showed reversible disturbance in evoked potentials at glucose levels below 2.6mmol/l in a small cohort of asymptomatic term babies. It was suggested that this finding indicated need to keep BGLs above this level however this neurophysiological outcome does not equate to permanent neurological injury.

In newborn animal models, hypoglycaemia has to be both severe and prolonged to produce brain injury.\textsuperscript{7,8} Human data also points hypoglycaemic brain injury in term babies usually being the result of prolonged very low BGLs. In the retrospective series of Montassir et al,\textsuperscript{9} many of the babies had recorded BGL below 0.9 mmol/l and in that of Burns et al,\textsuperscript{10} 86% had
levels below 1.5 mmol/l. In the series of Montassir et al, babies with brain injury were exposed to low blood glucose for significantly longer than those without, 14 hrs vs 1.7 hrs. However none of the proposed pathological levels are clear cut and there is probably considerable inter-individual variation in vulnerability to low blood glucose and absolute blood glucose level is only one of the factors which defines that vulnerability, other factors will include duration of exposure and perinatal risk factors such as intra-partum hypoxia, prematurity and symptoms. Any baby with blood glucose ≤ 2.5 mmol/l who has symptoms that might be due to hypoglycaemia should be considered vulnerable.

Preterm babies. Preterm babies have an impaired ability to produce ketones (an alternative brain fuel) response to low glucose levels, so are more vulnerable. Lucas et al found glucose levels below 2.5mmol/l were associated with worse neurodevelopmental outcome. Duvanel et al reported that preterm growth restricted infants with recurrent moderate hypoglycaemia (5 episodes with plasma glucose levels >0.6 and <2.6 mmol/L) or 1 single severe hypoglycaemic episode (0 to 0.6 mmol/L) had lower psychomotor development scores at 3.5 and 5 years age.

Intervention threshold vs pathological threshold. Authorities in neonatal hypoglycaemia highlight the importance of differentiating between an interventional threshold and a pathological threshold. An interventional threshold indicates a range where low BGL would not usually be injurious but, because of the uncertainty, intervention is indicated to lift the BGL above this range. A pathological threshold reflects a level below which BGL is likely to be injurious if left untreated. These arbitrary thresholds for newborn blood glucose have been selected to strike a balance between the rare but serious risk of under-treatment (hypoglycaemic neurological injury) and the everyday risks of over-treatment e.g. separation of mother and baby, interruption of establishing breast feeding etc.

Notwithstanding the uncertainty as to safe blood glucose levels, the therapeutic goal should be to not tolerate BGLs between intervention and pathological thresholds for longer than the effect of one feed, and to increase BGLs below pathological levels as a matter of urgency with intravenous glucose.

Intervention Threshold.

- During the first 24 hours in well babies born after 34 weeks: ≤ 2.0 mmol/l.
- After 24 hrs in well babies born after 34 weeks: ≤ 2.5 mmol/l.
- At any time in any unwell baby, term or preterm,: ≤ 2.5 mmol/l.
**Pathological Threshold:** Blood glucose should be considered to require urgent intervention in any baby with a **BGL ≤ 1.5 mmol/l** or any baby with a **BGL ≤ 2.5 mmol/l** with symptoms that might be due to hypoglycaemia…see below.

**Incidence of Neonatal Hypoglycaemia:**

The true incidence will vary depending on the definition applied by an individual unit. In general terms, the higher the interventional threshold and the earlier after birth the screening starts, the higher will be the incidence of hypoglycaemia. The study of Harris et al described prospective screening BGL (SBGL) measures from early after birth in 514 ‘at risk’ babies. Fifty per cent of these babies had an SBGL <2.6 mmol and 20% had a measure less than 2.0 mmol/l. Fifty per cent of these low measures occurred in the first 6 hours when there is a natural nadir in blood glucose levels. None of the babies were reported as symptomatic and the authors emphasise that the significance of asymptomatic hypoglycaemia in terms of long term outcomes remains unclear.

**Symptoms of Neonatal Hypoglycaemia:**

Most infants with low blood glucose levels will be asymptomatic. But an SBGL should always be measured in any baby with possible symptoms of hypoglycaemia. If that SBGL is ≤ 2.5 mmol/l, it should be considered that those symptoms may be due to hypoglycaemia.

Symptoms of hypoglycaemia may include:

- **Poor feeding** – This is often the first, albeit non-specific, symptom of neonatal hypoglycaemia. Infants who do not demand feed or who fail to have a nutritive feed may have hypoglycaemia or develop hypoglycemia. This may be a sleepy baby not demanding or an unsettled baby who doesn’t feed when put to the breast. Infants should normally have at least one code 5 or 6 feed (nutritive feed) within the first 6 hours and two code 5 or 6 feeds within the first 12 hours. A screening blood glucose should be performed:
  - At 6 hours, if a baby has not had at least one code 5 or 6 breast feed including the initial skin to skin feed.
  - At 12 hours, if a baby has not had at least two code 5 or 6 breast feeds including the initial skin to skin feed.

These babies should have an SBGL to ensure the poor feeding is not secondary to hypoglycaemia. If the SBGL is within normal range, these infants should be referred to the lactation team and / or senior midwife to evaluate feeding.

- **Jitteriness and irritability.**
- **Apnoea and cyanosis.**
- **Hypotonia and lethargy.**
• Seizures.

Blood Glucose Measurement:

Screening BGL (SBGL): Screening for hypoglycaemia is performed with a blood reagent strip. Currently available blood glucose screening meters were shown to estimate laboratory BGL +/- 0.95 mmol/L. Laboratory BGL averaged 0.17 to 0.56 mmol/L below the screening BGL. The difference may be due to glycolysis despite the use of NaFK2-oxalate tubes, making laboratory formal BGL an unreliable measure without additional efforts to prevent glycolysis (eg ice or immediate analysis).\textsuperscript{17} However, it is important that before treatment is commenced a formal blood glucose level (FBGL) is performed to validate low SBGL.\textsuperscript{18,19}

Formal BGL: performed for confirmation of hypoglycaemia \textit{though do not delay treatment} waiting for this result if SBGL ≤1.5 mmol/l.

1. On postnatal wards: place blood sample in a lithium heparin tube and transport immediately to biochemistry. Phone the laboratory (58279 / 58442) to ensure immediate spinning down of sample and analysis. Undue delay will result in falsely low BGL and inappropriate management.

2. In RPA Newborn Care: Use the i-Stat glucose cartridge located in NICU or the ABL 90 Flex blood gas analyser.

Prevention of Neonatal Hypoglycaemia

Prevention of hypoglycaemia must be the primary goal. When babies are admitted to the NICU for other reasons such as prematurity, the routine is glucose screening and there should be a low threshold for instituting IV therapy. It is the babies who would not otherwise be admitted to NICU who present the challenge in terms of prevention.

Any baby at risk of hypoglycaemia needs attention paid to early establishment of breast feeding and screening blood glucose level (SBGL) with a cot side screening device such as the Optium-Xceed currently in use at RPA.

Classification of risk: Babies are classified into two groups:

1) High risk babies and 2) Increased risk babies, depending on their likelihood of neonatal hypoglycaemia. These groups are summarised in appendix 1. In addition to the criteria below for defining control of maternal diabetes, consider reading the recent diabetes clinic notes, click on 'diabetes progress notes' in the diagnostic results section in Powerchart.

High risk babies: Infants at high risk are to be admitted to Newborn Care and have a SBGL by 1 hour of age or before the procedure, if umbilical catheters are to be inserted.

High risk babies include:
1. **Babies of any diabetic mother** with evidence of poor recent control:
   - Most recent HbA1c >6g% and/or recent daily BGL mainly more than 8 mmol/L
   - **Or** birth weight above the 95th centile (see Appendix 2 for 95th centiles)
   - **Or** SBGL after first feed on Delivery Suite/Recovery is ≤ 2.0 mmol/L

2. **Preterm babies** born before 35 weeks

3. **Very low birth weight babies** less than 2200g as per admission policy.

4. **Macrosomic baby**: i.e. physical appearance of an infant of a diabetic mother in the absence of a history of maternal diabetes. These babies are large, have increased subcutaneous fat, increased muscle mass and are plethoric. Their head circumference will plot on a lower centile than their weight (see photograph). If unsure, these babies need an early neonatal medical review and an SBGL within 2 hours of birth.

5. **High risk babies with symptoms** which may be due to hypoglycaemia: If the SBGL is low (≤ 2.5mmol/L) in a symptomatic baby then urgent intravenous glucose is indicated. Confirm BGL with a formal blood glucose (FBGL) when inserting the IV line. Subsequent SBGL are not indicated in "jittery" babies who have a SBGL ≥ 2.5mmol/L and are feeding well.

**Increased risk babies:**

These infants may be transferred to the postnatal wards if otherwise well and undergo monitoring as per the ‘increased risk’ management and flow chart below. Infants of diabetic mothers with good recent control should have an additional SBGL performed after the first ‘skin to skin’ breast feed in the delivery/recovery suite.

1. **Babies of any diabetic mother** with evidence of good recent control:
   - HbA1c ≤6g% and/or the large majority of recent BGL measures are less than 8
mmol/L.

- And birth weight less than 95th centile. (see Appendix 2 for 95th centiles)
- And SBGL after first feed on Delivery Suite/Recovery is more than 2.0 mmol/l

2. **Preterm babies** born at 35 and 36 weeks as per admission policy.

3. **Low measured percentage body fat:** Percentage body fat as measured by the PeaPod of <5.8% in girls and <4.2% in boys.

4. **Wasted babies:** Most 'wasted' babies will have low % body fat measurements but it still needs to be considered clinically if % body fat measurement is not available or even if it is normal and the baby has a wasted appearance (see redundant skin on thighs in photos below). Contact neonatal RMO/NNP if unsure of assessment of wasting.

5. **Small for gestational age or low birth weight babies:** The weight percentile, which confers increased risk of hypoglycaemia increases, is unknown. Within this guideline, weight based increased risk will be defined by birth weight less than 5th percentile or less than 2500g. This can be referenced by entering the birth weight into the computer in the NEAP room but the table in Appendix 2 is provided for quick written reference.

6. **Babies born with low cord arterial pH (<7.1)**

7. **Babies who weigh more than 4.5 Kg even if not obviously macrosomic.**

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**Management of high risk babies admitted to Newborn Care**
See flow diagram in Appendix 3

**General Principles**
- In high risk babies born after 34 weeks including otherwise well infants of **poorly controlled diabetic mothers** Blood glucose levels should be maintained above 2 mmol/L in 1st 24 hours and above >2.5 mmol/L after 24 hours.
• In preterm babies born before 35 weeks OR sick term babies, blood glucose levels should be maintained above 2.5 mmol/l.

Feeding management.

• In high risk babies including otherwise well infants of poorly controlled diabetic mothers – Breast feed where possible. If the mother is unable to attend the nursery or there is concern about sucking intake, feed to 60mls/kg/day using expressed breast milk or semi-hydrolysed formula for the first 24 hours provided the blood glucose level remains above 2.0mmol/L. Supplementation with volumes less than 60mls/kg/day can be considered with Senior Medical approval. If the blood glucose level falls below 2mmol/L, follow the Newborn Care Management Flow Chart.

• In preterm babies born before 35 weeks OR sick term babies – see enteral feeding protocol. Blood sugar levels must be maintained >2.5mmol.

When to perform glucose screening

• All high risk babies admitted to the nursery should have a SBGL by 1 hour of age or pre-procedure if umbilical catheter insertion is planned.

• Thereafter, SBGL should be performed 30 minutes after each feed.

How long to perform blood glucose screening

• Babies admitted only for SBGL monitoring can be transferred to the postnatal ward if SBGLs are above 2.0mmol/l for the first 12 hours. SBGL monitoring after each feed should continue for a further 24 hours on the postnatal wards.

Management of Increased risk babies on the postnatal ward
See flow diagram in Appendix 4:

General Principles

• Blood glucose levels 2 to 2.5 mmol/L on day 1 should be managed with frequent feeds and continued SBGL monitoring. Medical review should be requested if feeding poorly or SBGL is persistently <2.5 mmol/l after 24 hours.

• Blood glucose levels between 1.5 and 2mmol/l – give a feed and recheck SBGL 30 minutes after completion of the feed or, if feed is prolonged, one hour after the commencement of the feed. If SBGL persists below 2mmol/l, admit to Newborn Care as per protocol for further management.
• Blood glucose levels below 1.5 mmol/l should be admitted to Newborn Care, have immediate IV treatment. Administer an intragastric tube feed if there is a delay in IV treatment. Send a laboratory BGL (for confirmation), insulin, cortisol, growth hormone before commencing glucose infusion.

Feeding management:

• It is essential that all ‘increased risk’ babies have their first feed in delivery suite or the Birth Centre or recovery as soon as possible after birth and same documented on the Newborn Care Plan (MR504). The second feed should occur within 6 hours of birth and then regularly thereafter, aiming for a minimum of five feeds within the first 24 hours.

When to perform blood glucose screening:

• Document BGLs on the Standard Newborn Observation Chart or SNOC (SMR110.014) and escalate any concerns via the Neonatal CERS.

• Infants of diabetic mothers with good recent control and < 95\(^{th}\) centile for birth weight should have their first SBGL after the first ‘skin to skin’ breast feed or no later than two hours of age.

• In other increased risk babies, the first blood glucose screening should occur no later than 6 hours and should preferably be performed after the baby is given their second feed. The timing is more important than the relationship to feed. So if the baby is late taking his/her second feed or that feed is prolonged, this SBGL should still occur no later than 6 hours.

• Thereafter, blood glucose screening should occur 30 minutes after each feed ensuring the baby receives regular good feeds during the first 24 hours.

How long to perform blood glucose screening?

• Cease SBGL, if subsequent readings are >2.5 mmol/L for 3 consecutive measurements and the baby appears well and is feeding well,

• If the second SBGL is 2 - 2.5 mmol/L, continue SBGL monitoring for additional 24 hours (see below for persistent SBGL ≤ 2.5mmol/L).

• After 24 hours age: Normal SBGL should be more than 2.5 mmol/L for well term babies and well preterm babies born after 34 weeks. If SBGL is persistently below 2.5 mmol/L beyond 24 hours the infant should be reviewed by a senior Neonatal doctor (either consultant or fellow).
4. PERFORMANCE MEASURES

Incidence of symptomatic neonatal hypoglycaemia,

5. DEFINITIONS

BGL = Blood glucose level
SBGL = Screening blood glucose level.

6. REFERENCES AND LINKS


Revised: Nick Evans May 2016
## Appendix 1: Summary Table of High Risk and Increased Risk Babies:

<table>
<thead>
<tr>
<th>High Risk Babies</th>
<th>Increased Risk Babies</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Infant of any diabetic mother with poor recent control</strong></td>
<td><strong>Infant of any diabetic mother with good recent control.</strong></td>
</tr>
<tr>
<td>• Maternal HbA1C &gt;6% and/or BGLs &gt;8mmol/l or</td>
<td>• Maternal HbA1C &lt;6% and/or BGLs &lt;8mmol/l and</td>
</tr>
<tr>
<td>• Infant SBGL ≤ 2.0 mmol/l after first feed or</td>
<td>• Infant SBGL &gt; 2mmol/l after first feed and</td>
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<tr>
<td>• Birth weight &gt;95th centile (see appendix 2)</td>
<td>• Birth weight &lt;95th centile (see appendix 2)</td>
</tr>
<tr>
<td><strong>Preterm babies born before 35 weeks.</strong></td>
<td><strong>Preterm babies born at 35 or 36 weeks.</strong></td>
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<tr>
<td><strong>Any baby with birth weight less than 2200g.</strong></td>
<td><strong>Babies with low percent body fat (PeaPod).</strong></td>
</tr>
<tr>
<td><strong>Baby with macrosomic appearance.</strong></td>
<td><strong>Baby with wasted appearance in spite of normal percent body fat measurement.</strong></td>
</tr>
<tr>
<td><strong>Baby with possible hypoglycaemic symptoms and SBGL ≤ 2.5 mmol/l.</strong></td>
<td><strong>IUGR babies with birth weight &lt; 5th centile (see appendix 2) or &lt; 2500g.</strong></td>
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<td></td>
<td><strong>Babies with cord pH &lt;7.0.</strong></td>
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<td></td>
<td><strong>Babies with birth weight &gt;4500g and not macrosomic.</strong></td>
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</tbody>
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Appendix 2: Quick reference tables for 5th and 95th centiles

<table>
<thead>
<tr>
<th>5th centiles</th>
<th>&lt;5&lt;sup&gt;th&lt;/sup&gt; Centile Boys</th>
<th>&lt;5&lt;sup&gt;th&lt;/sup&gt; Centile Girls</th>
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<td>&lt;2960g</td>
<td>&lt;2840g</td>
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<tr>
<th>95th centiles</th>
<th>&gt;95&lt;sup&gt;th&lt;/sup&gt; Centile Boys</th>
<th>&gt;95&lt;sup&gt;th&lt;/sup&gt; Centile Girls</th>
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<td>41 weeks</td>
<td>&gt;4450g</td>
<td>&gt;4250g</td>
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Appendix 3: Procedure for high risk babies flow chart

Infants at high risk are to be admitted to the nursery and have a SBGL by 1 hour of age or pre-procedure if umbilical catheterisation is planned.

- **First SBGL above 2.0 mmol/L**
  - Check SBGL 30 mins after feeds for 12 hours.
  - Continue to establish early regular breast feeding.
  - At least 5 feeds in 1st 24 hours

- **If SBGL above 2.0 mmol/L & feeding well, after 12 hours in SCN**
  - Transfer to Postnatal ward
  - Continue to do SBGL after feeds for another 24 hours
  - If SBGL above 2.5 mmol/L & feeding well, cease SBGL after 36 hours

- **Any SBGL 1.5-2.0 mmol/L**
  - Complimentary feed (4 mls/kg) urgently
  - SBGL 30 min after feed

- **Contact neonatal RMO/NNP urgently if SBGL ≤ 2.0mmol/l**

- **Any SBGL < 1.5 mmol/L or SBGL <2.5mmol/l with possible symptoms.**
  - Contact neonatal RMO/NNP.
  - Tube feed if there is a delay in IV treatment.
  - Immediate IV treatment.
  - With IV insertion, send FBGL, insulin, cortisol, growth hormone before commencing glucose infusion.

Rapid stepwise approach to low BGL:

**Formal or Screening BGL 1.5 – 2.0 mmol/L**

- Continue breast feeding
- EBM or formula complimentary feed (bottle or tube feeds) to 60mls/kg/day or appropriate volume to day of life.
- Commence IV 10% dextrose at 60 - 90 ml/kg/day, if SBGL not increased or maintained above 2.0 mmol/L
- With IV insertion, send FBGL, insulin, cortisol, growth hormone before commencing glucose infusion.

**Formal or Screening below 1.5 mmol/L**

- IV bolus of 10% dextrose at 2.5 ml/kg. Consider 5.0mls/kg if BGL less than 1.0 mmol/l.
- Ensure within 15 minutes of the bolus that BGL has increased to more than 2.0mmol/l
- Monitor BGL closely and continue IV 10% dextrose at 60 to 90 ml/kg/day to maintain normal blood glucose.
- If SBGL not maintained, increase dextrose concentration to 12.5% or 15%.
- If SBGL not maintained, consider glucagon infusion starting at 5μg/kg/hr titrating up according to SBGL.
Appendix 4: Procedure for increased risk babies flow chart

Infants of all diabetic mothers with good recent control and <95th centile birth weight, in delivery suite / recovery:
- Check SBGL 30 minutes after first skin to skin feed or no later than 2 hours of age

If ≤ 2.0 mmol/L, treat as ‘high risk’ in Newborn Care on Flow Chart 2.

First SBGL >2.0mmol/L (Normal)
- Check SBGL 30 mins after feeds for 12 hrs.
- Aim for a minimum 5 feeds in 1st 24 hrs.
- Cease BGL monitoring if SBGLs are above 2.5 mmol/L for 3 consecutive readings & baby is feeding well.

If >2.0 mmol, treat as ‘increased risk’ on PNW.

All other ‘increased risk’ babies, on postnatal ward:
- The first blood glucose screening no later than 6 hrs.
- Preferably after the baby is given his/her 2nd feed but timing no later than 6 hours more important than relationship to feed.

Any SBGL 1.5-2.0 mmol/L
- Complimentary feed (4mls/kg) ASAP & repeat SBGL 30 min after feed
- If SBGL is still 1.5 to 2mmol/L
- Contact neonatal RMO/NNP

Any SBGL <1.5mmol/L
- Contact neonatal RMO/NNP urgently

• Admit Newborn Care
• See high risk flow chart

If first or subsequent SBGL between 2.0 and 2.5 mmol/L continue SBGLs for another 24 hours.
- Beyond 24 hours senior paediatric review needed if SBGLs remain < 2.5mmol/l

First SBGL >2.0 mmol/L
- (Normal)

If ≤ 2.0 mmol/L, treat as ‘high risk’ in Newborn Care on Flow Chart 2.

Check SBGL 30 mins after feeds for 12 hrs.
- Aim for a minimum 5 feeds in 1st 24 hrs.
- Cease BGL monitoring if SBGLs are above 2.5 mmol/L for 3 consecutive readings & baby is feeding well.

Any SBGL 1.5-2.0 mmol/L
- Complimentary feed (4mls/kg) ASAP & repeat SBGL 30 min after feed
- If SBGL is still 1.5 to 2mmol/L
- Contact neonatal RMO/NNP

Any SBGL <1.5mmol/L
- Contact neonatal RMO/NNP urgently

• Admit Newborn Care
• See high risk flow chart

If first or subsequent SBGL between 2.0 and 2.5 mmol/L continue SBGLs for another 24 hours.
- Beyond 24 hours senior paediatric review needed if SBGLs remain < 2.5mmol/l