Kidz Medical Services
Glucose Homeostasis in Late-Preterm and Term Infant

Purpose:
To provide the clinicians of Kidz Medical Services with guidelines for the screening and the subsequent management of neonatal hypoglycemia in the late-preterm and term infants in the newborn nursery or mother baby unit.

Guideline:

I. Definition of Neonatal Hypoglycemia (NH):
   A. 2008 National Institutes of Health expert panel concluded:
      1. No substantial evidence-based progress has been made in defining NH.
      2. What constitutes clinically important NH, particularly regarding relation to brain injury, and that monitoring for, preventing, and treating NH remains largely empirical.
      3. In addition, simultaneous medical conditions that are associated with brain injury, such as HIE or infection, could alone, or in concert with NH, adversely affect the brain.
      4. For these reasons, the NIH report did not identify any specific value or range of plasma glucose concentrations that potentially could result in brain injury.
   B. Pathophysiology:
      1. Blood glucose concentrations as low as 30 mg/dL are common in healthy neonates by 1 to 2 hours after birth; these low concentrations, usually are transient, asymptomatic, and considered part of normal adaptation to postnatal life.
      2. Most neonates compensate for “physiologic” hypoglycemia by producing alternative fuels including ketone bodies, which are released from fat.
      3. Clinically significant NH reflects an imbalance between supply and use of glucose and alternative fuels and may result from a multitude of disturbed regulatory mechanisms.
      4. A rational definition of NH must account for the fact that acute symptoms and long-term neurologic sequelae occur within a continuum of low plasma glucose values of varied duration and severity.

II. Infants at risk:
   A. Because plasma glucose homeostasis requires glucogenesis and ketogenesis to maintain normal rates of fuel use, NH most commonly occurs in infants with impaired glucogenesis and/or ketogenesis, which may occur with excessive insulin production, altered counter regulatory hormone production, an inadequate substrate supply, or a disorder of fatty acid oxidation.
   B. NH occurs most commonly in infants who are small for gestational age, infants born to mothers who have diabetes, and late-preterm infants.
   C. It remains controversial whether otherwise normal infants who are large for gestational age are at risk of NH, largely because it is difficult to exclude maternal diabetes or maternal hyperglycemia (prediabetes) with standard glucose-tolerance tests.
D. A large number of additional maternal and fetal conditions also place infant at risk of NH.

<table>
<thead>
<tr>
<th>Maternal factors</th>
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<tbody>
<tr>
<td>Drugs: terbutaline, ritodrine, Chlorothiazide, labetalol, propranolol,</td>
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<td>Gestational or insulin-dependent Diabetes</td>
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<th>Perinatal Factors</th>
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<tr>
<td>Perinatal stress: NRFHR, birth trauma</td>
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<td>Post resuscitation</td>
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<th>Infant factors</th>
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<td>LGA</td>
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<td>IDM</td>
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<td>LPI – Late preterm infants 36 6/7 weeks and less</td>
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<td>SGA or IUGR</td>
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<td>Respiratory Distress</td>
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<td>Sepsis</td>
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<td>Hypothermia</td>
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<td>HIE</td>
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<td>Polycythemia</td>
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<td>Hormone disorders: Beckwith-Wiedemann, Glucagon deficiencies, thyroid disorders</td>
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<td>Hereditary defects: Galactosemia, G6PD, glycogen storage diseases</td>
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III. Infants to be screened for hypoglycemia:
A. Large for gestational age (LGA) or small for gestational age (SGA) infants to be screened.
   1. Infants who are LGA or SGA may develop low plasma glucose concentrations at as early as 3 hours of age, and these infants may be at risk of NH for up to 10 days after birth.
B. Use the WHO growth chart values to determine if full term babies are AGA, LGA or SGA
   1. Full term boys under 2.76 kg are under 10% therefore are SGA
   2. Full term boys over 4.0 kg are over 90% therefore are LGA
   3. Full term girls under 2.67 kg are under 10% therefore are SGA
   4. Full term girls over 3.85 kg are over 90% therefore are LGA
C. Late preterm infants (LPI) should all be on the glucose monitoring protocol regardless of size but should be plotted on the Fenton 2013 curve to determine if AGA, LGA or SGA by the AHP or MD.
D. IDM should all be screened.
   1. Infants born to mothers with diabetes may develop asymptomatic NH as early as 1 hour after birth and usually by 12 hours of age.
E. LGA, SGA, LPI and IDM all to be screened.
F. Routine screening and monitoring of blood glucose concentration is not needed in healthy term newborn infants after an entirely normal pregnancy and delivery.
   1. Screening should only be measured in term infants who have clinical manifestations or who are known to be at risk.
IV. Laboratory Data:
   A. When NH is suspected, the plasma or blood glucose concentration must be determined immediately by using one of the laboratory enzymatic methods.
   B. Although a laboratory determination is the most accurate method of measuring the glucose concentration, the results may not be available quickly enough for rapid diagnosis of NH, which thereby delays the initiation of treatment.
   C. Point-of-care (POC) test-strip results demonstrate a reasonable correlation with actual plasma glucose concentrations, but the variation from the actual level may be as much as 10 to 20 mg/dL.
   D. Unfortunately, this variation is greatest at low glucose concentrations. There is no point-of-care method that is sufficiently reliable and accurate in the low range of blood glucose to allow it to be used as the sole method for screening for NH.
   E. Because of limitations with “rapid” bedside methods, the blood or plasma glucose concentration must be confirmed by laboratory testing ordered stat. A long delay in processing the specimen can result in a falsely low concentration as erythrocytes in the sample metabolize the glucose in the plasma. This problem can be avoided by transporting the blood in tubes that contain a glycolytic inhibitor such as fluoride.

V. Clinical Signs:
   A. Clinical Signs of NH: Irritability, tremors, jitteriness, exaggerated moro reflex, high pitched cry, seizures, lethargy, floppiness, cyanosis, apnea, tachypnea, poor feeding
      1. Such signs usually subside quickly with normalization of glucose supply and plasma concentration
   B. The more serious signs (eg, coma and seizure activity) usually occur late in severe and protracted cases of hypoglycemia
      1. Severe signs are not easily or rapidly reversed with glucose replacement and normalization of plasma glucose concentrations
   C. Because avoidance and treatment of cerebral energy deficiency is the principal concern, greatest attention should be paid to neurologic signs. To attribute signs and symptoms to NH, Cornblath et al have suggested that the Whipple triad be fulfilled:
      1. A low blood glucose concentration
      2. Signs consistent with NH
      3. Resolution of signs and symptoms after restoring blood glucose concentrations to normal values

VI. Management:
   A. Plasma or blood glucose concentration should be measured as soon as possible (minutes, not hours) in any infant who manifests clinical signs.
   B. At-risk infants should be screened for NH with a frequency and duration related to risk factors specific to the individual infant.
   C. Any approach to management needs to account for the overall metabolic and physiologic status of the infant and should not unnecessarily disrupt the mother-infant relationship and breastfeeding.
   D. At-risk infants, LGA, IDM, SGA and LPI, should be fed within the first hour of life then the first screen ½ hour after feeding, then 2 hours after feeding then 3 hours (before next feeding) then before every feeding (every 2-3 hours).
   E. LGA and IDM screen for at least the first 12 hours of life.
F. LPI and SGA screen for at least the first 24 hours of life.
G. Screening before feedings should be continued if screens remain lower than 45 mg/dL.
H. A reasonable goal is to maintain plasma glucose concentrations in symptomatic infants between 40 and 50 mg/dL.
I. The target glucose concentration is greater than 45 mg/dL before each feeding.
J. If inadequate postnatal glucose homeostasis is documented, the clinician must be certain that the infant can maintain normal plasma glucose concentrations ≥ 45 on a routine diet through at least 3 feed-fast periods before discharge.
K. A reasonable cutoff for treating asymptomatic infants is 40 mg/dL.
L. It is recommended that the at-risk asymptomatic infant who has glucose concentrations of less than 40 mg/dL be refeed and that the glucose value be rechecked 1 hour after refeeding. Subsequent concentrations lower than 40 mg/dL, after attempts to refeed, necessitate treatment with intravenous glucose.
M. Persistent hypoglycemia can be treated with a minibolus (200 mg/kg [2 mL/kg] D10W) and/or intravenous infusion of D10W at 5 to 8 mg/kg per minute, 80 to 100 mL/kg per day; the goal is to achieve a plasma glucose concentration of 40 to 50 mg/dL (higher concentrations will only stimulate further insulin secretion).
N. Follow-up glucose concentrations and clinical evaluation must always be obtained to ensure that postnatal glucose homeostasis is achieved and maintained.

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<th>Major changes to Glucose Policy</th>
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<td>Feed at risk asymptomatic babies within 1 hour of life and check the first bedside glucose 30 minutes after feeding.</td>
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<td>If less than 40 mg/dL, send stat serum glucose, refeed and check bedside glucose 30 minutes after this feeding.</td>
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<td>After the two feedings if glucose less than 40 mg/dL, give IV D10W bolus.</td>
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<td>Feed at risk babies every 2-3 hours.</td>
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<td>Continue bedside glucose screening prior to every feeding for 12 hours for LGA/IDM and 24 hours for SGA/LPI.</td>
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<td>Must demonstrate adequate feedings with bedside glucose of ≥ 45 through 3 feed/fast periods to discontinue screening or discharge home.</td>
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References:


