Neonatal Hypoglycemia

MAJ Craig Barstow, MD

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MAJ Craig Barstow, MD

Director of Hospital Medicine, Womack Army Medical Center, Fort Bragg, North Carolina; Assistant Professor of Family Medicine at Uniformed Services University of Health Sciences, Bethesda, Maryland; Director of Ultrasound Education, Family Medicine Residency Program, Womack Army Medical Center; Physician, Scotland Memorial Hospital Emergency Department, Laurinburg, North Carolina

Dr. Barstow is a graduate of the Uniformed Services University of the Health Sciences – F. Edward Herbert School of Medicine in Bethesda, Maryland. He completed undergraduate studies at the U.S. Military Academy. Dr. Barstow joined the Womack Army Medical Center Family Medicine Residency Program in 2012, and created the fellowship program, accepting the first fellow in July 2015. He is the former program director of the hospitalist fellowship at Womack Army Medical Center. His areas of interest include inpatient family medicine, newborn care, and point-of-care ultrasound teaching.
Learning Objectives

1. Screen infants for neonatal hypoglycemia, in accordance to currently guidelines.

2. Assess the benefits and risks of bedside glucose analysis, versus laboratory enzymatic methods.

3. Taylor treatment to the specific clinical situation, while fostering optimal mother-infant contact and breastfeeding.

Audience Engagement System

Step 1

Step 2

Step 3
Neonatal Hypoglycemia

• Screening of Asymptomatic Newborns
• Symptomatic Newborns
• Prolonged hypoglycemia

Case 1

You are covering the newborn nursery over the weekend and the nurse calls you Friday night about a new delivery. The newborn is a term infant born to a G3, now P3 mother who is GBS negative and O+. The pregnancy was complicated by gestational diabetes treated with oral medication. The delivery was unremarkable. The nurse wants to know if you would like to screen the newborn for hypoglycemia.
Poll Question 1

Which asymptomatic infants are at risk for hypoglycemia?

A. Late term preterm newborns (34-36 6/7 weeks)
B. Large for Gestations Age (LGA) newborns
C. Small for Gestational Age (SGA) newborns
D. Infants born to diabetic mothers
E. All of the above

Newborns at Risk for Hypoglycemia

- Small for gestational age (SGA)
- Born to diabetic mother
- Late-term preterm (34-36 6/7)
- Large for gestational age (LGA)
When to screen?
Onset of hypoglycemia

Hypoglycemia manifests at 1-12 hours of life
• Born to diabetic mother
• Late-term preterm (34-36\textsuperscript{6/7})

Hypoglycemia manifests at 3 hours of life – 10 days
• Large for gestational age (LGA)
• Small for gestational age (SGA)

When to screen?

Initial feed within first hour of life and screen 30 minutes after 1\textsuperscript{st} feed
Feed every 2-3 hours after and screen before each feed

Screen 0-12 hours of life
• Born to diabetic mother
• Late-term preterm (34-36\textsuperscript{6/7})

Screen 0-24 hours of life
• Large for gestational age (LGA)
• Small for gestational age (SGA)

Committee on Fetus and Newborn. Postnatal glucose homeostasis in late-preterm and term infants. 
How to measure glucose?

- Centralized laboratory is the gold standard
- Plasma versus whole blood
- Plasma glucose concentrations are 10-15% higher than whole blood

- Point-of-care (POC) testing is readily available
  - Results are much quicker
  - May differ from plasma measurement by 10-20 mg/dL
  - Variation is greatest at low concentrations

How to Measure?

Use POC testing for immediate treatment decisions
Send confirmatory blood to centralized treatment prior to treatment
Do not wait for results before treating symptomatic hypoglycemia
Case 2

You make it through the night without any further calls. It is now Saturday morning and a nurse calls you again. A 2-hour old infant appears “jittery,” and the nurse would like to check the newborn’s glucose.

Poll Question 2

Which value is the lowest, normal glucose for a term newborn in the first hours of life?

A. 60 mg/dL
B. 47 mg/dL
C. 45 mg/dL
D. 35 mg/dL
E. 25 mg/dL
Neonatal Hypoglycemia

• Hypoglycemia occurs in 5-15% of neonates\(^1\)
• Prolonged hypoglycemia has been associated with permanent neurological injury
• Most infants with “low glucose” will be asymptomatic
• Historically, treatment has been recommended for glucose < 45-47 mg/dL


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Neonatal Hypoglycemia

• Early studies linked neonatal hypoglycemia with poor neurological outcomes
  • Transient and permanent structural brain abnormalities
  • Adverse developmental outcomes
  • Studies had significant design flaws
• Recent studies have failed to substantiate this finding
Infant Health and Development Program

• 745 preterm infant with birth weight < 2500g followed developmentally through age 18
• 20% lowest glucose < 35 mg/dL (37% glucose < 45)
• No difference in intellectual or academic achievement

Exact level and duration of hypoglycemia that causes neurological damage is unknown


Normal Glucose Homeostasis

• Fetal glucose is only slightly below maternal glucose
  • 9 mg/dL difference for normal maternal glucose
• Fetal insulin secreted in response to fetal glucose
• Fetal glucose is determined primarily by maternal glucose

Normal Glucose Homeostasis

- Glucose drops at birth and is 60-80% of maternal glucose
- Drops as low as 30 mg/dL in first 1-2 hours of life\(^1\)
  - Infants are asymptomatic
  - Probable normal physiological response
- Use alternative fuels
  - Ketone bodies
  - Lactate
- Rises above 45 mg/dL by 12 hours of life


Signs of Hypoglycemia

- Tremor
- Jitteriness
- Floppiness
- Sweating
- Lethargy
- Exaggerated Moro reflex
- High pitched cry
- Poor feeding
- Cyanosis
- Apnea
- Coma
- Seizures

Whipple’s Triad

1. Clinical signs of hypoglycemia
2. Symptoms occur during a documented period of hypoglycemia
3. Symptoms resolve with treatment of hypoglycemia


Differential Diagnosis

- Sepsis
- Inborn errors of metabolism
- Hyponatremia
- Neonatal encephalopathy due to perinatal asphyxia
Case 2 Continued

The initial heel stick glucose is 20 mg/dL. The nurse send a confirmatory plasma sample to the lab and feeds the newborn. An hour later, the recheck heel stick is 23 mg/dL. What would you like to do now?

Neonatal Hypoglycemia - Treatment

If symptomatic and glucose < 40 mg/dL → IV glucose

If asymptomatic

Birth to 4 hours of age
- If initial screen < 25 mg/dL
  - Feed and check in 1 hour

4 to 24 hours of age
- If initial screen < 35 mg/dL
  - Feed and check in 1 hour

If recheck < 25 mg/dL → IV glucose
If recheck 25-40 mg/dL -> refeed/IV glucose as needed
If recheck 35-45 mg/dL -> refeed/IV glucose as needed
If recheck > 45 mg/dL → IV glucose
Glucose dose 200mg/kg (dextrose 10% at 2 mL/kg)
    or
5-8 mg/kg mg/kg/min (80-100 mL/kg/d)

Target glucose 40-50 mg/dL


Treatment – Oral Dextrose

• Dextrose gel applied directly to buccal mucosa
• Allows for rapid correction of hypoglycemia
• Does not interrupt breast feeding and maternal care
Treatment – Oral Dextrose

2016 Cochrane Review
• Reduces mother-infant separation for treatment (RR 0.54)
• Increases rate of breastfeeding on after discharge (RR 1.10)
• No identified adverse outcomes
• No difference in neurodevelopmental outcome at 2-year follow-up

• Does not alter need for IV glucose


Case 2 Continued

It is now Sunday night. You started D10 at 6 mg/kg/min Saturday morning and titrated up to achieve a goal glucose of 50 mg/dL. You are currently waiting for a bed to open in the nearest NICU so you can transfer the newborn and the infant is now requiring 15 mg/kg/min of D10.
Poll Question 3

Which of the following are possible causes of persistent hypoglycemia in the newborn?

A. Birth asphyxia  
B. Sepsis  
C. Hyperinsulinism  
D. Inborn error of metabolism  
E. All of the above

Persistent Neonatal Hypoglycemia

Hypoglycemia that persists past 3 days of life

Prolonged neonatal hyperinsulinism (common)  
- Birth asphyxia  
- Intrauterine growth restriction  
- Toxemia

Genetic hypoglycemia disorders  
- Hyperinsulinism  
- Adrenal insufficiency  
- Glucose, glycogen or fatty acid  
- metabolic disorders

Toxins  
- Insulin  
- Sulfonylureas  
- Alcohol  
- Beta blockers  
- Salicylate

Pros-prandial hypoglycemia  
- Fundoplication  
- Gastric bypass
Prolonged Neonatal Hyperinsulinism

Mild and transient hyperinsulinism probably part of normal physiological response immediately after birth

- Some infants will have a prolonged period of relative hyperinsulinism due to perinatal stress
  - Birth asphyxia
  - Intrauterine growth restriction
  - Toxemia

- Most common cause of persistent hypoglycemia


Persistent Neonatal Hypoglycemia

Differential Diagnosis

- Hyperinsulinism
- Adrenal insufficiency
- Beckwith-Wiedemann syndrome

- Toxins and drugs
- Post-fundoplication and gastric bypass

Persistent Neonatal Hypoglycemia

Delay evaluation until after 48-hours of life to exclude transitional hypoglycemia
Draw labs when patient is symptomatically hypoglycemic
- Bicarbonate
- Beta-hydroxybutyrate (BOHB)
- Lactate
- Free fatty acids

If labs not available during symptomatic hypoglycemia, a period of fasting may be necessary to make the diagnosis or to determine safety for discharge


Genetic Hyperinsulinism

- Incidence of approximately 1 in 50,000 births
- May be as high as 1 in 2,500 births in some populations
  - Parts of Finland
  - Arabian peninsula
- May be born with macrosomia
  - Suggests prenatal hyperinsulinemia
- 45% present in soon after birth
- 77% will present within first 6 months

Hyperinsulinism

• For prolonged hypoglycemia, start glucose at physiological rate of 4-6 mg/kg/min
• Increase infusion to maintain glucose above 45-50 mg/dL (70 mg/dL)
  • May require infusion rates as high as 15-20 mg/kg/min
• Insertion of venous umbilical catheter strongly encouraged
• Consider early referral to tertiary care center
• Fasting test may be necessary to make the diagnosis
• Exaggerated response to glucagon (> 30 mg/dL) is highly suggestive of hyperinsulinism


Practice Recommendations

• Screen late preterm (34-36\(^{6/7}\)) small for gestational age (SGA), large for gestation age (LGA) and newborns of diabetic mothers for hypoglycemia in the postpartum period. (SOR B)
• For newborns with blood glucose < 25 mg/dL within the first 4 hours of life and < 35 mg/dL after the first 4 hours of life despite feeding, start a glucose infusion. (SOR B)
• Consider transfer to a tertiary care center for newborns with persistent hypoglycemia in whom you suspect a diagnosis of congenital hyperinsulinemia, adrenal insufficiency, or metabolic disorders. (SOR C)
Contact Information

• Craig Barstow, MD
• craig.h.Barstow.mil@mail.mil

Questions
Additional Reading
