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Reducing Professional Liability in Neonatal Hypoglycemia

Jonathan K Muraskas, MD, Jay P Goldsmith, MD

A 34-year-old primigravida with positive prenatal care is admitted at 34 and 0/7 weeks for preterm labor and spontaneous rupture membranes approximately 4 hours prior to presentation. There is no clinical evidence for chorioamnionitis. Pregnancy has been complicated by gestational diabetes requiring metformin. The most recent ultrasound, approximately two weeks prior to this admission, demonstrated an estimated fetal weight greater than the 95th percentile at 32 weeks gestation. Labor progressed, and the mother delivered a 2985 g LGA newborn male by spontaneous vaginal delivery at 34 and 0/7 weeks. Apgar scores of 4 and 8 were assigned at 1 and 5 minutes, respectively, and the infant required stimulation and CPAP because of mild respiratory distress. Because of respiratory distress and prematurity, he was admitted to the neonatal intensive care unit. The initial glucose was 12 mg/dL. At approximately 40 minutes of life, an IV was started, a 2 cc/kg bolus of dextrose 10% was given, and a continuous IV rate was established at 80 cc/kg/day. A repeat point-of-care (POC) glucose drawn at 55 minutes of life was 22 mg/dL. Another dextrose 10% bolus at 2 cc/kg was given. At approximately 120 minutes of life, repeat glucose was 36 mg/dL. At 3 hours of life, a glucose value was 55 mg/dL and remained stable throughout the rest of the NICU course.

Despite lower glucose values, there were no clinical signs of hypoglycemia documented. The baby had an unremarkable NICU course consistent with transient tachypnea of the newborn. He was discharged at approximately 36 and 5/7 weeks postmenstrual age and was nippling ad lib with a normal discharge physical exam. The discharge summary listed diagnoses as late preterm male, infant of a diabetic mother, transient tachypnea of the newborn, and hypoglycemia. At approximately eight years of age, this child was diagnosed with mild autism spectrum disorder (ASD). Throughout early grade school, he continued to score less than the 10th percentile relative to proficiency in literacy and mathematics. A malpractice claim was filed against the treating neonatologist, with the plaintiff neonatologist expert claiming that this is a meritorious case and produced literature that he described as "authoritative," demonstrating transient hypoglycemia as the sole causation for all of this child's adverse neurodevelopmental outcomes because no other diagnosis could be responsible. However, no consideration was given to multiple studies demonstrating no significant long-term neurodevelopmental deficits in this population. Furthermore, the plaintiff expert opines that hypoglycemia was listed as a diagnosis in the discharge summary, and the diagnosis of hypoglycemia in a late preterm infant required a more aggressive treatment. This case is still active.

Hypoglycemia describes a low concentration of glucose in the blood. Hypoglycemia affects up to 1 million newborns every year. The annual cost in the United States exceeds 2 billion dollars.

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Questions regarding this diagnosis that often arise at the bedside are:

1. How low a glucose concentration is too low?

2. At what level of serum glucose concentration does brain damage occur?
3. How long can serum glucose be low before irreversible brain damage occurs?

Hypoglycemia screening and management practices vary significantly across the United States. Significant "pathologic" hypoglycemia has not been defined by a single number that can be applied universally to all patients. A consistent definition of hypoglycemia does not exist for the first 48 hours of life. Lower glucose values in the first two hours of life are a normal physiologic adaptation to extrauterine life. Most clinicians consider plasma glucose values lower than 35 mg/dL abnormal in the first 48 hours of life, regardless of gestational age. In an attempt to guide clinicians, the AAP has relied on analysis of the lower range of glucose that occurs during the establishment of postnatal glucose homeostasis and advised actionable ranges of 25–40 mg/dL for the first 4 hours of life and 35–45 mg/dL from 4 hours to 24 hours of age. Glucose levels rise and should be similar to older children after the first 48 hours of life. There is no consistent threshold or lower limit single value for plasma glucose concentrations below which neurologic impairment or injury invariably begins or develops. (1) Most reasonable clinicians feel that asymptomatic hypoglycemia is benign for short periods at any level and that prolonged hypoglycemia (i.e., <25 mg/dL) is necessary for many hours to cause brain injury.

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Blood glucose levels are not necessarily a reflection of brain glucose levels. Whole blood glucose values tend to be 10–15% lower than plasma glucose. Therefore, bedside point of care (POC) glucose values done on whole blood are 10–15% lower than plasma glucose levels performed in the laboratory. Whole blood glucose can drop if allowed to stand at room temperature. Glucose oxidase test strips read by the eye or meter are often too unreliable and variable to initiate therapy in an asymptomatic newborn. POC bedside devices can provide a rapid screening of whole blood glucose. (2)

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Documentation is always the best defense against allegations of malpractice, and treating hypoglycemia in newborns is no exception. The newborn's clinical condition, glucose value, the method by which it was measured, treatment, and clinical response are essential and the standard of care. Most newborns with plasma glucose between 25 and 45 mg/dL without symptoms are usually fed or given glucose gel. Symptomatic hypoglycemia should always be treated with IV glucose with good documentation. Symptomatic hypoglycemia has been associated with neurologic impairment, including developmental delay, cortical visual deficits, cognitive difficulties, and epilepsy. Hypoglycemia could also be secondary to neonatal diseases such as hypoxic-ischemic encephalopathy, respiratory distress syndrome, and sepsis. Signs can include tremors, apnea, jitteriness, cyanosis, irritability, lethargy, tachypnea, grunting, hypotonia (hypertonia during seizures), poor feeding, tachycardia, and seizures. Neuroimaging

of newborns with confirmed symptomatic hypoglycemia classically involves the occipital lobe, although more diverse patterns of injury have been described (3).

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Common malpractice allegations in managing low glucose values include failure to initiate blood glucose monitoring when identifiable risk factors are present. Lower delivery volume—Level 1 and Level 2 nurseries—are more vulnerable to allegations of delay in initiating IV glucose therapy and delayed transfer to a higher level of care in the presence of low glucose values. Allegations can also include not heeding both nursing and parental concerns, such as poor feeding, hypotonia, jitteriness, or low body temperature. As noted, failure to recognize and document abnormal clinical signs with low glucose values, treatment, and resolution with normoglycemia can be problematic (4). Providers should be cautious when listing hypoglycemia as a discharge diagnosis, especially if there is no evidence of clinical signs or symptoms. A preferred diagnosis is "laboratory hypoglycemia." A skilled plaintiff lawyer can blow up the medical record to show a discharge diagnosis of hypoglycemia and go through every adverse effect a low blood sugar can potentially cause in a child who has low glucose values in the nursery. This topic can make a defense difficult when there is a paucity of documentation to refute many of these allegations. The mantra of "if you did not document it, you did not do it" in a trial is pervasive.

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There has been no convincing evidence that one or more brief episodes of low glucose concentrations below a specific value cause brain injury or that the duration of low glucose values is dangerous. However, a retrospective study of transient glucose values <35, <40, and <45 mg/dL in the newborn period was associated with lower achievement test scores at ten years of age in one study (5). The ongoing HypoEXIT trial is the first study to compare neurodevelopmental outcomes using two different glucose thresholds for intervention. In this multicenter, noninferiority trial, asymptomatic at-risk infants-infants of diabetic mothers, late preterm neonates, or newborns with birthweights <10%-ile or >90%-ile with hypoglycemia are stratified into different protocols: a traditional threshold group with plasma glucose <47 mg/dL as the cutoff for treatment and a low threshold group using a value less than 36 mg/dL. Treatment options were the same in both groups and determined by providers. At 18 months, the two groups had no significant differences in psychomotor test scores. (6) In the randomized Sugar Babies trial, a mid-childhood follow-up study (at 10–11 years), which included many late preterm and term newborns with multiple episodes of glucose values <2 mmol/L (<36 mg/dL), did not demonstrate any adverse educational achievement in the non-treated (placebo) group (7).

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The present consensus, using evidence-based medicine, is that transient asymptomatic low glucose values and symptomatic hypoglycemia promptly treated in the newborn period should not result in adverse neurological outcomes.

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References:

1. Hubbard EM, Hay Jr WW. The term newborn: hypoglycemia. Clin Perinatol 2021;48:534-544
2. Stanley CA, Rozance PJ. Re-evaluating "transient neonatal hypoglycemia": mechanism and implications for management. J Pediatr 2015;166:1520–1525
3. Burns CM, Rutherford MA. Patterns of cerebral injury and neurodevelopmental outcomes after symptomatic neonatal hypoglycemia. Pediatrics 2008;122:65–74
4. Srinivasakumar P, Muraskas JK. Myriad unknowns regarding neonatal hypoglycemia pose difficulties for managing patients, mitigating legal risks. AAP News: Pediatricians and the Law. August 2023
5. Kaiser JR, Bai S. Association between transient newborn hypoglycemia and fourth-grade achievement test performances: a population-based study. JAMA Pediatr 2015;169:913–921
6. Van Kempen AAMW, Eskes PF et al. Lower versus traditional treatment thresholds for neonatal hypoglycemia. NEJM 2020;382:534-544
7. St Clair SL, Darren WT Dai, Harris DL et al. Mid-Childhood outcomes after dextrose gel treatment of neonatal hypoglycaemia: follow-up of the sugar babies randomized trial. Neonatology 2023; 120(1):90-101. DOI: 10.1159/00052771

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