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ABM Protocols

ABM Clinical Protocol #1: Guidelines for Glucose Monitoring and Treatment of Hypoglycemia in Breastfed Neonates

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A central goal of the Academy of Breastfeeding Medicine is the development of clinical protocols for managing common medical problems that may impact breastfeeding success. These protocols serve only as guidelines for the care of breastfeeding mothers and infants and do not delineate an exclusive course of treatment or serve as standards of medical care. Variations in treatment may be appropriate according to the needs of an individual patient.

PURPOSE

TO PROVIDE GUIDANCE in the first hours / days of life to:

- Prevent hypoglycemia in breastfed infants
- Monitor blood glucose levels in at risk term and late-preterm breastfed infants
- Manage documented hypoglycemia in breastfed infants
- Establish and preserve maternal milk supply during medically necessary supplementation for hypoglycemia

BACKGROUND

Physiology

The term *hypoglycemia* refers to a low blood glucose concentration. Transient hypoglycemia in the immediate newborn period is common, occurring in almost all mammals. In healthy, normal term human infants, even if early enteral feeding is withheld, this phenomenon is self-limited, as glucose levels spontaneously rise within 2 to 3 hours.[1–3] This early self-limited period of hypoglycemia should not be considered pathologic. There is little practical value in measuring, or treating, the blood glucose concentrations of asymptomatic, normal term babies in the first 2 hours after birth.[4–6] Furthermore, even in those situations in which low blood glucose concentrations do develop secondary to prolonged intervals (>8 hours) between breastfeedings,[2] a marked ketogenic response occurs The enhanced capability of the neonatal brain to use ketone bodies provides glucose-sparing fuel to the brain, protecting neurologic function.[2,7–9]

Studies have not shown that treating transiently low blood glucose levels results in better short- or long-term outcomes compared with no treatment, and in fact there is no evidence that asymptomatic hypoglycemic infants benefit from treatment at all.[10] Koivisto et al.[11]

found no difference in neurologic outcome between asymptomatic hypoglycemic infants and euglycemic control infants, with 94% and 95% of each group normal on 1- to 4-year follow-up. There was a significant (12%) increase in neurologic abnormalities in *symptomatic* hypoglycemic infants and a 50% incidence of neurologic abnormalities when seizures were present. The compensatory provision of alternate fuels constitutes a normal adaptive response to transiently low nutrient intake during the establishment of breastfeeding,[2,12] resulting in breastfed infants tolerating lower plasma glucose levels without any significant clinical manifestations or sequelae.[12] Therefore, the monitoring of blood glucose concentrations in healthy, appropriately grown neonates is unnecessary, and potentially harmful to parental well-being and the successful establishment of breastfeeding.[4,6,13,14]

Definition of hypoglycemia

The definition of hypoglycemia in the newborn infant has remained controversial because of a lack of significant correlation among plasma glucose concentration, clinical symptoms, and long-term sequelae.[12,15,16] In addition, blood glucose test results vary enormously with the source of the blood sample, the assay method, and whether whole blood, plasma, or serum glucose concentration is determined. Plasma or serum glucose concentrations are 10% to 15% higher than in whole blood.[17]

Breastfed, formula-fed, and mixed-fed infants follow the same pattern of glucose values with an initial fall in glucose over the first 2 hours, followed by a gradual rise in glucose over the next 96 hours, whether fed or not.[1,18,19] Breastfed infants tend to have slightly lower glucose and higher ketone bodies than artificially fed infants.[2,18,20,21]

The incidence of "hypoglycemia" varies with the definition.[22] Many authors have suggested numeric definitions of hypoglycemia, usually between 30 and 50 mg/dL (1.7 to 2.8 mmol/L) and varying by postnatal age.[1,4,15,18,22–26] Cornblath et al.[12] summarized the problem:

> Significant hypoglycemia is not and can not be defined as a single number that can be applied universally to every individual patient. Rather, it is characterized by a value(s) that is unique to each individual and varies with both their state of physiologic maturity and the influence of pathology.

A recent metaanalysis (studies published 1986 to 1994) of low plasma glucose thresholds in full-term normal newborns who were mostly mixed-fed (formula and breastfeeding) or formula-fed, presented recommended low thresholds for plasma glucose based on hours after birth (Table 1). The authors specifically noted that given the lower plasma glucose levels in normal breastfed infants, the low thresholds for exclusively breastfed infants might even be lower.[27] Recommendations based on this threshold approach are provided in Table 1.

Given this information, it is clear that the routine monitoring of blood glucose in healthy term infants is not only unnecessary, but is potentially harmful to the establishment of a healthy mother–infant relationship and successful breastfeeding patterns.[6,13,14,28,29] This recommendation has been supported by the World Health Organization,[4] the AAP,[30] and the National Childbirth Trust of the United Kingdom.[31] They all conclude that early and exclusive breastfeeding is safe to meet the nutritional needs of healthy term infants and that healthy, full-term infants do not develop symptomatic hypoglycemia simply as a result of underfeeding.

Testing methods

Bedside glucose testing strips are inexpensive and practical, but are not reliable with significant variance from true blood glucose levels.[14,26,32] Bedside glucose tests may be used for screening, but laboratory levels must confirm results before a diagnosis of hypoglycemia can be made, especially in asymptomatic infants.[4,14,17,28]

TABLE 1. RECOMMENDED LOW THRESHOLDS: PLASMA GLUCOSE LEVEL

Hour after birth	*≤5th Percentile PGL (mg/dL)*
1–2 (nadir)	28 (1.6 mmol/L)
3–47	40 (2.2 mmol/L)
48–72	48 (2.7 mmol/L)

From Ref. 27.

TABLE 2. AT-RISK INFANTS FOR WHOM ROUTINE MONITORING OF BLOOD GLUCOSE IS INDICATED

Small for gestational age (SGA); <10th percentile for weight
Large for gestational age (LGA); >90th percentile for weight*
Discordant twin; weight 10% below larger twin
Infant of diabetic mother, especially if poorly controlled
Low birth weight (<2500 g)
Perinatal stress; severe acidosis or hypoxia-ischemia
Cold stress
Polycythemia (venous Hct >70%) / hyperviscosity
Erythroblastosis fetalis
Beckwith-Wiedemann syndrome
Microphallus or midline defect
Suspected infection
Respiratory distress
Known or suspected inborn errors of metabolism or endocrine disorders
Maternal drug treatment (e.g., terbutaline, propranolol, oral hypoglycemics)
Infants displaying symptoms associated with hypoglycemia (see Table 3)

*This remains controversial. Some recommend in unscreened populations in whom LGA may represent undiagnosed and untreated maternal diabetes.

From: Schaefer-Graf UM, Rossi R. Bührer C, et al. Rate and risk factors of hypoglycemia in large-for-gestational-age newborn infants of non-diabetic mothers. *Am J Obstet Gynecol* 2002;187:913–917; Cahill JB, Martin KL, Wagner CL, Hulsey TC. Incidence of hypoglycemia in term large for gestational age infants (LGA) as a function of feeding type. *ABM News Views* 2002;8:20.

RISK FACTORS FOR HYPOGLYCEMIA

Neonates at increased risk for developing neonatal hypoglycemia should be routinely monitored for blood glucose levels irrespective of the mode of feeding. At risk neonates fall into two main categories:

1. Excess use of glucose, which includes the hyperinsulinemic states
2. Inadequate production or substrate delivery[33]

The infant categories as shown in Table 2 are at increased risk for hypoglycemia.[5,12,33–36]

CLINICAL MANIFESTATIONS OF HYPOGLYCEMIA

The clinical manifestations of hypoglycemia are *nonspecific*, occurring with a variety of other neonatal problems. Even in the presence of an arbitrary low glucose level, the physician must assess the general status of the infant by observation and physical examination to rule out other disease entities and processes that may need additional laboratory evaluation and treatment. Some common clinical signs are listed in Table 3.

A diagnosis of hypoglycemia also requires that symptoms abate after normoglycemia is restored. Transient, single, brief periods of hypoglycemia are unlikely to cause permanent neurologic damage.[5,10,28]

GENERAL MANAGEMENT RECOMMENDATIONS (TABLE 4)

Early and exclusive breastfeeding meets the nutritional and metabolic needs of healthy, term newborn infants. Healthy term infants do not develop symptomatic hypoglycemia simply as a result of underfeeding.[4,5,30]

1. Routine supplementation of healthy, term infants with water, glucose water or formula is unnecessary and may interfere with establishing normal breastfeeding and normal metabolic compensatory mechanisms.[2,20,30,31]
2. Healthy term infants should initiate breastfeeding within 30 to 60 minutes of life and continue on demand, recognizing that crying is a very late sign of hunger.[30,37] Early breastfeeding is not precluded just because the infant meets the criteria for glucose monitoring.

TABLE 3. CLINICAL MANIFESTATIONS OF POSSIBLE HYPOGLYCEMIA

Irritability, tremors, jitteriness
Exaggerated Moro reflex
High-pitched cry
Seizures or myoclonic jerks
Lethargy, listlessness, limpness, hypotonia
Coma
Cyanosis
Apnea or irregular breathing
Tachypnea
Hypothermia; temperature instability
Vasomotor instability
Poor suck or refusal to feed

TABLE 4. GENERAL MANAGEMENT RECOMMENDATIONS

Early and exclusive breastfeeding meets the nutritional and metabolic needs of healthy, term newborn infants.
1. Routine supplementation is unnecessary.
2. Initiate breastfeeding within 30 to 60 minutes of life and continue on demand.
3. Facilitate skin-to-skin contact of mother and infant.
4. Feedings should be frequent; 10 to 12 times per 24 hours in the first few days after birth.

Glucose screening is performed only on at-risk or symptomatic infants.
1. Routine monitoring of blood glucose in all term newborns is unnecessary and may be harmful.
2. An at-risk infant should be screened for hypoglycemia with a frequency and duration related to the specific risk factors of the individual infant.
3. Monitoring continues until normal, preprandial levels are consistently obtained.
4. Bedside glucose screening tests must be confirmed by formal laboratory testing.

3. Initiation and establishment of breastfeeding is facilitated by skin-to-skin contact of mother and infant. Such practices will maintain normal infant body temperature and reduce energy expenditure (thus enabling maintenance of normal blood glucose) while stimulating suckling and milk production.[21,30]
4. Feedings should be frequent, 10 to 12 times per 24 hours in the first few days after birth.[30]

Glucose screening should be performed only on at-risk infants and those with clinical symptoms compatible with hypoglycemia.

1. Routine monitoring of blood glucose in asymptomatic, term newborns is unnecessary and may be harmful.[4,5,31,38,39]
2. At-risk infants should be screened for hypoglycemia with a frequency and duration related to the specific risk factors of the individual infant.[5] It is suggested that monitoring begin within 30 to 60 minutes for infants with suspected hyperinsulinemia, and no later than 2 hours of age for infants in other risk categories.
3. Monitoring should continue, until normal, preprandial levels are consistently obtained.
4. Bedside glucose screening tests must be confirmed by formal laboratory testing.

MANAGEMENT OF DOCUMENTED HYPOGLYCEMIA (TABLE 5)

Asymptomatic infant:

1. Continue breastfeeding (approximately every 1 to 2 hours) or feed 3 to 5 mL/kg (up to 10 mL/kg)[4] of expressed breast milk or

TABLE 5. MANAGEMENT OF DOCUMENTED HYPOGLYCEMIA

Asymptomatic infant
1. Continue breastfeeding (approximately every 1 to 2 hours) or feed 3 to 10 mL/kg of expressed breast milk or substitute nutrition.
2. Recheck blood glucose concentration before subsequent feedings until the value is acceptable and stable.
3. Avoid forced feedings.
4. If glucose remains low despite feedings, begin intravenous glucose therapy.
5. Breastfeeding may continue during IV glucose therapy.
6. Carefully document response to treatment.

Symptomatic infant or infants with plasma glucose levels <20 to 25 mg/dL (<1.1 to 1.4 mmol/L)
1. Initiate intravenous 10% glucose solution.
2. Do not rely on oral or intragastric feeding to correct extreme or symptomatic hypoglycemia.
3. The glucose concentration in symptomatic infants should be maintained >45 mg/dL (>2.5 mmol/L).
4. Adjust intravenous rate by blood glucose concentration.
5. Encourage frequent breastfeeding.
6. Monitor glucose concentrations before feedings as the IV is weaned until values stabilize off intravenous fluids.
7. Carefully document response to treatment

substitute nutrition (pasteurized donor human milk, elemental formulas, partially hydrolyzed formulas, routine formulas).
2. Recheck blood glucose concentration before subsequent feedings until the value is acceptable and stable.
3. If the neonate is unable to suck or feedings are not tolerated, avoid forced feedings (e.g., nasogastric tube) and begin intravenous (IV) therapy (see the following). Such an infant is not normal and requires a careful examination and evaluation in addition to more intensive therapy.
4. If glucose remains low despite feedings, begin IV glucose therapy and adjust intravenous rate by blood glucose concentration.
5. Breastfeeding may continue during IV glucose therapy when the infant is interested and will suckle. Wean IV glucose as serum glucose normalizes and feedings increase.
6. Carefully document signs, physical examination, screening values, laboratory confirmation, treatment and changes in clinical condition (i.e., response to treatment).

Symptomatic infants or infants with plasma glucose levels <20 to 25 mg/dL (<1.1 to 1.4 mmol/L)

1. Initiate intravenous 10% glucose solution.
2. Do not rely on oral or intragastric feeding to correct extreme or symptomatic hypoglycemia. Such an infant is not normal, and requires an immediate and careful examination and evaluation in addition to IV glucose therapy.
3. The glucose concentration in symptomatic infants should be maintained >45 mg/dL (>2.5 mmol/L).
4. Adjust intravenous rate by blood glucose concentration.
5. Encourage frequent breastfeeding after the relief of symptoms.
6. Monitor glucose concentrations before feedings as the IV is weaned, until values are stabilized off intravenous fluids.
7. Carefully document signs, physical examination, screening values, laboratory confirmation, treatment, and changes in clinical condition (i.e., response to treatment).

SUPPORTING THE MOTHER

Having an infant who was thought to be normal and healthy and who develops hypoglycemia is both concerning to the mother and family, and may jeopardize breastfeeding. Mothers should be reassured that there is nothing wrong with their milk, and supplementation is usually temporary. Having the mother hand-express or pump milk that is then fed to her infant can overcome feelings of maternal inadequacy as well as help establish a full milk supply. It is important to provide stimulation to the breasts by manual or mechanical expression with appropriate frequency (eight times in 24 hours) until her baby is latching and suckling well to protect her milk supply. Keeping the infant at the breast, or returning the infant to the breast as soon as possible is important. Skin-to-skin care is easily done with an IV and may lessen the trauma of intervention, while also providing physiologic thermoregulation, contributing to metabolic homeostasis.

RECOMMENDATIONS FOR FUTURE RESEARCH

1. Well-planned, well-controlled studies are needed that look at plasma glucose concentrations, clinical symptoms, and long-term sequelae so the levels of glucose necessary for intervention can be better understood.
2. The development of more reliable bedside testing methods would increase the efficiency of diagnosis and treatment of significant glucose abnormalities.
3. A clearer understanding of the role of other glucose-sparing fuels and methods to measure them in a clinically meaningful way and time frame would aid in understanding which babies are truly at risk of neurologic sequelae, and thus must be treated.

CONCLUSION

Healthy, full-term infants are programmed to make the transition from their intrauterine constant flow of nutrients to their extrauterine

intermittent nutrient intake without the need for metabolic monitoring or interference with the natural breastfeeding process.[3] Homeostatic mechanisms ensure adequate energy substrate is provided to the brain and other organs, even when feedings are delayed. The normal pattern of early, frequent, and exclusive breastfeeding meets the needs of healthy full-term infants. Routine screening or supplementation are not necessary and may harm the normal establishment of breastfeeding.

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