JOHNS HOPKINS ALL CHILDREN'S HOSPITAL
MATERNAL, FETAL, AND NEONATAL INSTITUTE

Neonatal Transitional Hypoglycemia Clinical Pathway

JOHNS HOPKINS
All Children's Hospital

Johns Hopkins All Children's Hospital
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Neonatal Transitional Hypoglycemia Clinical Pathway

Rationale:

This clinical pathway was proposed as a consensus amongst Johns Hopkins All Children's Hospital (JHACH) Neonatologists, Pediatric Endocrinologists, Pharmacists, and Dieticians to standardize the clinical approach and management of neonates with transitional hypoglycemia. It addresses the following clinical problems:

1. Defining neonatal transitional hypoglycemia
2. Managing neonatal transitional hypoglycemia

Inclusion criteria:

- All neonates admitted into the Neonatal Intensive Care Unit (NICU) who are ≥ 35 weeks' gestation age (GA)

Exclusion criteria:

- Patients not admitted into the NICU
- Neonates that are NPO
- Neonates that are critically ill or on respiratory support
- Preterm neonates < 35 weeks' GA

Background:

Fetal glucose levels are dependent on maternal glucose supply and placental transfer. Immediately after birth, a neonate's blood glucose concentration represents roughly 70% of maternal concentration. It may fall rapidly to a nadir of less than 30 milligrams (mg)/deciliter (dL) within 1 to 2 hours (Adamkin, 2011; Heck, 1987). Typically, these concentrations rise above 45 mg/dL by 12 hours after birth and increase over the next 2 to 3 days to reach the normal range for older infants and children (> 70 mg/dL) (Cornblath, 2000). The Pediatric Endocrine Society (PES) defines this period of hypoglycemia (< 60 mg/dL) occurring in the first 48 hours of life as neonatal transitional hypoglycemia (Stanley, 2015).

Neonatal transitional hypoglycemia occurs in up to 15% of healthy neonates and tends to be asymptomatic (Hay, 2009). However, this incidence may reach up to 60% in neonates who are preterm, small for gestational age (SGA), large for gestational age (LGA), intra-uterine growth restricted (IUGR), or born to mothers with diabetes (Edwards, 2021). Fifty percent of these higher-risk neonates will develop at least one episode of hypoglycemia, while 20% may experience more than one episode (Edwards, 2021). Additional risk factors for neonatal transitional hypoglycemia include perinatal asphyxia, prolonged labor, hypothermia, sepsis, and maternal use of medications such as beta-agonists and beta-blockers (Edwards, 2021).

In neonates, this early period of low blood glucose concentrations may be crucial for stimulating physiological processes essential for postnatal survival, including the promotion of glucose production through gluconeogenesis and glycogenolysis (Rozance, 2012). Additionally, a decrease in blood glucose concentration enhances oxidative fat metabolism, stimulates appetite, and may aid adaptation to fast-feed cycles (Rozance, 2012). Historically, the management of neonatal transitional hypoglycemia involves supplemental feedings or intravenous (IV) dextrose with admission to the NICU.

Oral 40% glucose gel, consisting of 40% glucose, water, and glycerin, is an established first-line treatment for hypoglycemia in adults and children. An emerging body of literature, including randomized controlled trials, now supports the use of glucose gel to treat hypoglycemia in neonates. Initial concerns with using oral glucose gel in neonates involved the potential of hyperglycemia, choking, vomiting, and rebound hypoglycemia. Multiple studies have shown that neonates did not exhibit rebound hypoglycemia but rather maintained blood glucose concentrations within the normal range. In 2013, Harris et al. published the results of a randomized, double-blind, placebo-controlled clinical trial demonstrating the efficacy of buccal administration of a glucose gel in reversing hypoglycemia in neonates at negligible risk. This method of administration was found to be effective due to the high vascularization of the mucosa, allowing an absorption rate similar to that of IV administration. The standard dose described in the study was 0.2 grams (g) glucose/kilogram (kg) body weight, which is essentially equivalent to the dose for IV dextrose treatment in neonates with hypoglycemia (2 milliliters [mL]/kg body weight of 10% dextrose in 100 mL of water, which equals 0.2 g dextrose/kg body weight). Their study showed that using a 40% glucose gel with feeding was more effective than feeding alone in reversing neonatal transitional hypoglycemia, did not require NICU admission, and was compatible with exclusive breastfeeding.

A single-center retrospective study reported a 73% reduction in NICU admissions and a 49% reduction in formula supplementation for the primary diagnosis of hypoglycemia after implementation of an oral glucose algorithm (Bennett, 2016). Another single-center study found that oral glucose gel was effective in stabilizing neonates with very low blood glucose and reducing the need to initiate IV dextrose-containing fluids (Romald, 2019). 76% of late preterm and term neonates with asymptomatic hypoglycemia in this study responded well to oral glucose gel and did not require IV dextrose. Of the neonates who were stabilized with glucose gel, 79% required only one dose, 18% required two doses, and 3% required 3 doses. The study also suggested that it may be reasonable to administer an oral glucose gel as a bridge while preparing IV dextrose administration.

Oral glucose gel is simple to administer, cost-effective, and well-tolerated. In studies, it has primarily been used for asymptomatic hypoglycemia in the first few hours after birth, when the neonate’s blood glucose remains low after the first feed. This step would replace the current recommendations for asymptomatic neonatal hypoglycemia from the 2011 American Academy of Pediatrics (AAP) guidelines on postnatal glucose homeostasis (Adamkin, 2011). Per the current AAP guidelines, neonates with symptomatic hypoglycemia and blood glucose concentrations less than 40 mg/dL should receive IV dextrose. According to these guidelines,

asymptomatic neonates with a glucose < 25 mg/dL should receive IV dextrose, and asymptomatic neonates with a glucose level of 25 – 40 mg/dL after the first feed should refeed or receive IV dextrose as needed. Note, blood glucose concentrations that fall below 10 mg/dL for more than 12 hours have been shown to cause neurological damage, including seizures, psychomotor disturbances (leading to learning deficits), cerebral palsy, and/or intellectual disabilities, and should be treated with IV dextrose (Bennett, 2015).

Clinical Management:

40% glucose gel:

- Dosing: 0.2 g/kg/dose (0.5 mL/kg/dose)
- Administration:
    - Draw up the dose in an oral syringe
    - Give ½ dose into one cheek and massage the cheek, and then give the other ½ dose into the other cheek, and massage the cheek

What to feed:

- The first choice is mother's own milk (MOM)
- If unable to obtain MOM and the neonate is ≥ 35 weeks' GA, provide 20 kilocalories (kcal)/ounce (oz) term formula
- Avoid increasing the caloric content of the feeds as this minimally affects the carbohydrate load

Discharge parameters:

- Patients are appropriate for discharge when:
    - Off IV fluids for 24 hours
    - Has three consecutive blood glucose concentrations within normal limits (goal blood glucose > 60 mg/dL)
- Discharge formulas:
    - The first choice is MOM
    - If unable to obtain MOM and the neonate is ≥ 35 weeks' GA, provide 20 kcal/oz term formula
    - The patient must be on feeds for 24 hours with three blood glucose concentrations within normal limits (goal blood glucose > 60 mg/dL)

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Neonatal Transitional Hypoglycemia Clinical Pathway
0 – 4 Hours of Life

Does the patient have symptomatic hypoglycemia?
(e.g., irritability, tremors, jitteriness, high-pitched cry, seizures, lethargy, floppiness, cyanosis, apnea, tachypnea)

Exclusion Criteria:
- Patients not admitted into the NICU
- Neonates that are NPO
- Neonates that are critically ill or on respiratory support
- Preterm neonates < 35 weeks' GA
- Neonates > 4 hours of life

NO

Initial feeding within 1 hour of birth, screen blood glucose 30 minutes after 1st feed

Initial screening blood glucose result

< 25 mg/dL	≥ 25 – < 40 mg/dL	≥ 40 mg/dL
Contact provider for IV dextrose	Feed patient and recheck glucose in 1 hour	Continue feeds every 2 – 3 hours and obtain glucose prior to each feed

YES

OFF PATHWAY
Obtain blood sugar and contact the provider for IV dextrose

Subsequent screening blood glucose result

< 25 mg/dL	≥ 25 – < 40 mg/dL	≥ 40 mg/dL
Contact provider for IV dextrose	Administer 40% glucose gel*, feed patient, and recheck glucose in 1 hour	Continue feeds every 2 – 3 hours and obtain glucose prior to each feed

*40% glucose gel:
- Dosing: 0.2 g/kg/dose (0.5 mL/kg/dose)
- Administration:
  - Draw up the dose in an oral syringe
  - Give ½ dose into one cheek and massage the cheek, and then give the other ½ dose into the other cheek, and massage the cheek

- If the patient becomes symptomatic at any time, call the provider for IV dextrose
- Patient should not receive more than 2 doses of glucose gel in 24 hours; contact the provider for IV fluids
- If after 1st 24 hours, patient is not taking 60 mL/kg/day, contact provider for IV fluids or consider nasogastric feeds
- Continue checking glucose until there are 3 consecutive screenings within normal limits

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Neonatal Transitional Hypoglycemia Clinical Pathway
>4 – 24 Hours of Life

Exclusion Criteria:
- Patients not admitted into the NICU
- Neonates that are NPO
- Neonates that are critically ill or on respiratory support
- Preterm neonates < 35 weeks' GA
- Neonates > 24 hours of life

Does the patient have symptomatic hypoglycemia?
(e.g., irritability, tremors, jitteriness, high-pitched cry, seizures, lethargy, floppiness, cyanosis, apnea, tachypnea)

NO

YES

OFF PATHWAY
Obtain blood sugar and contact the provider for IV dextrose

Blood glucose result

< 35 mg/dL

Contact provider for IV dextrose

≥ 35 – < 45 mg/dL

Administer 40% glucose gel*, feed patient, and recheck glucose in 1 hour

≥ 45 mg/dL

Continue feeds every 2 – 3 hours and obtain glucose prior to each feed

*40% glucose gel:
- Dosing: 0.2 g/kg/dose (0.5 mL/kg/dose)
- Administration:
  - Draw up the dose in an oral syringe
  - Give ½ dose into one cheek and massage the cheek, and then give the other ½ dose into the other cheek, and massage the cheek

- If the patient becomes symptomatic at any time, call the provider for IV dextrose
- Patient should not receive more than 2 doses of glucose gel in 24 hours; contact the provider for IV fluids
- If after 1st 24 hours, patient is not taking 60 mL/kg/day, contact provider for IV fluids or consider nasogastric feeds
- Continue checking glucose until there are 3 consecutive screenings within normal limits

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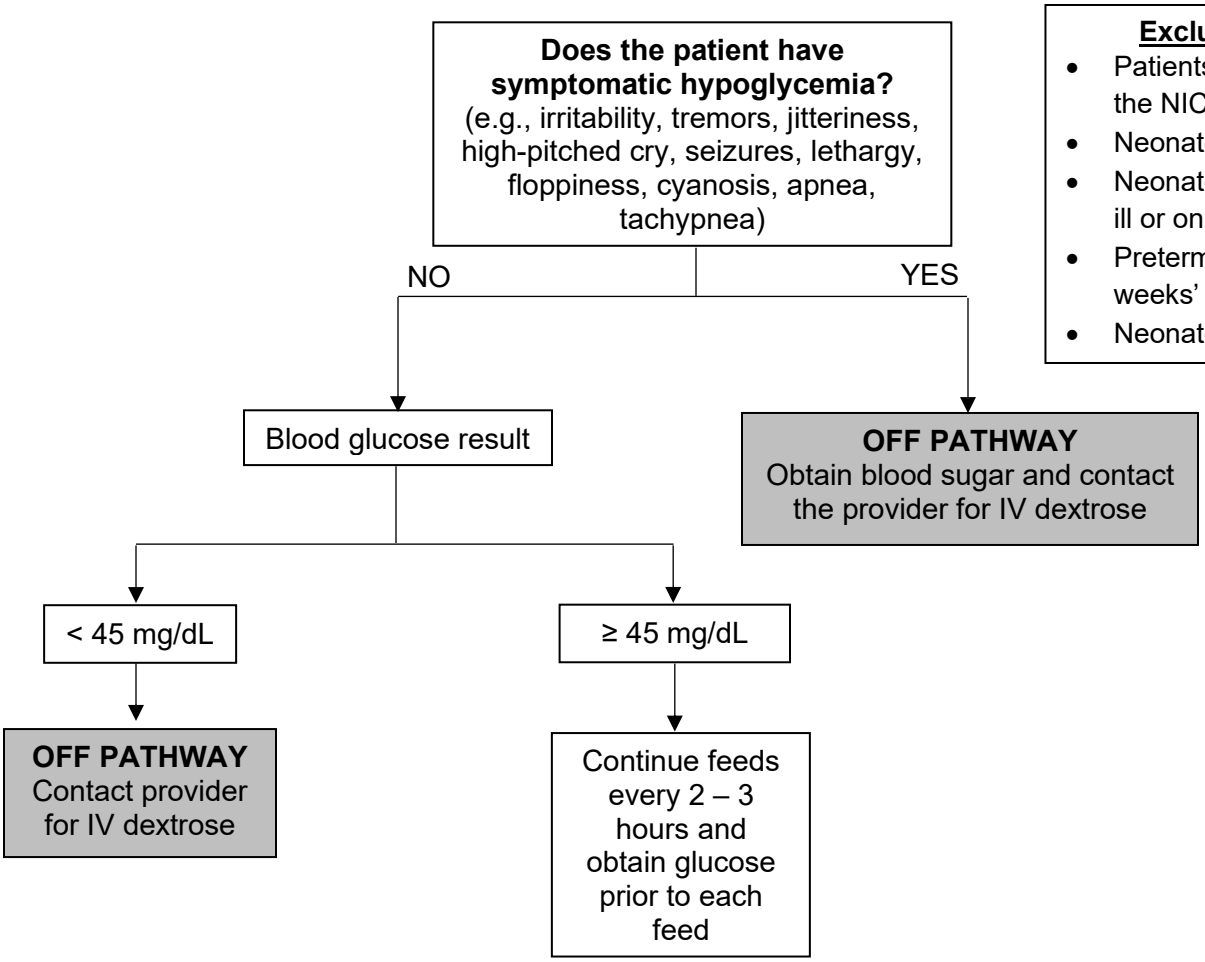
Neonatal Transitional Hypoglycemia Clinical Pathway
>24 – 48 Hours of Life



Exclusion Criteria:

- Patients not admitted into the NICU
- Neonates that are NPO
- Neonates that are critically ill or on respiratory support
- Preterm neonates < 35 weeks' GA
- Neonates > 48 hours of life

- If the patient becomes symptomatic at any time, call the provider for IV dextrose
- If after 1st 24 hours, patient is not taking 60 mL/kg/day, contact provider for IV fluids or consider nasogastric feeds
- Continue checking glucose until there are 3 consecutive screenings within normal limits

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Outcome Measures:

1. Timely blood glucose screening
    a. Definition: Percentage of at-risk neonates who receive their first blood glucose check within 1 hour of birth
    b. Why it matters: Ensures early detection of hypoglycemia and adherence to screening protocol
    c. Target: ≥ 95%
2. Avoidance of IV dextrose therapy
    a. Definition: Percentage of at-risk neonates with hypoglycemia successfully managed with feeding alone, avoiding IV dextrose
    b. Why it matters: Promotes non-invasive management and supports rooming-in and breastfeeding
    c. Target: ≥ 85%
3. Exclusive breastfeeding at discharge
    a. Definition: Percentage of at-risk neonates discharged home on exclusive breastfeeding
    b. Why it matters: Indicates successful feeding support despite hypoglycemia risk and management
    c. Target: ≥ 75%

Clinical Pathway Team

Neonatal Transitional Hypoglycemia Clinical Pathway

Johns Hopkins All Children's Hospital

Maternal, Fetal, and Neonatal Institute

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Disclaimer:

Clinical Pathways are intended to assist physicians, physician assistants, nurse practitioners, and other healthcare providers in clinical decision-making by describing a range of generally accepted approaches for diagnosing, managing, or preventing specific diseases or conditions. The physician must make the ultimate judgment regarding the care of a particular patient, taking into account the patient's individual circumstances.

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