NEONATAL HYPOGLYCEMIA

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WHAT IS NEONATAL HYPOGLYCEMIA?

• Glucose concentration low enough to cause signs and symptoms of impaired brain function
• Normal threshold for neurogenic response < 60 mg/dl
• For safety goal should be blood glucose level > 70 mg/dl

WHY NOT FOCUS ON A SPECIFIC GLUCOSE VALUE?

• Brain responses to hypoglycemia vary. Response depends on various factors including:
  • Alternative fuels
  • Previous hypoglycemic events
• No single glucose value is known to cause brain damage in everyone. Value is influenced by duration and degree of hypoglycemia
• Values may be difficult to interpret
WHEN IS HYPOGLYCEMIA “NORMAL” IN A NEONATE?

- Transitional hypoglycemia may occur during the first 3 days of life
  - > 50 mg/dl
- Infant of mother with diabetes
- Transitional hypoglycemia should be resolved before discharge from the hospital

WHEN TO WORRY

- Infant displays signs and symptoms of hypoglycemia
- Blood glucose level < 50 mg/dl any time

WHIPPLE’S TRIAD

- Signs and symptoms of hypoglycemia
- Documented low blood glucose level
- Resolution of symptoms when blood glucose level is returned to normal
NEONATES AT RISK

• Babies with symptoms of hypoglycemia
• Large for gestational age (mother does not have to have diabetes)
• Babies who experienced perinatal stress

WHAT IS PERINATAL STRESS

• Birth asphyxia or ischemia
• Cesarean section for fetal distress
• Maternal eclampsia/ pre-eclampsia
• Maternal hypertension
• Intrauterine growth restriction (IUGR), small for gestational age (SGA)
• Meconium aspiration
• Hypothermia
• Hematologic concerns: erythroblastosis fetalis, polycythemia

NEONATES AT RISK

• Premature or postmature delivery
• Infant of a diabetic mother
• Family history of genetic form of hypoglycemia
• Sibling with history of hypoglycemia
• Concerns for congenital syndrome associated with hypoglycemia
CONGENITAL SYNDROMES ASSOCIATED WITH HYPOGLYCEMIA

• Overgrowth syndrome (Beckwith Wiedemann)
• Midline facial malformations
• Microphallus

DO NOT DISCHARGE BEFORE PROVEN SAFE FROM HYPOGLYCEMIA

• Episode of hypoglycemia requiring IV dextrose or symptomatic
• Inability to consistently maintain post-prandial glucose levels
  • ≥50 mg/dl up to 48 hours of age and ≥ 60 mg/dl after 48 hours of age
• Family history of genetic form of hypoglycemia
• Congenital syndrome associated with hypoglycemia

SIGNS AND SYMPTOMS OF NEONATAL HYPOGLYCEMIA

• Difficulty breathing
• Mottled skin
• Shaky
• Seizure activity
• Irritability
• Extreme hunger
CHALLENGES IN RECOGNIZING NEONATAL HYPOGLYCEMIA

- Neonates do not always display symptoms of hypoglycemia
- Previous episodes of hypoglycemia can decrease neurogenic response to future episodes for 24 hours (hypoglycemia unawareness)
- Hepatic glucose release is impaired
- HAAF: Hypoglycemia Autonomic Failure

GLUCOSE UTILIZATION

- The brain requires the most glucose
- Infants and young children require more glucose than adults due to their larger brain size
- The brain is able to use ketones or lactate as alternative fuel
- In Hyperinsulinism or Fatty Acid Oxidation Disorders these fuels will not be available in sufficient amounts

PROTECTION FROM HYPOGLYCEMIA

- Suppression of insulin secretion when blood glucose levels are below the normal postabsorptive mean (85 mg/dl)
- Glucagon secretion with as blood glucose level falls
- As blood glucose fall to < 65 mg/dl, growth hormone and cortisol increase
METABOLIC PROTECTION AGAINST HYPOGLYCEMIA

- Release of glucose stores from the liver
- With prolonged fasting glucose utilization is restricted to the liver
- Free Fatty Acids can replace glucose in skeletal and heart muscle – not in the brain
- As ketones rise they can partly increase the brain's energy needs

HOW DO WE TEST FOR NEONATAL HYPOGLYCEMIA?

- Heel Stick
- Ensure the foot is warm
- Repeat level less than 70 mg/dl immediately
- If blood glucose remains <70 mg/dl send confirmatory to the lab

WHEN DO YOU NEED TO SEND A CONFIRMATORY?

- Any blood glucose < 50 in infant < 48 hours of age should be repeated on bedside glucometer. If repeat < 50 mg/dl - send confirmatory
- Any blood glucose < 60 mg/dl > 48 hour of age should be repeated on bedside glucometer. If repeat < 50 mg/dl - send confirmatory
THE BLOOD SUGAR IS LOW, NOW WHAT

- Re-check on glucometer, send confirmatory if remains low
- If blood glucose > 50 mg/dl feed
- If blood glucose < 50 mg/dl start dextrose

HOW SHOULD NEONATAL HYPOGLYCEMIA BE TREATED?

- Treatment goal should be to keep blood glucose level > 70 mg/dl
- IV dextrose should be initiated as soon as hypoglycemia noted
- IV dextrose may be concentrated to avoid fluid overload

FREQUENT FEEDS AS TREATMENT FOR NEONATAL HYPOGLYCEMIA

- Dextrose should be the only therapy used to treat hypoglycemia
- Frequent/ continuous feeds will lead to the development of feeding aversion
CAUSES OF NEONATAL HYPOGLYCEMIA

• Hyperinsulinism
  • Stress Induced
  • Genetic Mutation
  • No Identifiable Mutation
• Glycogen Storage Disease (GSD)
• Fatty Oxidation Disorder (FFA)

GLUCOSE GOALS

• Neonates with a suspected hypoglycemia disorder and older children with a confirmed hypoglycemia disorder:
  • Maintain blood glucose > 70 mg/dl
• High-risk neonates without a suspected congenital hypoglycemia disorder:
  • < 48 hours old, maintain BG > 50 mg/dl
  • > 48 hours old, maintain BG > 60 mg/dl

TESTING FOR NEONATAL HYPOGLYCEMIA

• Fasting Study:
  • Neonates should be able to fast 24 hours
  • Need to ensure that babies are safe to fast > 70 mg/dl
  • “Skip a feed”
  • Fasting Study
FASTING A NEONATE

• 24 hours
• NPO except for ¼ NSS
  • Po or IV hydration
• Prepare family
• Plan for “skip a feed” if suspect stress induced hypoglycemia with values > 50 mg/dl

CRITICAL SAMPLE

• Basic Metabolic Panel
• Beta-hydroxybuterate
• Ammonia
• Lactate
• Cortisol
• Growth Hormone
• Insulin

CRITICAL SAMPLE

• C-Peptide
• Free Fatty Acids
• IGF-BP1
• Free and total carnitine
• Acylcarnitine Profile
• Urine Organic Acids- try bagging. If not sooner obtain first void after fast. Obtain within 2-4 hours of fast ending
PREPARING TO OBTAIN THE CRITICAL SAMPLE

- Ask for help
- Label tubes ahead of time
- Now volume required for each test
- Have a blood drawing IV
  - Don’t have placed too early
  - Don’t wait too long to have placed

CAUSES OF NEONATAL HYPOGLYCEMIA

- Finding: Low beta hydroxy buterate (BHOB) and low free fatty acids (FFA)
- Hyperinsulinism
- Hypopituitarism
- Transitional Neonatal Hypoglycemia
- Perinatal Stress Hyperinsulinism
CAUSES OF NEONATAL HYPOGLYCEMIA

• Findings: Low BHOB and elevated FFA

• Fatty Acid Oxidation Defects

CAUSES OF NEONATAL HYPOGLYCEMIA

• Findings: Elevated lactate

• Gluconeogenesis defects
  • GSD (Glycogen Storage Disease)

CAUSES OF NEONATAL HYPOGLYCEMIA

• Findings: Elevated BHOB

• Ketotic Hypoglycemia
• Glycogenoses
• Growth Hormone (GH) Deficiency
• Cortisol Deficiency
PREPARING THE FAMILY FOR THE FAST

• Review the importance— to ensure their child is safe
• Be clear that their baby may “hang in the 50s mg/dl” for “a long time”
• Review the process of obtaining a confirmatory sample
• Review the glucagon stim

SAFE DISCHARGE FOR A NEONATE WITH HYPOGLYCEMIA

• You must be sure that the baby can safely fast between feedings
• You must be certain that if the baby will be able to skip a feeding
• Family must be taught blood glucose monitoring
• Family must have glucometer and supplies prior to discharge
• Family must be aware of blood glucose values to call for
• Family must have rescue plan
• If being discharged with glucagon, teaching must be completed
• Family must have glucagon prior to discharge

ENDOCRINE FOLLOW UP FOR A NEONATE WITH HYPOGLYCEMIA

• The baby stayed > 70 mg/dl for 6 hours, what happens when they start sleeping longer?
• When does the fast need to repeated?
• How long does the family need to follow in Endocrine clinic?