Hypoglycemia is commonly seen in the neonate. Evidence indicates that hypoglycemia has long term neurological implications. Prompt identification and treatment is critical to ensure optimum outcomes.

NICU, neonatal glucose metabolism, hypoglycemia, glucose gel

Evidence-Based Update: Using Glucose Gel to Treat Neonatal Hypoglycemia

Purpose and Goal: CNEP # 2070

- Understand the challenges of managing neonatal hypoglycemia.
- Learn about using glucose gel to treat neonatal hypoglycemia.

None of the planners, faculty or content specialists has any conflict of interest or will be presenting any off-label product use. This presentation has no commercial support or sponsorship, nor is it co-sponsored.

Requirements for successful completion:

- Successfully complete the post-test
- Complete the evaluation form
Date

- December 2017 – December 2019

Learning Objectives

- Describe normal glucose homeostasis.
- Describe the characteristics of neonatal hypoglycemia.
- Describe the use of glucose gel for the treatment of hypoglycemia.

Introduction

- Hypoglycemia is commonly seen in the neonate
- It is the most common neonatal metabolic disorder
  - It is a leading cause of admission to the NICU
  - It affects as many as 5-15% of all neonates
- Most newborns experience transient hypoglycemia
- Prolonged hypoglycemia is not normal
  - The brain is dependent on glucose
  - Untreated hypoglycemia → poor outcomes

Fetal Glucose Homeostasis

- Glucose is a primary source of fetal energy
- Fetal glucose needs are met by the placenta
- A continuous supply of glucose is provided
- Glucose is stored as glycogen
  - Glycogen is initially stored in the placenta
  - By 24 weeks, it is stored in the liver
  - By 40 weeks, it is stored in cardiac and skeletal muscle
**Neonatal Glucose Homeostasis**

- Glucose is a primary source of neonatal energy
- Neonatal glucose needs are met by intermittent feeds
- Additionally, fetal glycogen stores are available
  - By term, glycogen liver stores are twice those of adults
  - By term, glycogen cardiac stores are 10 times those of adults
  - Increased glycogen stores balance removal of the placenta
  - Glycogen stores are depleted within 18-24 hours
- Breakdown of stored glycogen is hormone dependent
  - Insulin
  - Glucagon
  - Catecholamines
  - Corticosteroids
- There is a normal surge of hormonal activity at birth
  - Transient increase of serum glucose levels
  - Followed by ↓ in glucose levels within 3-4 hours

**Hypoglycemia**

- No uniform standards define neonatal hypoglycemia
- Several professional groups have developed guidelines
  - American Academy of Pediatrics
  - Pediatric Endocrine Society
  - Academy of Breastfeeding Medicine
  - Canadian Paediatric Society
- But none of these groups agree on a definition
- It is difficult to define hypoglycemia by a single number
  - American Academy of Pediatrics definition
  - First published in 1993 and revised in 2011
  - Glucose levels <45 mg/dL
National Consensus Guidelines
- Offer screening and treatment recommendations
- While offering individual practice support
- The consensus for when to treat is currently:
  - For symptomatic neonates
    - Glucose levels <45 mg/dL
  - For asymptomatic neonates
    - Glucose levels <40 mg/dL
  - For infants after 24 hours of age
    - Glucose levels <50 mg/dL

Causes of Hypoglycemia
- Hypoglycemia represents an imbalance
  - Between the utilization
  - And the supply of available glucose
- It results from ↓ glucose production and ↑ glucose utilization
  - Diminished glucose supply
  - Inadequate glycogen stores
    - SGA infants
    - Premature infants
  - Impaired glucose production
    - Hyperinsulinism
    - Endocrine Disorders
    - Inborn Errors of Metabolism
  - Increased glucose utilization
    - Sepsis
    - Cold Stress
    - Perinatal Stress/Hypoxia
    - Hyperinsulinism
**Pathophysiology of Hypoglycemia**

- Maternal-Placental transfer of energy substrates
  - Including glucose
  - Meets fetal metabolic demands
  - Meets fetal energy demands
- When the umbilical cord is cut
  - The maternal source of glucose abruptly ends
  - Neonatal glucose levels abruptly fall
    - Over the first 2-4 hours
  - Neonatal glucose homeostasis is initiated
    - Metabolic adaptations
    - Endocrine adaptations
    - Utilization of energy substrates
      - Glycogen
      - Ketone bodies
      - Amino acids
      - Fatty acids
      - Lactate
      - Glycerol
- Glucose is the primary energy source for the brain
  - It is critical for brain metabolism
  - It is just as vital as oxygen
- Neonates have a high rate of glucose utilization
  - The neonatal brain is disproportionately large
  - The brain uses up to 95% of available glucose
- Preterm infants are at higher risk of hypoglycemia
  - Proportionally larger brain size
  - Markedly decreased glycogen stores

**Infants of Diabetic Mothers**

- More than 100,000 infants born each year
• More than 50% will develop hypoglycemia
• Hypoglycemia is related to hyperinsulinism
  • Fetal exposure to glucose → pancreatic overstimulation
  • Fetal pancreatic overstimulation → hyperinsulinism
  • Fetal hyperinsulinism → decreased utilization of glycogen

Clinical Manifestations

• Hypoglycemia may be detected by routine monitoring
• Neonates are frequently asymptomatic
• Signs can be subtle and non-specific
  • Jitteriness
  • Tremors
  • Irritability
  • Hypotonia
  • Apnea
  • Bradycardia
  • Cyanosis
  • Tachypnea
  • Poor suck
  • Poor feeding
  • Weak cry
  • High-pitched cry
  • Hypothermia
  • Seizures

Identifying Infants at Risk

• Recognition of infants at risk is critical
• Infants at risk should be closely monitored
• There are 4 main groups of at risk infants:
  • Preterm, Post-Term and SGA infants
- Preterm infants have \( \downarrow \) glycogen stores
- SGA infants have \( \downarrow \) glycogen stores
- Post-term infants have \( \downarrow \) glucose transfer
- Infants of Diabetic Mothers
  - Hyperinsulinism
- Extremely Low Birthweight Infants
  - Glucose intolerant
  - Insulin resistant
- Infants Exposed to Maternal Medications
  - Terbutaline
  - Metformin
  - Valproate

**Evaluation and Treatment**

- At risk infants should be screened within 1 hour of birth
  - Pre-feed glucose screens are recommended
  - Serum glucose confirmation is recommended
    - Glucose screens are 15\% lower than serum levels
    - RBC metabolism continues in serum samples
    - Glucose levels may be artificially decreased
    - Transporting serum on ice reduces metabolism
  - Follow up screens should be every 1 hour until stabilized
  - Once stabilized, every 4-6 hour screening is adequate
- Treatment goals are prevention and prompt resolution
- Adequate oral feeds are essential
  - Breastfeeding should be encouraged
  - Formula supplements are not best practice
- Continuous glucose infusions may be necessary
  - Especially if hypoglycemia is persistent
- The use of 40\% glucose gel may be beneficial
Treatment with Glucose Gel

- None of the published guidelines discuss glucose gel
- Treatment recommendations include
  - Oral feeding with breastmilk or formula
  - IV dextrose for symptomatic infants
  - IV dextrose for asymptomatic infants when feeding alone does not resolve the hypoglycemia
- Hypoglycemia often requires NICU admission
  - Separates the baby from the mother
  - Delays breastfeeding and bonding
- Even one bottle of formula
  - Negatively affects the infant gut
  - Changes gut flora for up to 4 weeks
- 40% glucose gel offers a treatment alternative
- Glucose gel has not been studied extensively in neonates
  - It was first studied in 1990 and again in 2000
  - Randomized controlled studies have recently been conducted
  - Several studies show that glucose gel
    - Is inexpensive
    - Is noninvasive
    - Is readily available
    - Is easy to administer
  - Several individual hospitals have used glucose gel
  - Several individual protocols have been developed
- Oral glucose gel is the first line treatment
  - Older infants
  - Diabetic adults
- Glucose is the one of the sugars formed
  - When breastmilk is metabolized
  - It does not negatively affect the gut
- Studies show that glucose gel
  - Is more effective than feeding
• Decreases the use of formula
• Supports the use of colostrum
• Supports exclusive breastfeeding
• Rebound hypoglycemia has not been found
  • Glucose gel is well tolerated
  • There are no adverse effects
• 40% gel provides 400 mg/kg glucose
  • It consists of 40% glucose
  • Plus water and glycerin
• It can be administered in the infants’ cheeks
  • Buccal mucosa is highly vascularized
  • Absorption rate is equal to IV dextrose
• Dosing is weight based
  • 2.0 kg → 1.00 ml
  • 2.5 kg → 1.25 ml
  • 3.0 kg → 1.50 ml
  • 3.5 kg → 1.75 ml
  • 4.0 kg → 2.00 ml
  • 4.5 kg → 2.25 ml
  • 5.0 kg → 2.50 ml
• The dose can be easily divided
  • Deliver ¼ or ½ to each cheek
  • Gently massage cheek
  • Repeat as needed
• When exclusively breastfeeding
  • Gel can be given after a feed
• When supplementing by bottle
  • Gel can be given before a feed

Long-Term Outcomes

• Significant hypoglycemia has been linked to brain injury
• Long-term outcomes include:
  • Smaller head size
  • Developmental delay
  • Poor neurodevelopmental outcomes
• Brain injury has been correlated by MRI
  • Impaired cognitive development
  • Increased cognitive disability
• Mild to moderate transient hypoglycemia
  • Has not been consistently linked to poor outcomes
• The use of glucose gel to treat hypoglycemia
  • Has shown decreased NICU admissions
  • Has shown decreased treatment failure
• The use of glucose gel has been shown to
  • Support successful breastfeeding
  • Support normal neurodevelopment
  • Improve parent satisfaction
  • Decrease costs of treatment

Summary

• Hypoglycemia is a common neonatal disorder
• Infants may present without symptoms
• At risk infants should be monitored closely
• Prevention, early detection, and intervention are critical
• The use of glucose gel may prevent NICU admissions

References

Chan, S.W. 2013. Neonatal Hypoglycemia. Up-To-Date: http://www.uptodate.com/contents/neonatal-hypoglycemia?source=search_result&search=neonatal+hypoglycemia&selectedTitle=1~32#H1


**Evaluation**

- Required fields

**Your information**

*Your name

*Your email address
Test

- Glucose is the primary source of energy for the brain.
  - True
  - False

- Hypoglycemia is caused by decreased glucose production and increased glucose utilization.
  - True
  - False

- Infants are frequently asymptomatic and hypoglycemia is often detected by routine monitoring.
  - True
  - False

- Formula feeding or IV dextrose infusions are the only available options for treating neonatal hypoglycemia.
  - True
  - False
• Glucose gel is inexpensive, easy to administer, noninvasive and has been shown to have no negative side effects.
  ○ True
  ○ False

• Untreated hypoglycemia can result in brain damage and poor neurodevelopmental outcomes.
  ○ True
  ○ False

**Evaluation**

We hope you found this educational offering both interesting and informative. We’d like to hear from you and appreciate you taking the time to answer these evaluation questions.

*Were you able to complete this activity in the allotted time?*
  ○ Yes
  ○ No

Were you informed of the following disclosures?

*Purpose of learning activity*
  ○ Yes
  ○ No

*Requirements for successful completion of this CNE activity*
  ○ Yes
  ○ No

*Presence or absence of conflict of interest of planning committee members*
  ○ Yes
  ○ No
*Presence or absence of conflict of interest of content specialist(s)/author(s)/feedback person(s)
  ○ Yes
  ○ No

*Were your personal objectives successfully achieved?
  ○ Yes
  ○ Somewhat
  ○ No
  If not, why not?

*What one thing might you do differently in your practice after this session?

Please evaluate the brief:

*Presentation organized
  ○ Excellent
  ○ Very good
  ○ Good
  ○ Fair
  ○ Poor

*Materials offered relevant content
  ○ Excellent
  ○ Very good
  ○ Good
  ○ Fair
  ○ Poor
*Assistance provided as needed
  - Excellent
  - Very good
  - Good
  - Fair
  - Poor
  - Not applicable

*Overall strength of presentation
  - Excellent
  - Very good
  - Good
  - Fair
  - Poor

Stated objectives achieved?

*Describe normal glucose homeostasis.
  - Excellent
  - Very good
  - Good
  - Fair
  - Poor

*Describe the characteristics of neonatal hypoglycemia.
  - Excellent
  - Very good
  - Good
  - Fair
  - Poor
*Describe the use of glucose gel for the treatment of hypoglycemia.

- Excellent
- Very good
- Good
- Fair
- Poor