Not So Sweet: Evaluation and Management of Infants of Diabetic Mothers

Clinical Advances in Pediatrics
September 27, 2017
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Disclosures
• None
• But…. I am a neonatologist NOT an endocrinologist 😊

Objectives
1. Review fetal anomalies and conditions associated with maternal diabetes
2. Describe initial evaluation and management for infants of a diabetic mother
3. Discuss current recommendations regarding the management of hypoglycemia

Clinical Case
• 37.3 week gestation infant
• 29 y/o G3P3 mother
• Pregnancy complicated by A2GDM and pre-eclampsia
• Maternal medications: PNV, Glyburide 7.5mg BID

Risk Factors
• Family history
• Prepreg. weight >110% ideal
• BMI >30
• Significant weight gain in early adulthood or b/w pregnancies
• Excess gestational weight gain
• Age >25
• Maternal BW >9lb or <8lb
• Previous baby >9lb
• Higher parity
• H/o unexplained perinatal loss
• Previous infant with congenital anomalies
• Glycosuria at first prenatal visit
• Polycystic ovary syndrome
• Use of glucocorticoids
• Essential hypertension or pregnancy-related hypertension
• Metabolic syndrome
• Non-Caucasian Race

How is gestational diabetes diagnosed during pregnancy?
What risk factors predispose mothers to gestation diabetes?
Definitions

**Overt diabetes:**
- Women who meet any of the following criteria at their initial prenatal visit:
  - Fasting glucose >126
  - A1C >6.5
  - Random glucose >200

**Gestational Diabetes:**
- Women with onset or first recognition of abnormal glucose tolerance during pregnancy
- ACOG 2017 Practice Guidelines:
  - All women screened with OGTT at 24-28 weeks
  - Two-Step Screen:
    - 50 gm, 1 hour OGTT
    - If abnormal: 100 gm, 3 hour OGTT

Modified White Classification

- Gestational diabetes -
  - Non-medication dependent: Class A
  - Insulin or medication dependent: Class B
- Pre-existing diabetes -
  - Class B - developed > 20 Y/O; history < 10 years, no vascular complications.
  - Class C - developed 10 – 19 Y/O, or history 10-19 years, no vascular complications.
  - Class D - developed < 10 Y/O, history > 20 years, vascular complications are present.
  - Class F – with nephropathy.
  - Class R – with retinopathy (retinal damage).
  - Class T – with kidney transplant.
  - Class H – with coronary artery or other heart disease.

Clinical Case

- Mother’s Diabetic History:
  - Abnormal 3hr GTT at 28.4 weeks
  - Starts with diet control then Glyburide added
    - Glyburide dose increased to 7.5mg BID secondary to elevated fasting glucose
  - Clinic visit day prior to delivery:
    - BG: avg 105
    - Fasting 77-107 (5/10 elevated)
    - PP B: 87-153 (3/9 elevated)
    - PP L: 76-151 (4/9 elevated)
    - PP D: 87-136 (2/8 elevated)

- What perinatal morbidities are associated with gestational diabetes?
- Why does macrosomia develop?

Perinatal Adverse Outcomes

- Preeclampsia
- Polyhydramnios
- Macrosomia
- Birth trauma
- Operative delivery
- Stillbirth

The Placenta & Macrosomia

- Maternal nutrients are transported across the placenta
- Hormones are NOT transported across the membranes
  - Fetal endocrine responses are mediated by nutrients transported
    - Increased levels of insulin and insulin-like growth factor
- Placental growth is associated with macrosomia
- Alterations in expression of glucose and AA transporters
- Growth acceleration begins at 25-28 weeks
  - Brain not affected; head growth is normal
Clinical Case
- Delivered via induced vaginal delivery at 37 3/7 weeks
- APGARs: 8/9  BW: 3.12 KG
- Initial blood glucose 32
  - Improves to 54 after feeds
- Transferred to NICU at 25hr due to hyperbilirubinemia
- Allowed to breastfeed ad lib. Mother requests Enfamil supplementation
- H&H 17.9/55, Retic 4.3%

• What is the pathogenesis for the infants hypoglycemia?
• If the infant remained hypoglycemic, what would be the management?
• Why is hyperbilirubinemia associated gestational diabetes?

Hypoglycemia
- Carry over of the fetal hyperinsulinemic state with cessation of maternally derived hyperglycemia
- Counter-regulatory hormones and stores insufficient and immature
  - Inadequate glycogen supply
  - Impaired glucose production
  - Increased glucose utilization
- Degree of hypoglycemia correlates with maternal glucose control, especially at the time of delivery

• Clinical Manifestation:
  - Jitteriness/tremors
  - Hypotonia
  - Change in level of consciousness
  - Apnea, bradycardia or cyanosis
  - Tachypnea
  - Poor suck/feeding
  - Weak or high-pitched cry
  - Hypothermia
  - Seizures

• Definition: Blood glucose concentration at which intervention should be initiated to avoid significant morbidity, especially neurologic sequelae
  - Exact cut off remains elusive. 40-50mg/dl commonly used
• Glucose concentration measured in whole blood is 15% lower than plasma

• Common even without GDM
  - 10% of normal term infants cannot maintain plasma glucose >30 if 1st feeding is delayed for 3-6 hours after birth
• Infants at risk for hypoglycemia:
  - Premature infants
  - LGA or SGA
  - Infants who require intensive care
  - Infants whose mothers were treated with beta adrenergic or oral hypoglycemia agents
  - Infants with polycythemia
Hypoglycemia

- Monitoring the at risk infant
  - Within 1-2 hours after birth
  - Before feedings
  - Continued for 12-24 hours AND until feedings are well established and glucose values have normalized
  - Evaluate for other causes if persistent or severe

Hypoglycemia

- Differential Diagnosis
  - Beckwith-Wiedmann
  - Alloimmune hemolytic disease of the newborn
  - Perinatal asphyxia
  - Maternal sulfonylurea or terbutaline use
  - Hyperinsulinemic hypoglycemia of infancy
  - Sepsis
  - Polycythemia
  - Hypothermia
  - Hepatic dysfunction
  - Endocrine disorders
  - Inborn errors of metabolism

Hypoglycemia

Treatment: 2011 AAP Clinical Report

- Parenteral glucose infusion if symptomatic with glucose <40
- Initial oral feeding to the following asymptomatic infants:
  - <4 hours old and glucose <25
    - if blood glucose fails to increase- parental glucose
    - if blood glucose increases to 25-40- oral feeding or parental glucose
  - 4-24 hours old and glucose <35
    - if blood glucose fails to increase- parental glucose
    - if blood glucose increases to 35-45- oral feeding or parental glucose

Hypoglycemia

- Treatment
  - Parental therapy
    - Initial bolus of 2ml/kg of 10% dextrose
    - Followed by glucose infusion at a GIR of 6-8
    - Central venous access required if >D12.5% is needed to achieve desired GIR
    - Attempt to taper as feedings are advanced
  - Recheck blood sugar 1 hour after any interventions

Hyperbilirubinemia

- Polycythemia
- Macrosomia leading to bruising at birth
- Delayed clearance

Clinical Case

- Hypocalcemic on DOL #1 with Ca of 7.8
- Worsens on DOL #5- Ca 6.8, iCa 0.93
  - Phos 6.8
  - PTH 46.9 (normal)
  - T4 1.6, TSH 2.12
  - Calcitonin 3.3 (normal)
- Calcium levels improve, but remain low
- Discharged with outpatient follow up
• Why are IDMs at risk for hypocalcemia?
• This infant had hypoglycemia, hyperbilirubinemia and hypocalcemia, presumably related to gestational diabetes, what other conditions was she lucky to avoid?

Hypocalcemia
• Occurs in 5-30% of IDMs
• Lowest Ca at 24-72 hours
• Typically asymptomatic
• May be jittery. Rarely develop seizures
• Delay in the normal PTH surge postnatally
  – Maternal diabetes may cause increased urinary loss of magnesium, which blunts parathyroid hormone secretion
• Typically resolves without treatment

Morbidity in IDM

Congenital Malformations
• Cardiovascular: Conotruncal anomalies (TGA, TA, single ventricle), Defects (VSD, ASD, PDA, CoA), Structural (cardiomegaly, septal hypertrophy, single umbilical artery)
• Neurologic: caudal regression syndrome, anencephaly, spina bifida
• Renal: Hydronephrosis, renal agenesis, ureteral duplication
• GI: duodenal atresia, imperforate anus, small left colon syndrome

• Macrosomia and visceromegaly:
  – Premature birth
  – Congenital anomalies: club foot, shoulder dystocia, bronchial atresia, diaphragmatic hernia, vertebral anomalies
  – Metabolic disturbances: hypoglycemia, hypocalcemia, hypomagnesemia

• Cardiorespiratory:
  – Cardiac: PPHN
  – Respiratory: RDS, TTN-B

• Hematologic:
  – Polycythemia, Hyperbilirubinemia, Thrombocytosis

Congenital Malformations
• Neurologic/Skeletal:
  – Caudal regression syndrome
  – Agenesis or hypoplasia of femurs associated with agenesis of the lower vertebrae/sacrum
  – Anencephaly
  – Spina bifida

Congenital Malformations
• Gastrointestinal:
  – Small left colon syndrome
  – Situs inversus
  – Duodenal atresia
  – Imperforate anus

Congenital Malformations
• Cardiovascular:
  – VSD (most common), ASD, PDA
  – Conotruncal Anomalies- Transposition, Truncus
  – Single umbilical artery

• Renal:
  – Renal agenesis
  – Hydronephrosis
  – Ureteral duplication
Cardiopulmonary

- PPHN
- Hypertrophic Cardiomyopathy
  - Septal hypertrophy due to increased fat and glycogen deposition into the myocardium
  - Most are asymptomatic
  - May develop LVOT obstruction

Respiratory

- Respiratory Distress Syndrome
  - IDMs 4-6x times greater risk
  - Hyperinsulinemic state restricts substrate availability for surfactant biosynthesis and impedes fibroblast-pneumocyte factor
- Transient Tachypnea of the Neonate
  - Scheduled C/S without labor

Hematologic

- Polycythemia
  - Increased erythropoietin production due to state of relative hypoxemia from increased metabolic rate in hyperinsulinemic state
- Thrombocytopenia
- Hyperviscosity
  - Renal vein thrombosis

Long-term Complications

- Childhood obesity
- Increased risk of developing diabetes later in life
- ADHD (?)

Summary

- The prevalence of gestational diabetes is increasing due to increasing rates of obesity
- GDM increases the chances of adverse outcomes for both the mother and infant
- Diabetes cause molecular changes in the placental
- Glycemic control is key
- Macrosomia and hypoglycemia are the most common complications for the infant
- Congenital anomalies are related to hyperglycemia during organogenesis

References

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Questions?