INFANT OF A DIABETIC MOTHER

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Newborn Medicine

Disclosure
I have no conflict of interest to disclose

Objective
- Epidemiology
- Normal newborn transition
- Fetal adaptation to maternal hyperglycemia
- Abnormal postnatal metabolism
- Common clinical findings
- Medical management
- Morbidity and mortality / Outcomes
Which Baby Is IDM?

Epidemiology

- Nearly ½ IDM are admitted to the NICU
- Infants can be large or small for gestational age
  - SGA infants are results of maternal renal insufficiency
  - At even higher risk for perinatal asphyxia and adverse outcomes
- Higher risk for c-section due to macrosomia and poor transition to extrauterine life
- Premature delivery

Normal Transition

- Fetal glucose concentration is 55 mg/dl throughout gestation
- Clamping of umbilical cord disrupts placental glucose supply
- A rapid decline in the first few hours of life to as low as 30 mg/dl.
- Resolution of hypoglycemia by 4 hours of age to “normal” levels
- Gluconeogenesis in hepatocytes, mobilization of glycogen by glycolysis, release of lactate, amino acid, glycerol (and ketone bodies after the first few days)
- Process is enhanced by catecholamine and cortisol surges at time of birth
Fetal Adaptation to Maternal Hyperglycemia

• Fetal hyperglycemia, hyperinsulinemia, and macrosomia
  • Insulin-sensitive tissues: liver, cardiac muscle, and subcutaneous fat

• Increased metabolic rate, increased oxygen consumption, and fetal hypoxia
  • Increased erythropoiesis, polycythemia, hyperviscosity
  • Increased catecholamine production, hypertension and cardiac hypertrophy

• Normal brain and head growth result in disproportional head-to-shoulder ratio
  • Increased risk for shoulder dystocia/brachial plexus injury
Fetal Adaptation to Maternal Hyperglycemia

- Small left colon syndrome – transient obstruction, delayed innervation of ganglions
- Not to be confused with Hirschsprung's disease – no ganglion, irreversible

Fetal Adaptation to Maternal Hyperglycemia

- Excess glucose is teratogenic
- Pre-gestational diabetes leads to congenital anomalies:
  - Cardiac defects (TGA, DORV, VSD)
  - Caudal regression syndrome (sacral agenesis)
  - Neural tube defects

What Are The Common Findings On Exam
Common Findings

• Large for gestational age – BW > 90 %ile or gestational age, or > 4 kg
• Respiratory distress – delayed maturation due to hyperinsulinism
• Murmur
• Plethoric
• Bruising, brachial plexus injury
• Hypotonia, immature sucking, poor feeding
• Delayed passage of meconium
• Hyperbilirubinemia – due to polycythemia
• Hypocalcemia and hypomagnesemia – jittery, seizure activity,

Workup

• Serum glucose
  • < 40 mg/dL is abnormal in the first 24 hours;
  • Persistent low glucose despite a high glucose infusion rate > 8 mg/kg/min
• CBC
  • Hematocrit > 65 is concerning for polycythemia
  • Thrombocytopenia may occur due to bone marrow crowding
• Electrolyte measurement
  • Calcium, Magnesium, Bilirubin
• Arterial blood gas
  • Respiratory distress

Workup

• X-ray
  • Cardiomegaly, pulmonary vascular markings, retained fetal lung fluid, focal abnormalities, bone details, bowel gas pattern, presence of sacrum
• ECHO
  • Septal hypertrophy – left ventricular outflow obstruction
  • Structural anomalies – prostaglandin dependent lesions
• Barium enema
  • If GI obstruction is a concern
Workup

- Counter-regulatory hormones
  - During episode of hypoglycemia, obtain:
    - Serum insulin level → high
    - Free fatty acids → low
    - Ketones (beta-hydroxybuterate) → low
    - Cortisol → normal (to rule out adrenal insufficiency as etiology)

- Glucagon challenge
  - 200 mcg/kg IV or IM
  - Serum glucose at, 30, 45, and 60 minutes
  - Rise of glucose of at least 30 mg/dL above the baseline is diagnostic

Management

- Hypoglycemia
- Electrolyte abnormalities
- Respiratory support
- Cardiovascular support
- Birth trauma

Management - hypoglycemia

- Definition: an abnormally diminished content of glucose in the blood
- Early studies in the 1930s proposed the following:
  - Mild: 40-50 mg/dL
  - Moderate: 20-40 mg/dL
  - Severe: < 20 mg/dL
- Multicenter observational data in 1980s
  - An association between glucose value < 47 mg/dL and adverse neurodevelopmental outcome
  - Risk doubled if persistent for more than 3 days
  - Risk tripled if persistent for more than 5 days
Management - hypoglycemia

Maternal glycemic control during pregnancy and labor

Hypoglycemia occurs within the first few hours after birth

Often need glucose supplementation by IV infusion or nutritional hyperalimentation

Glucose gel

Medications
Management – Hypoglycemia

Early establishment of enteral feeding!
- Milk supply of a newly paras woman is inadequate in volume in the first few days
- Breast feeding is great! But it should be supplemented with formula until the milk flow is well established
- Typical intake volume by a term infant is 40-80 ml/kg/day in the first 24 hours
- It is ok to give a baby some formula
- Set the baby up for success!

Management – Hypoglycemia

IV dextrose therapy
- Initial glucose infusion rate is generally 4 – 6 mg/kg/min
- Can be higher in preterm infants, 6-8 mg/kg/min
- D50 bolus of 2 ml/kg can be given for extremely low glucose levels
- Dextrose concentration up to 30% may be required to delivery glucose infusion rates in the 15-30 mg/kg/min range
- Central line placement is necessary for infusion of dextrose concentration > 12.5%

How high/low should the serum glucose be during IV infusion?

Management – Hypoglycemia

- Glucose gel protocol [picture]
Management – Hypoglycemia

• First line medication: Diazoxide
  ▪ Binds to the intact SUR1 component of the pancreatic beta-cell K+ -ATP channels
  ▪ Effective dose range 5-15 mg/kg/day
  ▪ Common side effects: hypertrichosis (hairy babies), fluid retention, pHTN rare

• Second line medication: Octreotide
  ▪ For patients whom diazoxide therapy failed
  ▪ Long-acting somatostatin analogue
  ▪ Inhibits insulin secretion by hyperpolarization of beta-cells
  ▪ Effective dose range 5-25 mcg/dose every 4-6 hours
  ▪ May need continuous infusion if not responsive to bolus dosing

Management

• Full physician exam to assess for fractures, hematomas, brachial plexus injury
• Measure hematocrit in the first few hours of life
• Bilirubin monitoring throughout the hospital stay
• For jittery infants, check calcium and magnesium, supplement if necessary
• Seizures – call NICU
Morbidity and Mortality / Outcome

• Intrauterine exposure to hyperglycemia leading to fetal hyperinsulinism increases adipose tissue and pancreatic beta cells, leading to increased BMI and impaired glucose metabolism and obesity
• Risk present for both gestational and pre-gestational diabetes
• Can have poor neurodevelopmental outcome even with optimal glycemic control
• Smaller brain size, delayed brain maturation in infancy, low intelligence scores
• Impact on health in adulthood:
  • Impaired glucose tolerance
  • Blunted insulin secretion
  • Hypertension

References

• Riskin A, Davis-Papa K. Infant of a Diabetic Mother. [UpToDate]. 2018