A Spoonful of Sugar
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Grand Rounds 6/23/2017

No conflict of interest or disclosures
Praveen Chandrasekharan

Topics Discussed
• Asymptomatic hypoglycemia and its significance
• Who are at risk?
• Our practice in the past
• Newer therapy - dextrose gel
• Use of oral dextrose gel in our hospital
• Effectiveness of the therapy
• Outcomes
• Future studies
Hypoglycemia

- Neonatal hypoglycemia is the most common cause of preventable brain damage in the newborn period
- 5-15% of otherwise healthy neonates present with hypoglycemia
- Some of these infants fail to normalize their blood glucose by feeds alone and need intravenous dextrose therapy

Basis of Treatment - Asymptomatic Hypoglycemic Infants

- Controversy still surrounds the definition, significance and management of neonatal hypoglycemia
- Little evidence exists to guide treatment
- A blood glucose level maintained above 47 mg/dl was not associated with adverse neurologic outcome
- In our institution, we use a cut off level for blood glucose <45 mg/dl

Why do we chase numbers?

- Theory – transitional hypoglycemia is secondary to high insulin – impedes ketone production
- Blood glucose falls
- Decrease in insulin
- Increase in catecholamines, glucagon, glucocorticoids
- Stimulates gluconeogenesis and glycogenolysis and stabilizes blood sugar
- Glucose crosses the placenta by carrier mediated facilitated diffusion
- Glucose supply from placenta
- Brain glucose uptake is directly proportional to blood glucose concentration. If ketones are not available can cause damage

Hypoglycemia and Hospital Costs

• A large number of asymptomatic at risk neonates are screened for hypoglycemia
• This is due to the well established relationship between hypoglycemia and neurological impairment
• Approximately 10% of these asymptomatic neonates require admission to a neonatal intensive care unit
• This costs an estimated $2.1 billion annually in the United States alone

AAP Guidelines

Screening and Management of Postnatal Glucose Homeostasis in Late Preterm and Term SGA, IDA/LGA Infants

Incidence of Hypoglycemia in Babies at Risk

Treatment options for asymptomatic hypoglycemia

- Feeding
  - Breast feeding
  - Expressed breast milk
  - Formula
- Oral dextrose gel – Popular therapy now (focus of this talk)
- Intravenous dextrose

Oral Dextrose Gel (DG)

- 40% dextrose gel is commonly used for treating hypoglycemic adults
- Dextrose gel together with breastfeeding, expressed breast milk or formula increases blood sugar levels
- Potential advantages of this treatment are:
  - Oral administration in newborn nursery
  - Keeps mother and baby together
  - Easy to administer & low cost

Previous Trial: The Sugar Babies Study

- Randomized, double-blind, placebo-controlled trial by Harris et al. (230 infants: 115 DG and 115 placebo)
- Concluded that treatment with 40% dextrose gel is more effective than feeds alone
- Inexpensive and can be purchased commercially for $2 per baby or can easily be made in the hospital pharmacy
- They recommend DG be considered for first-line management of late preterm and term hypoglycemic babies in the first 48 h after birth
Oral Dextrose Gel Systemic Review – Weston et al.

- **Need for IV dextrose**
  - 0.78 (0.46 - 1.32)
  - 2 studies – 312 infants

- **Separation from mother**
  - 0.54 (0.31 - 0.93)
  - 1 study – 237 infants

- **Exclusive breast feeding**
  - 1.10 (1.01 - 1.19)
  - 1 study – 237 infants

Relative Risk (95% CI)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Relative Risk</th>
<th>95% CI</th>
<th>Studies</th>
<th>Infants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Need for IV dextrose</td>
<td>0.78</td>
<td>0.46 - 1.32</td>
<td>2</td>
<td>312</td>
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<td>Separation from mother</td>
<td>0.54</td>
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</tbody>
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**BMJ**

**Supporting ‘Baby Friendly’: a quality improvement initiative for the management of transitional neonatal hypoglycaemia**

Claire Stewart, Emma Sage, Peter Reynolds @ St. Peter’s Hospital, Surrey, UK – presented their work in 2014 and published in 2015

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**‘Baby Friendly’ study - Findings**

Pre and post 6 months after implementation of protocol:
- Number of infants – 380 pre vs. 339 post implementation
  - 73% decrease in the number of babies admitted to NICU
  - 83% decrease in total admission days
  - 88% increase in breast feeding rates at 3 months

After review, our multidisciplinary committee added glucose gel to the neonatal hypoglycemia protocol.

- Weight base dosing of dextrose gel was established.
- Mandatory educational sessions were provided to all RNs focused on use of the new algorithm and technique to administer the gel.

To treat neonatal hypoglycemia in NBN at Women and Children's Hospital and Millard Fillmore Suburban Hospital, use of 40% dextrose gel was started in November 2014.
Oral Dextrose Gel Reduces the Need for Intravenous Dextrose Therapy in Neonatal Hypoglycemia


Objectives

- To determine whether treatment with 40% dextrose gel is more effective than feeding alone in reversing neonatal hypoglycemia in term and near term babies in the first 48 hours after birth admitted to NBN
- To determine the effect of treatment with 40% dextrose gel on number of NICU admissions for intravenous fluids

Methods

- After IRB approval, a retrospective study was conducted pre and post Dextrose Gel use: 05/2014 to 10/2014 and 11/2014 to 04/2015
- Asymptomatic hypoglycemic (blood glucose <45 mg/dl) infants in newborn nursery (NBN) were given up to a maximum of 3 doses of 40% oral Dextrose Gel (200mg/Kg or 0.5ml/Kg applied to buccal mucosa)
- Transfer to NICU for IV fluids was considered treatment failure
Inclusion and Exclusion Criteria

- **Inclusion Criteria**
  - Infants at risk for neonatal hypoglycemia (small for gestational age, large for gestational age, an infant of a diabetic mother) who were asymptomatic
  - 35 weeks gestation or greater
  - Age < 48 hours after birth

- **Exclusion Criteria**
  - Symptomatic hypoglycemia
  - Congenital malformations

### Baseline Characteristics: Pre and Post Dextrose Gel Therapy

<table>
<thead>
<tr>
<th>Parameters</th>
<th>May 1, 2014 to Oct 31, 2014</th>
<th>Nov 1, 2014 to April 30, 2015</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total live births</td>
<td>2937</td>
<td>2654</td>
<td></td>
</tr>
<tr>
<td>Total asymptomatic infants with hypoglycemia (%)</td>
<td>248 (8.4)</td>
<td>250 (9.4)</td>
<td>0.20</td>
</tr>
<tr>
<td>Improved with feeds in controls/feeds + DG in cases (%)</td>
<td>144 (58)</td>
<td>184 (74)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Transferred to NICU (%)</td>
<td>104 (42)</td>
<td>66 (26)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Infant of Diabetic Mother (%)</td>
<td>74 (30)</td>
<td>70 (28)</td>
<td>0.69</td>
</tr>
<tr>
<td>Total LGA, SGA, IUGR %</td>
<td>82 (33)</td>
<td>100 (40)</td>
<td>0.11</td>
</tr>
</tbody>
</table>

### Responders Vs. Treatment Failures

- Infants who responded to that dose
- Infants who required another dose
- Infants who failed and required IV
Economic Impact of using oral dextrose gel

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Cost USD (mean ± S.D)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost for a NICU admission to treat hypoglycemia with IV dextrose therapy</td>
<td>31,820 ± 13,272</td>
</tr>
<tr>
<td>Cost for a regular NBN admission</td>
<td>4415 ± 819</td>
</tr>
<tr>
<td>Cost for treating hypoglycemia successfully with oral dextrose gel</td>
<td>5037 ± 873</td>
</tr>
</tbody>
</table>

Summary of our study

- Number of infants transferred from NBN to NICU for hypoglycemia decreased from 35/1000 to 25/1000 live births
- Total NICU admissions for asymptomatic hypoglycemia decreased from 20.6% to 14.8%
- After introduction of DG, only 26% of asymptomatic hypoglycemic neonates in NBN were transferred to NICU for IVF compared to 42% during the control phase (feeds alone)

Are there any preservatives in DG? by Joe Palumbo & Emily Polischuk

- There is 0.6 mg of methyl-paraben per gram of dextrose gel
- In 200mg/kg of dextrose gel per dose there is 0.12 mg/kg of methyl-paraben
- With a limitation of three doses per patient placed on this product it is unlikely that a patient will go above the 10 mg/kg daily intake cutoff
- Conclusion - Due to this the oral glucose product can be used safely in this hospital
Neurodevelopment outcome with DG – Harris et al.

- Neurosensory impairment (cognitive, language or motor score below 1 SD or cerebral palsy or blind or deaf)
- Processing difficulty (executive function or global motion perception worse than 1.5 SD from the mean)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Dextrose gel vs. Placebo</th>
<th>Relative Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neurosensory impairment</td>
<td>38% vs. 34%</td>
<td>1.11 (0.75 – 1.63)</td>
</tr>
<tr>
<td>Processing difficulty</td>
<td>10% vs. 18%</td>
<td>0.52 (0.23 to 1.15)</td>
</tr>
</tbody>
</table>

Prevent hypoglycemia before it occurs

- The incidence of hypoglycemia was low in babies who prophylactically received a single dose of 200 mg/kg dextrose gel (relative risk (RR) 0.68; 95% CI 0.47 to 0.99)
- Number needed to treat was 10 (5 – 115)
- No difference in the rate of NICU admission among groups treated with different doses of dextrose gel
- Breastfeeding rates were not different
- No adverse events

Studies at Pediatric Academic Society - 2017

- Clinical process model utilizing dextrose gel for neonatal hypoglycemia improves outcome – University of Minnesota
- Prophylactic dextrose gel does not prevent neonatal hypoglycemia: Baylor, Texas
- Implementation of Dextrose Gel in Newborn Nursery and subsequent NICU Transfers
Dextrose Gel - In a nutshell

- Many centers have started implementing dextrose gel along with feeding for treatment of hypoglycemia
- So far no adverse events have been reported
- Quality improvement and retrospective studies have shown mixed results
- More RCTs and follow up studies for oral dextrose gel are required
- Ongoing trial for prevention of hypoglycemia (hPOD)