MEDICAL UNIVERSITY OF SOUTH CAROLINA
VALUE INSTITUTE
Evidence-Based Practice Brief
Hypoglycemia in Normal Newborns

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ASK THE QUESTION

Question(s): In normal newborns, what is the effect of using dextrose or glucose gel as treatment for hypoglycemia?

SEARCH FOR EVIDENCE

Databases: PubMed, CINAHL

PubMed search strategy: hypoglycemia (filter: birth-1 month); “neonatal hypoglycemia”

Filters: English, Humans, Published 2011-Present

CRITICALLY ANALYZE THE EVIDENCE

The current policy regarding hypoglycemia in the normal newborn population (N-49) is based on the American Academy of Pediatrics (AAP, 2011) guideline for Postnatal Glucose Homeostasis in Late-Preterm and Term Infants, which was re-affirmed in 2015. Around the time of this re-affirmation, the Pediatric Endocrine Society (PES, 2015) released recommendations for Evaluation and Management of Persistent Hypoglycemia in Neonates, Infants and Children. A recent evidence-based practice brief (Newnam, K., 2017) contrasted the recommendations from both medical organizations, reporting that:

• PES expanded the risk criteria for screening to include: perinatal stress, pre-mature or post-mature, family history of genetic hypoglycemia, congenital syndromes or abnormal physical features, and
• PES criterion for administering IV dextrose is < 50mg/dL in infants with transient asymptomatic neonatal hypoglycemia because “newborn alternate fuels often not present in first few days”.

The PES guideline did not provide recommendations for screening times, treatment or prevention.

There were five research articles found addressing the effect of using dextrose or glucose gel as treatment for hypoglycemia, including one Cochrane systematic review (Weston et al., 2016). Their meta-analysis of two RCTs showed no evidence of a difference between dextrose gel and placebo regarding the need for IV treatment (typical RR 0.78, 95% CI 0.46-1.32), but did find that infants treated with dextrose gel were less likely to be separated from their mothers for treatment (RR 0.54, 95% CI 0.31-0.93) and were more likely to be exclusively breastfed after discharge (RR 1.10, 95% CI 1.01-1.18).

Three articles (Bennet et al., 2016; Rawat et al., 2016; Scheans et al., 2017) were quality improvement initiatives based on the protocol by Harris et al. (2013) for term newborns at risk of neonatal hypoglycemia, which included:
• Blood glucose testing by heel lance 1 hour after birth, then every 3-4 hours before feeds for the first 24 hours, and every 6-8 hours for subsequent 24 hours; continuous glucose monitor placed if hypoglycemic and remained in place for at least 48 hours (up to 7 days).
• If hypoglycemic at any point, gel 200 mg/kg (0.5 mL/kg) was massaged into the buccal mucosa and baby was encouraged to feed; if feeding poor baby was given expressed breastmilk or formula by syringe.
• Blood glucose was tested 30 minutes after gel administration; treatment repeated if baby remained hypoglycemic or if hypoglycemia recurred; up to six doses of gel could be given over 48 hours.

All 3 QI studies showed a decrease in NICU admissions for IV dextrose and improvements in exclusive breastfeeding. Rawat et al. (2016) reported an absolute risk reduction for IV dextrose therapy after the introduction of dextrose gel of 15.54% (95% CI 7.32–23.76) for an overall cost savings of $642,951 USD over the 6-month study period.

Additionally, secondary analysis of data from the Harris et al. (2013) study determined that the changes in blood glucose concentration after oral dextrose treatment were significantly higher than with placebo (marginal change: +3.0 mg/dL; 95% CI 0.7-5.3; p = 0.01), and that breastfeeding was associated with reduced requirement for repeat gel treatment (OR 0.52; 95% CI 0.28-0.94; p = 0.03).

PICO Question: In normal term neonates, what is the effect of using dextrose or glucose gel as treatment for hypoglycemia?

<table>
<thead>
<tr>
<th>Author/Date/ Journal</th>
<th>Purpose of Study</th>
<th>Study Design</th>
<th>Sample &amp; Setting</th>
<th>Outcomes</th>
<th>Design Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weston et al., 2016, Cochrane Database of Systematic Reviews</td>
<td>To assess the effectiveness of dextrose gel in correcting hypoglycemia and in reducing long-term neuro-developmental impairment</td>
<td>Systematic review</td>
<td>2 RCTs (312 infants)</td>
<td>No evidence of a difference between dextrose gel and placebo for major neurosensory disability at two-year follow-up (RR 6.27, 95% CI 0.77-51.03; 1 study, quality of evidence very low)</td>
<td>No evidence of a difference between dextrose gel and placebo regarding the need for IV treatment (typical RR 0.78, 95% CI 0.46-1.32; 2 studies, quality of evidence very low) Infants treated with dextrose gel were less likely to be separated from their mothers for treatment (RR 0.54, 95% CI 0.31-0.93; 1 study, quality of evidence moderate) -were more likely to be exclusively breastfed after discharge (RR 1.10, 95% CI 1.01-1.18; 1 study, quality of evidence moderate)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>-1 low risk of bias (Harris et al., 2013); 1 high risk of bias</td>
<td>Study Limitations =</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Systematic Review</td>
<td>Review did not address focused clinical question</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>Search was not detailed or exhaustive</td>
<td>Quality of the studies was not appraised or studies were of low quality</td>
</tr>
</tbody>
</table>
| | | | | Methods and/or results were inconsistent across studies |}
<table>
<thead>
<tr>
<th>Study</th>
<th>Overview</th>
<th>Findings</th>
<th>Limitations</th>
</tr>
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<tbody>
<tr>
<td>Bennett et al., 2016, Nursing for Women’s Health</td>
<td>To evaluate the implementation of a new treatment algorithm for newborns at risk for neonatal hypoglycemia that included oral administration of 40% glucose gel</td>
<td>Estimated rise in blood glucose concentration following dextrose gel was 0.4 mmol/L (95% CI -0.14-0.94; 1 study)</td>
<td>Events and thus have wide confidence intervals and the results are uncertain</td>
</tr>
<tr>
<td>Harris et al., 2017, The Journal of Pediatrics</td>
<td>To determine the change in blood glucose concentration after oral treatment of infants with hypoglycemia in the first 48 hours after birth</td>
<td>Increase in blood glucose concentration was greater after buccal dextrose gel than after placebo (marginal change: +3.0 mg/dL; 95% CI 0.7-5.3; p = 0.01) and greater after infant formula than after other feedings (marginal change: +3.8 mg/dL; 95% CI 0.8-6.7; p = 0.01)</td>
<td>Non-Experimental/Observational Studies (case-control, cohort, cross sectional, longitudinal, descriptive, epidemiologic, case study/series, survey)</td>
</tr>
</tbody>
</table>

**Study Limitations**

- None

**Publication Bias**

(e.g. pharmaceutical company sponsors study on effectiveness of drug)

**Increase Quality Rating** if:

- Large effect (When the relative risk of association between two factors is large or very large)
- Plausible confounders (When plausible residual confounding is directly impacting the magnitude of effect)

**Level of evidence for studies as a whole:**

- High
- Moderate
- Low
- Very Low
<table>
<thead>
<tr>
<th>Study</th>
<th>Description</th>
<th>Quality Improvement (pre-post)</th>
<th>Results</th>
<th>Study Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rawat et al., 2016, Biomed Hub</td>
<td>To study the effect of implementing dextrose gel supplement with feeds in late preterm/term infants affected by asymptomatic hypoglycemia on reducing IV dextrose therapy</td>
<td>Before and after implementation of a new protocol with glucose gel as first-line intervention for asymptomatic infants at risk for neonatal hypoglycemia -see below for protocol and risk factors</td>
<td>Number of infants transferred from the newborn nursery to the NICU for hypoglycemia decreased from 35/1,000 to 25/1,000 live births (p &lt; 0.01) -NICU admissions for asymptomatic hypoglycemia decreased from 20.6 to 14.8% - absolute risk reduction for IV dextrose therapy after the introduction of dextrose gel was 15.54% (95% CI 7.32–23.76) - number needed to treat was 7 (95% CI 4.2–13.7) 26% of asymptomatic hypoglycemic neonates in the newborn nursery were transferred to the NICU for IV dextrose compared to 42% with feeds alone Exclusive breastfeeding improved from 19 to 28% (p = 0.03) Dextrose gel protocol resulted in an overall cost savings of $642,951 over the 6-month period USD -$2,593 per patient USD</td>
<td>Study Limitations = None</td>
</tr>
<tr>
<td>Scheans et al., 2017, Neonatal Network</td>
<td>To study a nurse-driven protocol for neonatal hypoglycemia (NH) that included oral administration of glucose gel</td>
<td>Before and after implementation of a new protocol with glucose gel as first-line intervention for neonatal hypoglycemia</td>
<td>During the first year, admission rates to the NICU for NH decreased by 73% -40 additional families remained together on the mother baby unit Exclusive breastfeeding rates in the newborns with NH</td>
<td>Study Limitations = None</td>
</tr>
</tbody>
</table>

Quality Improvement (pre-post, controlled pre-post, historical comparison, time series)
- Intervention not evidence-based
- Improvement method was not clearly identified or the need for improvement was not described
- Stakeholders, organizational culture, patients, or interventions were not clearly described or appropriate
- Interventions were not described in enough detail to be replicated by others
- Baseline and outcome data were not collected and reported appropriately or in the same manner
- Data collection tools were not validated to measure intended outcomes
- Any modifications made to the intervention were not based on pilot studies
Bennett et al. (2016) protocol and implementation recommendations:

**BOX 3**
Basic Steps in Our Glucose Gel Algorithm

- Neonates are placed skin to skin and breastfed within the first hour of life.
- A BG level is obtained 30 minutes after this feeding is completed.
- If the BG level is <35 mg/dl, the nurse administers a weight-based dose of 40% glucose gel by syringe to the neonate’s buccal cavity and then places the neonate with the mother to feed.
- A BG level is then repeated 1 hour after gel administration.
- If this BG level is >35 mg/dl, the neonate’s BG levels are assessed before feedings until two consecutive readings are <45 mg/dl.
- If the neonate’s BG level is <35 mg/dl, a second dose of the gel is administered, and the neonate is again placed with the mother to feed.
- In the event that a second dose is needed, a BG level is obtained 1 hour after gel administration.
- If hypoglycemia is not reversed after the second dose of 40% glucose, the physician is contacted for further orders.

*Note: BG = bedside glucose.*

**BOX 5**
Suggestions for Implementing a Practice Change to Use Oral Glucose Gel for Neonatal Hypoglycemia

- Find a physician champion.
- Distribute the Harris et al. study (2013) and this article to key stakeholders.
- Collect data on the following:
  - The number of neonates who receive IV glucose and/or formula supplementation to treat neonatal hypoglycemia.
  - The initial blood glucose levels of these neonates.
  - How long they received IV glucose.
- If the pediatric staff is hesitant to implement, find a physician champion who will support a trial within her/his patient population.
- Track the blood glucose levels of those neonates and present your findings to key stakeholders.
- Evaluate the potential financial impact to the hospital, including price of IV glucose, cost of neonates’ stays in the NICU, and the increased length of stay for both women and neonates.
Rawat et al. (2016) Protocol for Asymptomatic Infants at risk for Hypoglycemia:

**Fig. 1**

Newborn nursery protocol for the screening and management of asymptomatic hypoglycemia. OG = Orogastric; PO = per or; SNS = supplemental nursing system.
REFERENCES


# Appendix A: GRADE criteria for rating a body of evidence on an intervention

Developed by the GRADE Working Group

## Grades and interpretations:

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>Further research is very unlikely to change our confidence in the estimate of effect.</td>
</tr>
<tr>
<td>Moderate</td>
<td>Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.</td>
</tr>
<tr>
<td>Low</td>
<td>Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.</td>
</tr>
<tr>
<td>Very low</td>
<td>Any estimate of effect is very uncertain.</td>
</tr>
</tbody>
</table>

## Type of evidence and starting level

<table>
<thead>
<tr>
<th>Evidence Type</th>
<th>Starting Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Randomized trial</td>
<td>High</td>
</tr>
<tr>
<td>Observational study</td>
<td>Low</td>
</tr>
<tr>
<td>Any other evidence</td>
<td>Very low</td>
</tr>
</tbody>
</table>

## Criteria for increasing or decreasing level

**Reductions**
- Study quality has serious (−1) or very serious (−2) problems
- Important inconsistency in evidence (−1)
- Directness is somewhat (−1) or seriously (−2) uncertain
- Sparse or imprecise data (−1)
- Reporting bias highly probable (−1)

**Increases**
- Evidence of association† strong (+1) or very strong (+2)
- Dose-response gradient evident (+1)
- All plausible confounders would reduce the effect (+1)

†Strong association defined as significant relative risk (RR 2-5 or 0.5-0.2) based on consistent evidence from two or more studies with no plausible confounders
Very strong association defined as significant relative risk (RR >5 or <0.2) based on direct evidence with no threats to validity