Prevention of Neonatal Hypoglycemia With Oral Glucose Gel for High-Risk Newborns

Mark Deyo-Svendsen, MD; Sara Herrmann, MD; Christina Andrist, DO; Michael Phillips, MD; Matthew Cabrera Svendsen, MD; Rachel Oldfather

ABSTRACT

Background: Neonatal hypoglycemia (glucose <47) is the most common metabolic problem in newborns (incidence 5% - 15%) and can cause adverse outcomes, even in the absence of noticeable symptoms. Oral glucose gel (OGG) is safe and effective for treatment of neonatal hypoglycemia. In order to reduce interventions such as intravenous (IV) dextrose administration and neonatal intensive care unit (NICU) transfer, in October 2017, we implemented a protocol in our Level 1 rural community hospital to identify newborns with asymptomatic hypoglycemia based on risk factors and treat them with OGG. Risk factors include large or small size for gestational age, maternal gestational diabetes, preterm and late preterm birth, and newborns requiring resuscitation.

Methods: Chart review was performed for all infants born at our hospital from October 1, 2016 through September 30, 2018. Data for year 1—the period before protocol implementation (October 2016-September 2017)—was compared to post implementation data from year 2 (October 2017-September 2018).

Results: There was a significant risk reduction in newborns requiring interventions due to hypoglycemia after protocol implementation ($P = 0.029$, Student t test). In year one, 7 of 310 total newborns required IV dextrose or NICU transfer related to neonatal hypoglycemia. In year two, 108 out of 250 total newborns were tested for asymptomatic hypoglycemia based on risk factors identified in the protocol. Of those tested, 31 newborns demonstrated hypoglycemia and received OGG. None of the 250 newborns required further associated interventions.

Conclusion: Protocol-based hypoglycemia testing based on risk factors with subsequent OGG administration was effective in reducing the need for IV dextrose and NICU transfer from our Level 1 rural community hospital.

• • •

Author Affiliations: Department of Pediatrics, Mayo Clinic Health System – Northwest Wisconsin, Menomonie, Wis (Hermann, Andrist); Department of Family Medicine, Mayo Clinic Health System – Northwest Wisconsin, Menomonie, Wis (Phillips, Deyo-Svendsen); Department of Family Medicine, Mayo Clinic Health System – Southeast Minnesota, Austin, Minn (Svendsen), University of Minnesota Medical School, Minneapolis, Minn (Oldfather).

Corresponding Author: Mark Deyo-Svendsen, MD, Mayo Clinic Health System Red Cedar, 2321 Stout Rd, Menomonie, WI 54751; phone 715.235.9671; email deyosvendsen.mark@mayo.edu.

INTRODUCTION

Neonatal hypoglycemia is the most common metabolic problem in newborns and is a preventable cause of neurological impairment.[1] The incidence of neonatal hypoglycemia ranges from 5% to 15% in the first few days after birth[2,3] and increases to more than 50% in newborns with certain risk factors. For example, milestone data indicate hypoglycemia rates of 19% to 52% in premature newborns, 42% to 54% in newborns small for gestational age, 10% to 47% in newborns large for gestational age, and 33% to 48% in newborns born to mothers with diabetes.[4,5]

Because of the critical role glucose plays in brain metabolism, short- and long-term neurological impairment can result from neonatal hypoglycemia—even if asymptomatic—depending on the severity and duration.[6,7] Transient hypoglycemia can be physiologic following birth,[6] but hypoglycemia also may be the initial presenting sign for complex metabolic disorders, such as hyperinsulinemia, glycogen storage disease, congenital disorders of glycosylation, galactosemia, fatty acid oxidation defects, growth hormone deficiency, and adrenal insufficiency.[8]

The definition of neonatal hypoglycemia and the glucose value at which adverse outcomes occur is controversial. The Pediatric Endocrine Society opined that neurological injury may occur at a glucose level less than 47 mg/dL,[9] and others support this risk threshold.[7] However, after evaluating newborns with asymptomatic hypoglycemia and poor long-term neurodevelop-

Table. Risk Factors Contributing to Neonatal Hypoglycemia Per Chart Review

Newborns Screened	Year 1[a]	Year 2[b]
Large for gestational age	34	29
Gestational diabetes mellitus	22	19
Small for gestational age	12	10
Maternal type 1 and type 2 diabetes mellitus	2	0

[a]October 1, 2017 to September 30, 2017, pre-implementation.
[b]October 1, 2017 to September 30, 2018, post-implementation.

mental outcomes, the American Academy of Pediatrics (AAP) indicated that injury may occur when glucose levels are below 30 mg/dL.[10]

Traditionally, oral glucose gel (OGG) has been used to reverse hypoglycemia in persons with diabetes. Sublingual and buccal administration of OGG is preferred over the oral route,[11] because it avoids first-pass metabolism and improves bioavailability for fast treatment results. The 2013 Sugar Babies Study[12] found that compared to formula feeding, OGG reduces treatment failure, as defined by hypoglycemia after 2 treatment attempts. It also found OGG to be both safe and effective for neonates.

The AAP generally endorses selective screening for hypoglycemia in high-risk newborns. Specifically, in 2011, the AAP Committee on Fetus and Newborn guidelines provided screening guidance for newborns who are late-preterm, small or large for gestational age, or born to mothers with diabetes.[10] Based on these guidelines, we implemented a neonatal hypoglycemia protocol to identify and treat newborns with asymptomatic hypoglycemia in our nursery.[10] The goal of this quality improvement initiative was to reduce interventions such as intravenous (IV) dextrose administration and neonatal intensive care unit (NICU) transfer.

Our Level 1 rural hospital is part of an integrated network of hospitals and clinics in the Midwest United States, serving approximately 45,000 people.[13] Eight family medicine physicians and 3 obstetrician-gynecologists provide prenatal care; 13 family medicine physicians and 2 pediatricians provide newborn care. The family birth center offers newborn care annually to 250 to 350 patients. In general, the rural population served by our nursery may benefit from actions taken to ensure adequate care as close to home as possible. Most families practice "rooming-in" (ie, the newborn is cared for in the postpartum room), and not all newborns designated as high risk are required to receive care in the nursery.[14] Medicaid is the most common payer for maternity care services (64%). Teenage pregnancy (16.7%), poverty (13.9%), and delayed or no prenatal care (4 or fewer prenatal visits 4.2%; 18.4% not in the first trimester) contribute to a high-risk population. The primary and repeat cesarean delivery rates are 15% and 9%, respectively, totaling 24% of deliveries. Most newborns (93.8%) are normal birth weight.[14]

METHODS

The hypoglycemia protocol in this study was designed to follow the AAP's 2011 clinical statement on the postnatal management of hypoglycemia in late-term and term newborns (Appendix).[10] Newborns identified as high-risk (Appendix) were provided early feeding and a glucose level was obtained. Those with a glucose level less than 45 mg/dL were provided OGG 0.2 grams/kg.[15] The newborn's mouth first was dried with gauze, then OGG was applied with a gloved finger and massaged into the buccal mucosa. Doses greater than 1 mL were divided and administered bilaterally to promote buccal absorption and to reduce swallowing. Following this procedure, nurses immediately offered feeding with human milk or at least 15 mL of formula. Providers were notified if newborns did not feed. Blood glucose levels were rechecked 30 minutes after feeding.

A labor and delivery registered nurse reviewed charts of all newborns born at our hospital from October 1, 2016 to September 30, 2018. Year 1 (October 1, 2016-September 30, 2017) data included newborns treated for hypoglycemia with formula, human milk, or IV dextrose infusion. These data were compared to post-implementation data from Year 2 (October 1, 2017-September 30, 2018).

The Institutional Review Board for Mayo Clinic Health System Northwest Wisconsin approved this research project in October 2017, prior to protocol implementation.

RESULTS

In year one, 122 neonates were screened for hypoglycemia. Seventy were identified with specific hypoglycemia risk factors, and 12 had hemodynamic instability or required resuscitation. Of the 310 total newborns, 7 with neonatal hypoglycemia required IV dextrose or NICU transfer due to hypoglycemia (2.25%, 95% CI, 1.80%-2.71%).

In year two, 108 neonates were screened for hypoglycemia. Fifty-eight had specific hypoglycemia risk factors, and 22 had hemodynamic instability or required resuscitation (Table). None of the 250 newborns required IV dextrose or NICU transfer due to hypoglycemia. This was a significant reduction in risk ($P = 0.029$, Student t test). Relative risk reduction is undefined as there were zero interventions in year 2.

It should be noted that 59 newborns with symptomatic hypoglycemia (37 in year 1; 22 in year 2) did not meet protocol criteria and were excluded from the study. Newborns transferred to a NICU for causes unrelated to hypoglycemia also were excluded; these newborns required resuscitation or were experiencing persistent tachycardia, respiratory distress, and hypothermia. All excluded patients were tested and treated as appropriate.

DISCUSSION

A hypoglycemia protocol adapted from the 2011 AAP guidelines[10] was implemented in our Level 1 rural community hospital nurs-

ery. Newborns identified with asymptomatic hypoglycemia based on risk factors were treated with OGG. In the year following protocol implementation, no newborns required treatment with IV dextrose or transfer to a higher level of care for treatment related to asymptomatic hypoglycemia.

Study limitations include the small sample size and the fact that the study design utilized retrospective chart review. Additionally, in year 1, infants were tested only if signs of hypoglycemia were present; if hypoglycemia was present, newborns were treated with early feeding or IV dextrose. It is not known whether at-risk infants were observed differently for signs of hypoglycemia—and potentially offered early feeding without testing—than those who were not at risk. Had this occurred, it may have resulted in lower year 1 interventions. Without this potential bias, the impact of testing and treating at-risk infants with OGG might have been even greater.

The findings from this quality improvement initiative support newborn screening for asymptomatic hypoglycemia based on select risk factors and subsequent treatment with OGG, and they are consistent with other recent reports of reduced interventions for hypoglycemia with the use of OGG in asymptomatic newborns. One retrospective analysis found that OGG effectively managed newborns deemed high risk for hypoglycemia and reported high-risk identifiers for newborns more likely to require a second dose of OGG or IV fluids with dextrose;[16] another reported a reduction in NICU transfer, improvement in breastfeeding rates, and an overall associated reduction in cost of care with OGG.[17]

Beyond reducing interventions for newborns, our findings have additional implications for practice. There is concern that intravenous infusion separates the mother and newborn and using formula to treat hypoglycemia may disrupt breastfeeding.[12,18] Particularly in a smaller newborn unit, starting and maintaining an IV might require transfer to a higher level of care facility.[12] Administration of OGG can occur quickly in the nursery while simultaneously encouraging maternal bonding. OGG has been shown to reduce hospital costs and supports breastfeeding.[12,17,19] OGG is a practical, cost-effective method to manage neonatal hypoglycemia in comparison to IV dextrose and formula.

CONCLUSION

Our findings indicate that protocol-based identification of newborns at risk for hypoglycemia with subsequent administration of OGG is an effective method to address asymptomatic neonatal hypoglycemia. It eliminated the need for more aggressive interventions, including peripheral IV line placement and IV dextrose infusion, and decreased the number of newborns transferred to a neonatal intensive care unit.

Acknowledgment: The authors wish to thank Tina Kippes, RN, Department of Nursing, Mayo Clinic Health System Northwest Wisconsin, for her work in compiling data for this project.

Funding/Support: None declared.

Financial Disclosures: None declared.

REFERENCES

1. Su J, Wang L. Research advances in neonatal hypoglycemic brain injury. *Transl Pediatr*. 2012;1(2):108-115. doi:10.3978/j.issn.2224-4336.2012.04.06

2. Lubchenco LO, Bard H. Incidence of hypoglycemia in newborn infants classified by birth weight and gestational age. *Pediatrics*. 1971;47(5):831-838.

3. Cranmer H. Neonatal hypoglycemia. Medscape. Published April 12, 2018. Updated April 30, 2020. Accessed July 27, 2020. https://emedicine.medscape.com/article/802334-overview

4. Harris DL, Weston PJ, Harding JE. Incidence of neonatal hypoglycemia in babies identified as at risk. *J Pediatr.* 2012;161(5):787-791. doi:10.1016/j.jpeds.2012.05.022

5. Kumar TJ, Vaideeswaran M, Arasar Seeralar T. Incidence of hypoglycemia in newborns with risk factors. *Int J Contemp Pediatr.* 2018;5(5):1952. doi:10.18203/2349-3291.ijcp20183538

6. Lucas A, Morley R, Cole TJ. Adverse neurodevelopmental outcome of moderate neonatal hypoglycaemia. *BMJ*. 1988;297(6659):1304-1308. doi:10.1136/bmj.297.6659.1304

7. Abramowski A, Hamdan AH. Neonatal Hypoglycemia. In: *StatPearls*. StatPearls Publishing; 2020. Accessed April 6, 2020. http://www.ncbi.nlm.nih.gov/books/NBK537105/

8. Gandhi K. Approach to hypoglycemia in infants and children. *Transl Pediatr.* 2017;6(4):408-420. doi:10.21037/tp.2017.10.05

9. Thornton P, Adamkin D. Hypoglycemia guidelines: AAP vs PES. *Contemp Pediatr*. 2016;33(6):22-27. Accessed July 27, 2020. https://www.contemporarypediatrics.com/view/hypoglycemia-guidelines-aap-vs-pes

10. Committee on Fetus and Newborn, Adamkin DH. Postnatal glucose homeostasis in late-preterm and term infants. *Pediatrics*. 2011;127(3):575-579. doi:10.1542/peds.2010-3851

11. Narang N, Sharma J. Sublingual mucosa as a route for systemic drug delivery. Int J Pharm Pharm Sci. 2010;3(Suppl 2):18-22. Accessed July 27, 2020. https://www.plantpills.co.uk/pdf/SUBLINGUAL-MUCOSA.pdf

12. Harris DL, Weston PJ, Signal M, Chase JG, Harding JE. Dextrose gel for neonatal hypoglycaemia (the Sugar Babies Study): a randomised, double-blind, placebo-controlled trial. *Lancet*. 2013;382(9910):2077-2083. doi:10.1016/S0140-6736(13)61645-1

13. United States Census Bureau. American Community Survey (ACS) demographic and housing estimates. 2018: ACS 5-year estimates. Dunn County. Accessed July 27, 2020. https://data.census.gov/cedsci/table?q=dunn%20county&g=0500000US55033&hidePreview=false&tid=ACSDP5Y2018.DP05&vintage=2018&layer=VT_2018_050_00_PY_D1&cid=DP05_0001E

14. Wisconsin Department of Health Services, Division of Public Health, Office of Health Informatics, Health Analytics Section. Wisconsin public health profiles, Dunn County. Published August 2016. Accessed July 27, 2020. https://www.dhs.wisconsin.gov/publications/p4/p45358-2016-dunn.pdf

15. Hypoglycemia prevention in newborns with oral dextrose: the dosage trial. ANZCTR identifier: ACTRN12613000322730. Updated July 7, 2018. Accessed July 27, 2020. https://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=363418&isReview=true

16. Gregory K, Turner D, Benjamin C, Monthé-Drèze C, Johnson L, Sen S. Evaluation of dextrose gel administration to infants with asymptomatic neonatal hypoglycemia: a single center experience. *Pediatrics*. 2018;142(1 MeetingAbstract):240. doi:10.1542/peds.142.1_MeetingAbstract.240

17. Makker K, Alissa R, Dudek C, Travers L, Smotherman C, Hudak ML. Glucose gel in infants at risk for transitional neonatal hypoglycemia. *Am J Perinatol*. 2018;35(11):1050-1056. doi:10.1055/s-0038-1639338

18. Crenshaw JT. Healthy Birth Practice #6: Keep mother and baby together— it's best for mother, baby, and breastfeeding. *J Perinat Educ.* 2014;23(4):211-217. doi:10.1891/1058-1243.23.4.211

19. Glasgow MJ, Harding JE, Edlin R, Children with Hypoglycemia and Their Later Development (CHYLD) Study Team. Cost analysis of treating neonatal hypoglycemia with dextrose gel. *J Pediatr.* 2018;198:151-155.e1. doi:10.1016/j.jpeds.2018.02.036

advancing the art & science of medicine in the midwest

WMJ

WMJ (ISSN 1098-1861) is published through a collaboration between The Medical College of Wisconsin and The University of Wisconsin School of Medicine and Public Health. The mission of *WMJ* is to provide an opportunity to publish original research, case reports, review articles, and essays about current medical and public health issues.

Visit www.wmjonline.org to learn more.