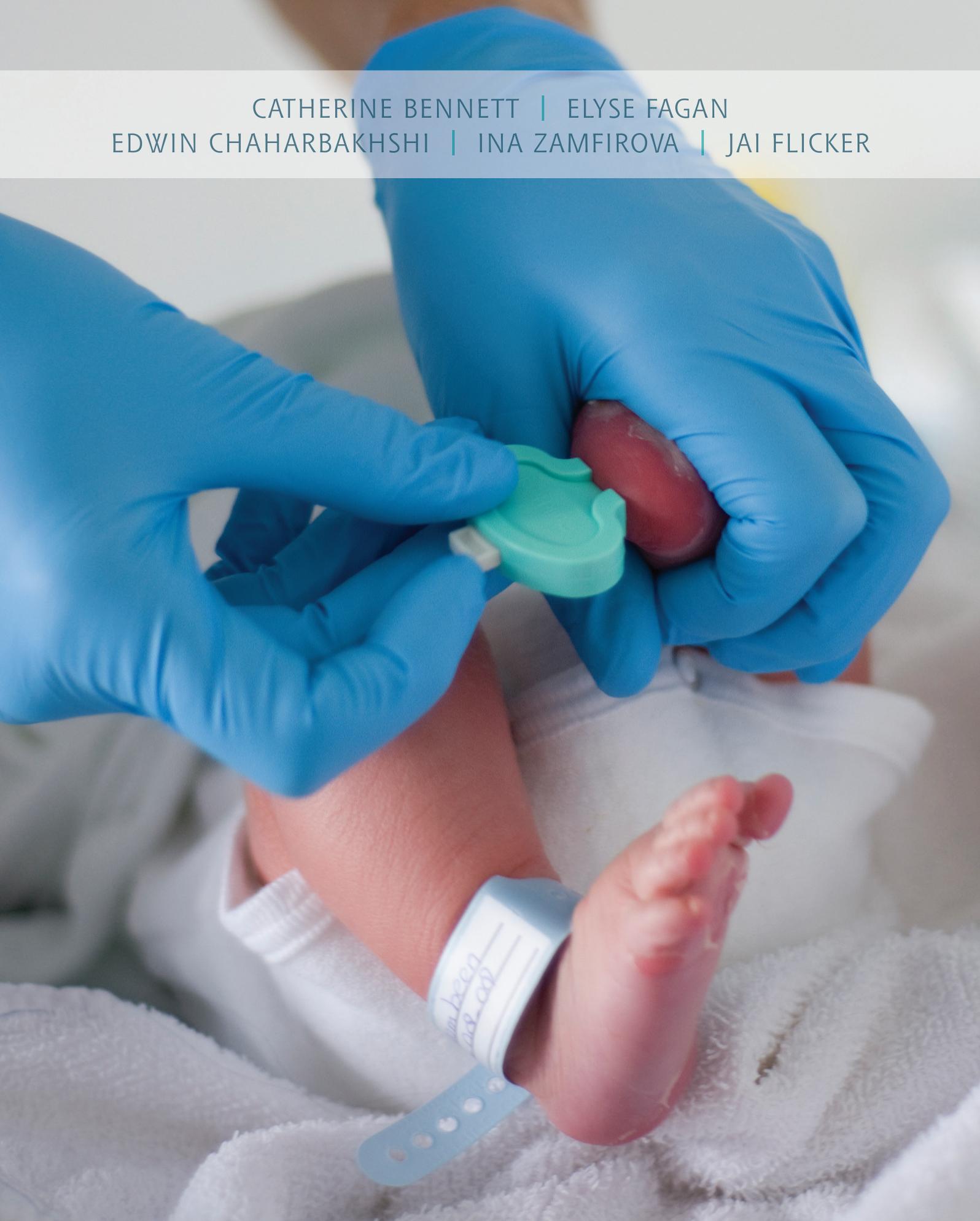


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IMPLEMENTING A PROTOCOL Using Glucose Gel to Treat Neonatal Hypoglycemia

Neonatal hypoglycemia is a leading cause of infant admission to the NICU and is associated with maternal diabetes and preterm birth (Harris, Weston, Signal, Chase, & Harding, 2013). This motivated us to take a deeper look into alternative protocols for the treatment of neonatal hypoglycemia. A promising treatment protocol described by Harris et al. (2013) inspired us to develop an algorithm based on the oral administration of 40% glucose gel. This safe and effective intervention resulted in a 73% decrease in NICU admissions for the diagnosis of neonatal hypoglycemia over a 14-month period. In addition, this new protocol algorithm more fully supported exclusive breastfeeding and mother–newborn bonding. We hope that by sharing our results we can contribute to the establishment of a new standard of care for neonatal hypoglycemia.

Abstract: Neonatal hypoglycemia is a leading cause of admission of neonates to the NICU. Typical treatment for neonatal hypoglycemia includes supplementation with formula or, in some cases, intravenous glucose administration. These treatments, though effective at treating hypoglycemia, interrupt exclusive breastfeeding and interfere with mother–infant bonding. Our institution developed a treatment algorithm for newborns at risk for neonatal hypoglycemia. The new algorithm called for the oral administration of 40% glucose gel. This intervention resulted in a 73% decrease in admission rates to the NICU for hypoglycemia, and it supported exclusive breastfeeding, skin-to-skin contact, and mother–infant bonding. <http://dx.doi.org/10.1016/j.nwh.2015.11.001>

Keywords: exclusive breastfeeding | glucose gel | neonatal hypoglycemia | NICU | skin-to-skin

THE NEED FOR A NEW PROTOCOL

Historically, determining evidence-based protocols for the treatment of neonatal hypoglycemia has been difficult because of a lack of clinical evidence defining pathologic glucose levels in neonates during the first hours of life (Committee on Fetus and Newborn & Adamkin, 2011). As recently as 2008, an expert panel at the Eunice Kennedy Shriver National Institute of Child Health and Human Development found that no threshold values had been established relating levels of glucose to pathologic neonatal hypoglycemia in infants, which remains true to this day (Cornblath et al., 2000; Hay, Raju, Higgins, Kahan, & Devaskar, 2009). This lack of scientific knowledge has led clinicians across the country to use a wide range of disparate interventions.

In 2011, in an effort to address this lack of an agreed-on treatment protocol for neonatal hypoglycemia, the American Academy of Pediatrics (AAP) published new management guidelines. These guidelines were necessary because, as the AAP explained, “The generally adopted plasma glucose concentration that defines neonatal hypoglycemia for all infants (<47 mg/dl) is without rigorous scientific justification” (Committee on Fetus and Newborn & Adamkin, 2011, p. 576).

Fetal glucose levels are dependent on maternal glucose supply and placental transfer, with a low-end normal value of 50 mg/dl. A physiologic decrease in glucose levels normally occurs immediately after birth and continues for the first 2 to 3 hours of life. Studies referenced by Hay et al. (2009) found levels as low as 23 mg/dl in healthy breastfed infants. The Committee on Fetus and Newborn and Adamkin (2011) found that levels of 30 mg/dl are common in healthy neonates during the initial 1 to 2 hours of life. After this temporary decrease, glucose levels in healthy neonates soon increase to 40 to 60 mg/dl. The only documented cases of neurological damage have occurred when glucose levels have dropped to low levels for many hours. For example, blood glucose levels that fall below 10 mg/dl for more than 12 hours have been shown to cause neurological damage including seizures, psychomotor disturbances (leading to learning deficits), cerebral palsy, and/or mental retardation (Committee on Fetus and Newborn & Adamkin, 2011).

The AAP set the new threshold for intervention at 25 mg/dl, which is more aligned with case studies than the widely accepted 47 mg/dl threshold. However, these new guidelines were

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We have found that the use of glucose gel is extremely inexpensive, far less invasive, and does not disrupt mother-infant bonding

not universally implemented, at least not within our hospital system, where protocols remained at higher thresholds, perhaps because of a lack of confidence in such dramatically lower numbers. Paradoxically, in some instances these new guidelines led to an increase in NICU admissions. This was because the AAP recommendation was to administer intravenous (IV) glucose to infants who sustain a blood glucose level of less than 25 mg/dl for more than 1 hour. In hospitals continuing to use higher thresholds, more neonates ended up receiving IV glucose, which is expensive, physically taxing to the neonate, and disruptive to mother–infant bonding. Alternatively, we have found that the use of glucose gel is extremely inexpensive, far less invasive, and does not disrupt mother–infant bonding.

SUPPORTING EXCLUSIVE BREASTFEEDING

According to Harris, Weston, Signal, Chase, and Harding (2013), the most frequent treatment for asymptomatic infants is supplemental feeding with formula, which interrupts exclusive breastfeeding. Although this readily available intervention may be tempting, the importance of exclusive breastfeeding should not be overlooked. In fact, the U.S. Department of Health and Human Services (2011) states that infants should be exclusively breastfed for at least the first 6 months of life to protect them from diarrhea, ear infections, pneumonia, asthma, sudden infant death syndrome, and obesity later in life. In its position statement on breastfeeding, the Association of Women's Health, Obstetric and Neonatal Nurses (AWHONN) states that, "Women should be encouraged and supported to exclusively breastfeed for the first six months of an infant's life" (AWHONN, 2015, p. 83). The AAP also recommends exclusive breastfeeding, taking a strong stand on the issue in its 2012 policy statement, stating, "Given the documented short- and long-term medical and neurodevelopmental advantages of breastfeeding, infant nutrition should be considered a public health issue and not only a lifestyle choice" (AAP, 2012, p. 827).

The benefits of exclusive breastfeeding for infants include significant decreases in respiratory and gastrointestinal tract infections, otitis media, necrotizing enterocolitis, sudden infant death, asthma, atopic dermatitis, eczema, food allergies, celiac disease, obesity, type 1 and type 2 diabetes mellitus, and childhood leukemia and lymphoma (AAP, 2012). There are potential maternal health benefits as well, including more rapid uterine involution, decreased postpartum blood loss, an increase in child spacing secondary to lactational amenorrhea, and decreased risk for postpartum depression, type 2 diabetes mellitus, rheumatoid arthritis, cardiovascular disease, and breast and ovarian cancer (AAP, 2012).



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Because the administration of glucose gel helps maintain normal glucose levels, a protocol using glucose gel reduces the necessity of supplemental feedings and therefore supports exclusive breastfeeding overall

In 1991, the World Health Organization and the United Nations Children's Fund launched the Baby-Friendly Hospital Initiative with the stated goal of protecting, promoting, and supporting exclusive breastfeeding. To investigate the relationship between Baby-Friendly hospital practices and the achievement of mothers' breastfeeding goals, Perrine, Scanlon, Li, Odom, and Grummer-Strawn (2012) reviewed results from the Infant Feeding Practices Study 11, conducted between 2005 and 2007. Of the 1,457 women studied, 85% prenatally stated their intention to continue exclusive breastfeeding for at least three months. However, only 32.4% accomplished that goal. The researchers found that the most influential practice supporting the continuation of exclusive breastfeeding at home was having relied exclusively on breast milk in the hospital (adjusted odds ratio, 2.3; 95% confidence interval, [1.8, 3.1]; Perrine et al., 2012).

A question commonly voiced by both nurses and parents regarding supplementation is, "Does one bottle really matter?" Evidence shows that supplementation with even one bottle of formula negatively affects an infant's gut flora for up to 4 weeks (Walker, 2014). For infants with a predisposition to certain allergies, just one bottle of formula given during the first 3 days of life can sensitize a neonate to cow's milk proteins and lead to dairy allergies later in life. In addition, early exposure to cow's milk proteins present in formula may increase an infant's risk of developing insulin-dependent diabetes mellitus (Walker, 2014). Glucose, on the other hand, is one of the sugars formed when breast milk is metabolized; therefore, it poses none of these risks for infants. Further, because the administration of glucose gel helps maintain normal glucose levels, a protocol using glucose gel reduces the necessity of supplemental feedings and therefore supports exclusive breastfeeding overall.

INCREASED SKIN-TO-SKIN CONTACT

For most of human history, a newborn's early survival depended on skin-to-skin contact with the mother for both warmth and successful feeding. During the early 1900s, when hospital births became the norm, birthing practices began changing dramatically. Immediately after birth, neonates were routinely whisked off to the nursery to be cleaned and wrapped and were brought to their mothers only for feedings. Care standards have been slowly progressing toward a more natural approach. Studies showing the mismanagement of neonate care in previous hospital practices have been in the literature for decades. A Cochrane review (Moore, Anderson, Bergman, & Dowswell, 2012) concluded that "early skin-to-skin contact between a mother and her baby at birth reduces crying, and helps the mother to breastfeed successfully" (Moore et al., 2012, p. 2). The placement of a newborn on the mother's chest immediately after birth allows for the progression of innate newborn behaviors for early initiation of breastfeeding. Neonates placed skin to skin immediately after birth for at least 50 minutes show increased rooting compared with neonates not placed skin to skin (Mizuno, Mizuno, Shinohara, & Noda, 2004).

A common treatment of neonatal hypoglycemia is the administration of IV glucose (Harris et al., 2013), an intervention that makes skin-to-skin contact more difficult. In some hospitals, this may require a neonate to be admitted to the NICU. Although the NICU is the ideal place for close observation of

symptomatic neonates, increased separation between asymptomatic neonates and their mothers remains a key issue, because vital bonding time is decreased at this crucial phase of development. According to Crenshaw (2007), the more time mothers spend with their newborns, the faster they learn to recognize and meet their infants' needs. Studies have shown that women who have continuous contact with their infants also produce more milk, breastfeed longer, and are more likely to exclusively breastfeed compared with women who have interrupted contact (Crenshaw, 2007). Infants who receive continuous maternal contact cry less, are able to be soothed more quickly, spend more time quietly sleeping, gain more weight per day, and are less likely to develop jaundice (Crenshaw, 2007).

WHY GLUCOSE GEL?

Oral glucose gel is a longstanding first-line treatment for hypoglycemia in adults and children. Hospital formularies commonly include 40% glucose gel for such purposes. The gel, consisting of 40% glucose, water, and glycerin, is also sold as an over-the-counter medication in most pharmacies. Although glucose gel is commonly used to treat hypoglycemia in children of other age groups, research using glucose gel for treatment of hypoglycemia in neonates is extremely limited. In 2013, Harris et al. published the results of a randomized clinical trial showing the efficacy of the buccal administration of glucose gel to reverse hypoglycemia in neonates with negligible risks. This method of administration was found to be particularly effective



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because the high vascularization of the mucosa allowed an absorption rate similar to that of IV administration. Their study showed that using 40% glucose gel with feeding was more effective in reversing neonatal hypoglycemia than feeding alone, did not require NICU admission, and was compatible with exclusive breastfeeding. In addition, this treatment was found to be simple to administer, cost effective, well tolerated, and not associated with any adverse effects (Harris et al., 2013). Newborns also did not exhibit rebound hypoglycemia but rather exhibited blood glucose levels remaining within normal range.

IMPETUS FOR QUALITY IMPROVEMENT

The negative impact of standard neonatal hypoglycemia treatment on breastfeeding and its disruption of continuous mother-infant contact prompted our team to look into alternative interventions. Our institution is a tertiary hospital in the mid-western United States and has more than 4,000 births per year. An audit of NICU admission indications between May 2013 and April 2014 showed that 10.6% of infants at risk for neonatal hypoglycemia were admitted to the NICU. The audit identified that these infants received IV glucose treatment until their hypoglycemia reversed. Our primary impetus for change was to decrease NICU admissions, thereby providing a cost savings to both the hospital and families, and also to decrease separation of women and their infants.

PLANNING AND IMPLEMENTATION STRATEGIES

The assistant manager of the postpartum unit, who facilitates our unit quality committee, shared the study by Harris et al. (2013) with the Newborn Advisory Committee (NAC) at our institution. The NAC is a multidisciplinary group including pediatricians, neonatologists, perinatal clinical nurse specialists (CNSs), and unit managers. Based on the study results, the NAC unanimously agreed to conduct a trial with glucose gel as a standard treatment for newborns with neonatal hypoglycemia. The gel was already available in the hospital pharmacy as a hypoglycemia antidote at a cost of less than \$3 per dose. The perinatal CNS team created a protocol algorithm to standardize the care and treatment of neonates at risk for hypoglycemia. These include neonates who are small for gestational age, large for gestational age, preterm, born to women with diabetes, and experiencing perinatal stress (Committee on Fetus and Newborn & Adamkin, 2011).

Glucose gel was administered as a first-line intervention to neonates with a blood glucose level less than 35 mg/dl at 30 minutes after the neonate's first feeding. Women who had identified breastfeeding as their preferred method were supported and encouraged to breastfeed. In cases of women who preferred formula, it was given immediately after the administration of the gel. Before the AAP publication providing guidelines for the treatment of neonatal hypoglycemia, our institution treated

BOX 1

Weight-Based Dosing of Glucose Gel

<i>Neonate Birthweight, kg</i>	<i>Dose of 40% Glucose Gel, g</i>	<i>Amount, ml</i>
2.0	0.4	1.00
2.5	0.5	1.25
3.0	0.6	1.50
3.5	0.7	1.75
4.0	0.8	2.00
4.5	0.9	2.25
5.0	1.0	2.50

Source: Harris, Weston, Signal, Chase, and Harding (2013).

any neonate with a blood glucose level less than 45 mg/dl with formula or IV glucose. Given the AAP threshold of 25 mg/dl, our hospital conservatively chose 35 mg/dl as the threshold to begin treatment of neonatal hypoglycemia with glucose gel during the first 4 hours of life.

Our pediatric pharmacist reviewed the Harris study (2013) and collaborated with the NAC to establish weight-based dosing of glucose gel. We followed the standard dose described in the Harris study, which was 0.2 g glucose/kg body weight. This is the standard dose that is used in IV glucose treatment for hypoglycemic neonates (2 ml/kg body weight of 10% dextrose in 100 ml of water, which equals 0.2 g dextrose/kg body weight) (see Box 1).

Throughout April 2014, all nursing staff members (approximately 150 people) working in the labor and birth unit and the postpartum unit attended a 1-hour educational presentation taught by two perinatal CNSs. This presentation covered the rationale for change, pathophysiology of neonatal hypoglycemia, results of the Harris study, and a step-by-step introduction to the new glucose gel algorithm. Samples of the gel, medicine cups, and syringes were presented to the staff so they could practice drawing up the proper amount of gel. In addition, we reviewed the proper technique for obtaining heel-stick blood samples.

The nurses were receptive, but the first few weeks after implementation presented challenges. For example, we had to refine gel administration techniques, because we found it difficult to give the full dose all at once. Over time, we identified the most effective administration method to be dividing the dose by four and administering each quarter in either the right or left buccal cavity and then massaging the infant's cheek gently to stimulate absorption. After approximately 4 weeks, most of the nursing staff had acclimated to the new procedure.

BOX 2

Risk Factors Associated With Neonatal Hypoglycemia

Neonates born to women with diabetes

Large for gestational age

Small for gestational age

Late preterm birth (gestational age, 34–36^{6/7} weeks)

Apgar scores less than 7 at 5 minutes of age

Source: Committee on Fetus and Newborn and Adamkin (2011).

DATA COLLECTION

We performed a retrospective chart review for 870 newborns at risk for neonatal hypoglycemia between March 2013 and May 2014 (see Box 2). After protocol implementation, the same criteria were used for review of 1,089 newborn charts between May 2014 and July 2015.

METHODS

An algorithm outlining the new protocol was developed by the perinatal CNSs and nurses working in the newborn nursery to guide the assessment, care, and treatment of neonates at risk for neonatal hypoglycemia; this has continued to be our guiding algorithm. The algorithm directs that newborns be fed within the first hour of life. Breastfeeding women are urged to breastfeed rather than use formula, and skin-to-skin contact is strongly encouraged throughout use of the algorithm (see Box 3).

RESULTS

Reduction of NICU Admissions

Since the implementation of the algorithm, there has been a 73% reduction in neonate admissions to the NICU for the primary diagnosis of hypoglycemia. During the 14 months before implementation, 92 of 870 neonates at risk for hypoglycemia (10.6%) were admitted to the NICU with the primary diagnosis of neonatal hypoglycemia. Implementation of the glucose gel algorithm began in May 2014. Between May 2014 and July 2015, 32 out of 1,089 neonates at risk for hypoglycemia (2.9%) were admitted to the NICU for the primary diagnosis of neonatal hypoglycemia (see Figure 1).

Infants Requiring Additional Doses of Glucose Gel

Neonates requiring a second dose of gel had success with neonatal hypoglycemia reversal: 52 of 63 (82.5%) were admitted to the postpartum unit with their mothers. Of the 26 neonates who received three doses, 13 were admitted to the NICU.

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 4

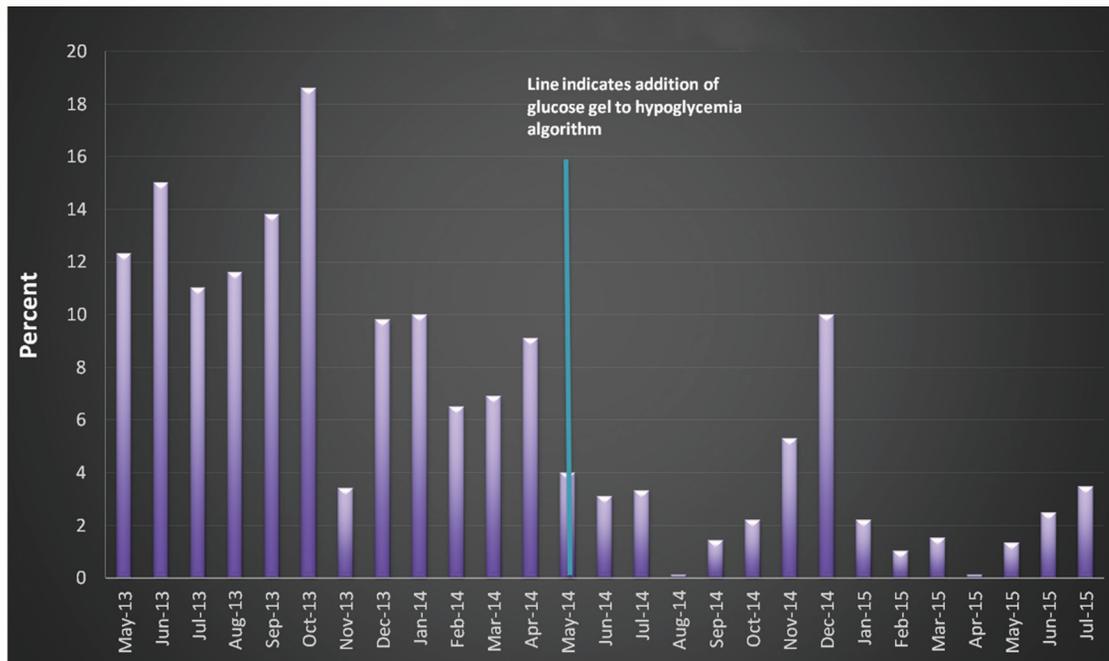
Signs and Symptoms of Neonatal Hypoglycemia

Irritability	Seizures
Exaggerated Moro reflex	Lethargy/apathy
Jitteriness and/or tremors	Apnea
Tachypnea	Cyanosis
High-pitched cry	

Source: Committee on Fetus and Newborn and Adamkin (2011).

Symptomatic Infants

Our algorithm calls for immediate bedside glucose assessment for any neonate exhibiting signs of neonatal hypoglycemia (see Box 4). If the bedside glucose level is less than 40 mg/dl, the neonate is given a dose of glucose gel and placed skin to skin with

FIGURE 1**Percentage of Infants Admitted to NICU for Neonatal Hypoglycemia**

his/her mother to breastfeed. Serum glucose is then obtained, and the neonate is closely observed. The bedside glucose level is reassessed 30 minutes after the glucose gel was administered. The physician is notified of the bedside or serum glucose level results and the condition of the neonate.

Effect on Exclusive Breastfeeding

Before the implementation of the glucose gel algorithm, most newborns with blood glucose levels less than 35 mg/dl received supplementation with formula or were separated from their mothers while receiving IV glucose in the NICU. We were unable to determine the number of those who were exclusively breastfed during that time period, but because our routine was to give supplementation to those with levels less than 40 mg/dl, the number was close to zero. During the 14 months after implementation, 494 of the 1,089 women with neonates at risk for hypoglycemia identified exclusive breastfeeding as their choice of feeding method, and 49% were successful in their goal. This is only slightly lower than the percentage for women with neonates with normal blood glucose levels (58%).

Neonates With Blood Glucose Levels at or Less Than 25 mg/dl

The AAP guidelines recommend IV glucose for neonates with blood glucose values less than 25 mg/dl an hour after the second feeding, which in our institution would require a NICU

admission. For this reason we wanted to examine how the administration of glucose gel affected neonates with glucose levels less than 25 mg/dl. Of the 1,089 neonates at risk for hypoglycemia, 49 had initial glucose levels at or less than 25 mg/dl. These asymptomatic neonates were given glucose gel and feedings as the first-line intervention. Seventeen of these neonates were admitted to the NICU, but only nine for the diagnosis of neonatal hypoglycemia (see Figure 2). Before the use of glucose gel, every neonate with a blood glucose level less than 25 mg/dl would have been admitted to the NICU.

DISCUSSION

In our study, administration of glucose gel reversed neonatal hypoglycemia in 88% of neonates at risk for hypoglycemia during the first 24 hours of life. We identified this to be the case in 246 of 278 neonates between May 2014 and July 2015. These neonates were able to stay with their mothers and avoid an admission to the NICU for IV glucose, and 49% of these did not receive formula supplementation. The addition of glucose gel to our hypoglycemia algorithm has supported family bonding and exclusive breastfeeding.

Before implementation, a potential concern was that a neonate's glucose level response to the administration of gel would be abnormally high, followed by rebound hypoglycemia. However, this did not occur in any of the neonates who received the gel. Of the 278 neonates who received glucose gel, none

FIGURE 2

Infants With Initial Glucose Levels <25 mg/dl (n = 49) and Place of Admission

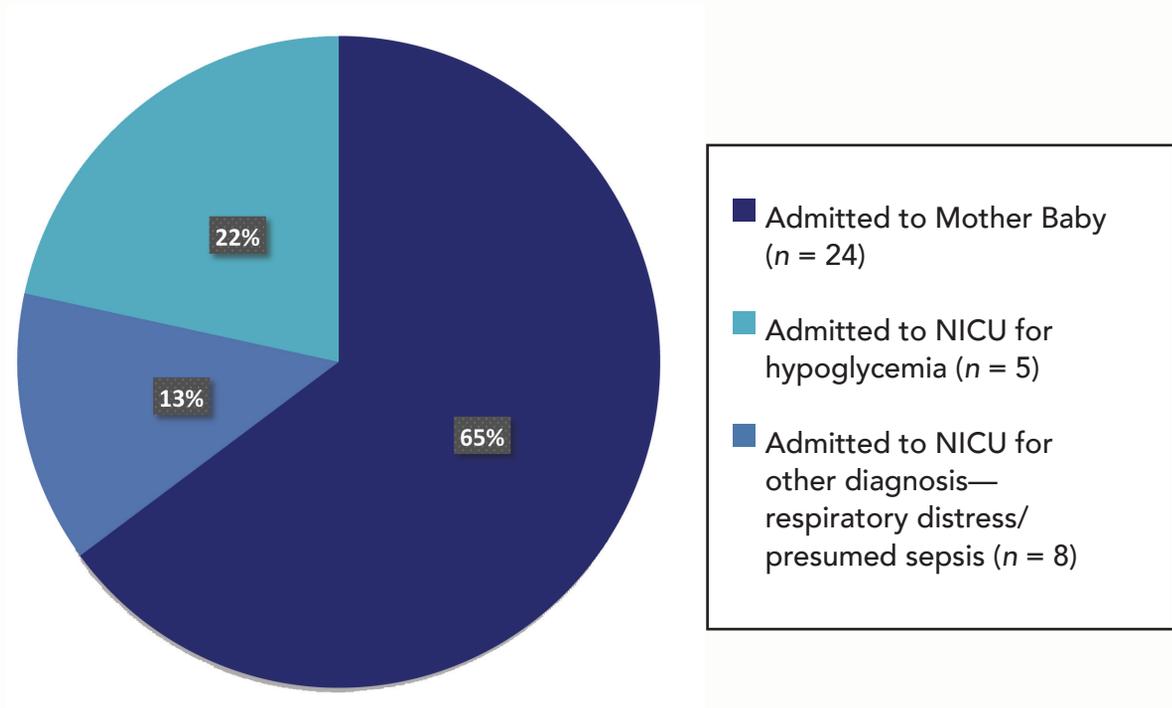


FIGURE 3

Glucose Levels One Hour After Administration of Dextrose Gel (n = 278)

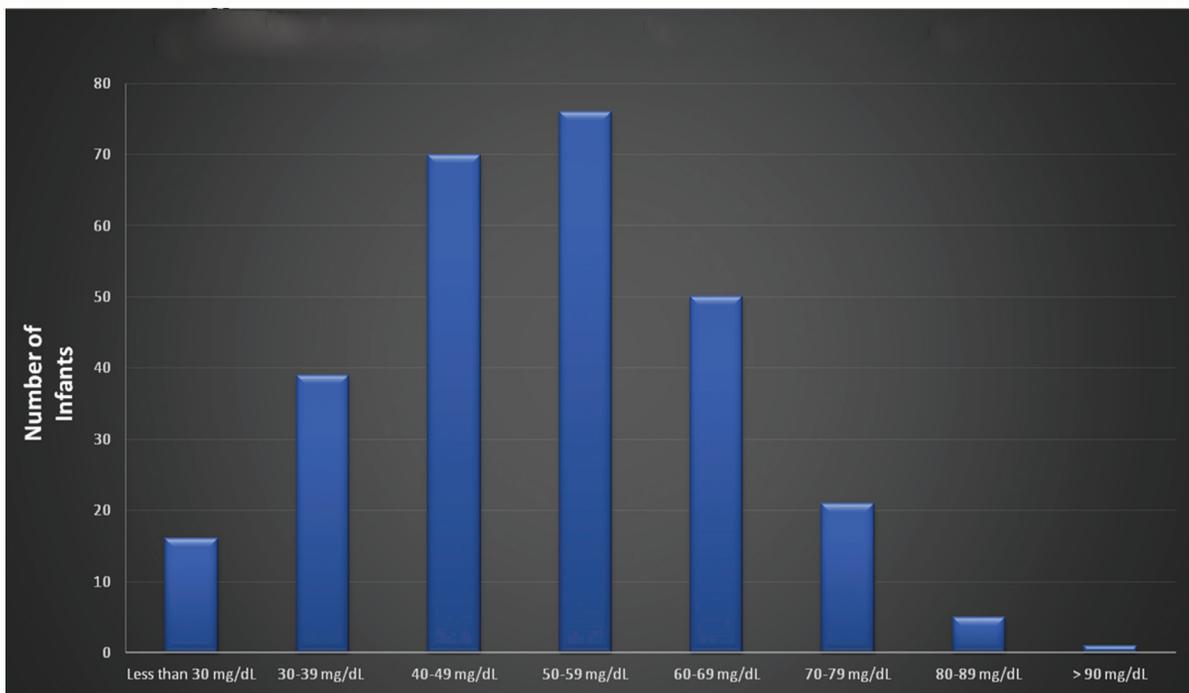


TABLE 1

Blood Glucose Levels Before and After Glucose Gel Administration for Exclusively Breastfed Infants

Gestational Age	Birth Weight, g	Reason on Algorithm	Blood Glucose Level Before Gel Administration, mg/dl	Blood Glucose Level 1 Hour After Gel Administration, mg/dl	Blood Glucose Level at 1 Hour Before Next Feeding, mg/dl	Subsequent Blood Glucose Level Before Next Feeding, mg/dl
39	3,590	IDM A2	28	42	59	47
40 ² / ₇	2,660	SGA	30	63	66	62
36 ⁶ / ₇	3,395	LPI	33	62	83	52
38 ³ / ₇	4,300	LGA	28	50	55	57
35 ⁴ / ₇	2,730	LPI	28	43	67	50
40	4,570	LGA	31	69	64	64

Note. IDM A2 = infant of a mother with adult type 2 diabetes; SGA = small for gestational age; LPI = late preterm infant; LGA = large for gestational age.

had levels greater than 90 mg/dl at 1 hour after administration. No hyperglycemia or rebound hypoglycemia was noted (see Figure 3 and Table 1).

IMPLICATIONS FOR CLINICIANS

Nurses are on the front line when caring for neonates with hypoglycemia. Nurses assess for signs of hypoglycemia, place neonates skin to skin with their mothers, assist with breastfeeding,

and perform the initial bedside glucose check. It is also nurses who see the disappointment and fear of parents when their neonate is taken to the NICU for treatment of hypoglycemia. This interaction with neonates and their families may account for the interest that nurses from other institutions across the country have shown at local and national poster presentations when they learn about our successful reversal of neonatal hypoglycemia with the oral administration of glucose gel.

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:
 - o The number of neonates who receive IV glucose and/or formula supplementation to treat neonatal hypoglycemia.
 - o The initial blood glucose levels of these neonates.
 - o 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.

Not only is an admission to the NICU devastating for parents and uncomfortable for neonates, it also carries a considerable financial burden. The 1-day charge for a NICU admission is estimated at \$4,000. In the current health care environment of population-based management, the focus is shifting from individuals to populations. Nurses and other clinicians are being challenged to do more with less while simultaneously being pushed to improve outcomes. In the abstract this seems like an impossible task. However, the use of glucose gel is a perfect example of a successful population-based management. By using innovative treatments such as oral glucose gel, we can significantly decrease health care costs and, at the same time, improve health outcomes for newborns. Nurses are in the perfect position to bring this practice change to the attention of their nursing and physician leaders (see Box 5).

CONCLUSION

With the growing trend toward population-based health management, decreasing expensive and/or unnecessary interventions is becoming increasingly important to the financial well-being of hospitals and to the health and well-being of patients. Use of oral glucose gel to treat neonatal hypoglycemia is inexpensive, noninvasive, and easy to administer. If the use of glucose gel is adopted by other institutions with results similar to ours, we have the potential to revolutionize the standard of treatment through the development of new clinical guidelines for newborns experiencing neonatal hypoglycemia. **NWH**



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