

Late-Onset Hypoglycemia in Term Newborns With Poor Breastfeeding

Laura M. Seske, MD,^{a,b} Stephanie L. Merhar, MD,^{a,b} Beth E. Haberman, MD^{a,b}

Brain injury as a result of significant neonatal hypoglycemia has been recognized for many years. Recently, several case reports from around the world have documented that neonatal hypoglycemia in term infants can result from inadequate intake related to breastfeeding.¹ Clinical manifestations can vary from no symptoms, to hypotonia and lethargy, to seizures.² The blood glucose level and duration of hypoglycemia that lead to neurodevelopmental sequelae have not been established.³ For many years, it was thought that hypoglycemic brain injury was localized to the occipital lobes; however, more recent research has shown that the damage can occur anywhere in the brain.^{4,5} There have been minimal follow-up data in this patient population to determine long-term prognosis.⁶ We report a cohort of 11 term neonates who were admitted to the Cincinnati Children's Hospital Medical Center (CCHMC) NICU for treatment of hypoglycemia that was not due to endocrinopathies, sepsis, hypoxic-ischemic encephalopathy, or maternal medical problems such as diabetes. All of the infants were discharged from their birth hospitals and within a few days were admitted to the NICU with hypoglycemia.

METHODS

A retrospective search was conducted to identify all neonates admitted to the CCHMC NICU from January 2010 to December 2013 with the following diagnosis codes: "neonatal convulsions" and/or "neonatal hypoglycemia." The research was conducted with approval of the CCHMC Institutional Review Board (Protocol 2014-0607). A chart review was performed for all 47 patients identified. Patients were excluded if they had any other diagnosis that could cause hypoglycemia such as: hypoxic-ischemic encephalopathy, meconium aspiration syndrome, sepsis, prematurity, micropenis, ambiguous genitalia, intrauterine growth restriction, small for gestational age, or those who were hypoglycemic immediately after birth. Eleven neonates were included who had isolated hypoglycemia with or without convulsions. All 11 of these infants were admitted to the CCHMC NICU after routine discharge from their birth hospitals. These neonates were born at 6 birthing centers in the greater Cincinnati area.

RESULTS

Case 1: A 39 1/7-week estimated gestational age boy born via vaginal delivery at 2905 g to a G1 P0. Mother was primarily breastfeeding but had reported supplementing with formula intermittently. The amount of formula used, mother's change in breasts during pregnancy and after delivery, and infant's ability to feed were not clearly documented and/or reported in the medical record. He presented to his primary medical doctor on day of life 3 for

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Address correspondence to Laura Seske, MD, Cincinnati Children's Hospital Medical Center, 3333 Burnet Ave ML 7009, Cincinnati, OH 45229. E-mail: laura.seske@cchmc.org

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^aDivision of Neonatology and Pulmonary Biology, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio; and
^bCenter for Prevention of Preterm Birth, Perinatal Institute, Cincinnati, Ohio

a normal newborn well-child check. On day of life 4, he was seen by a home health nurse and reportedly could not feed with a syringe due to lethargy and was referred to CCHMC emergency department, where his weight was 2600 g, decreased 10.5% from birth. Glucose was measured to be 20 mg/dL. He was given an intravenous 2-mL/kg bolus

of dextrose 10% in water. He had a seizure, which was treated with 1 dose of lorazepam. During his hospital course, he received phenobarbital for seizure prophylaxis. Magnetic resonance imaging (MRI) showed extensive areas of restricted diffusion involving the bilateral parietal and occipital lobes with subtle

restricted diffusion in the right frontal and temporal lobes. He was discharged from the hospital on maintenance phenobarbital.

In addition to the case presented in detail, 10 other cases were reviewed. The results of all 11 cases can be seen in Table 1. Briefly, 9 of the 11 were first-time mothers. Five

TABLE 1 Clinical Course of 11 Term Neonates with Hypoglycemia

Case No.	Gestational Age (wk)	Mode of Delivery	Birth Wt (g)	% Wt Loss From Birth	Maternal Obstetrical History	BF and/or PM	Supplementing With Formula	Age (d of life)	Presenting Symptoms	Glucose on Presentation (mg/dL)	Seizure	MRI Results
1	39 1/7	Vaginal	2905	10.5	G1P1	Yes	Yes	4	Lethargy, poor feeding, seizure in trauma bay of ED	20	Yes	Extensive areas of restricted diffusion involving the bilateral parietal and occipital lobes
2	38 3/7	Vaginal	2637	7.3	G1P1	Yes, + syringes of PM	No	4	Lethargy, poor feeding, seizures	20	Yes	Extensive severe injury to the posterior one-third of the supratentorial brain
3	38	Vaginal	2634	6.6	G1P1	Yes	No	3	Lethargy, poor feeding, no urine \times 12 h	36	No	No MRI done
4	39	Vaginal	3989	9.1	G10P4	Yes	No	2	Twitching in upper extremities	28	Twitching but EEG normal	No MRI done
5	40 1/7	Vaginal	3288	4.2	G2P2	Yes	No	3	Poor feeding, shallow breathing, tremors	13	Yes	Restricted diffusion in parietal and bilateral occipital lobes
6	37 3/7	Vaginal	3525	16	G1P1	Yes, + PM	No	3	Lethargy, hypotonia, apnea	<20	Yes	Diffuse brain injury involving frontal, parietal, and occipital
7	38 5/7	Vaginal	2525	0	G1P1	Yes, + PM	No	3	Cyanotic episode at home, lethargy, poor feeding	<20	Yes	Restricted diffusion involving both posterior parietal, temporal, and occipital lobes
8	40	Vaginal	3550	7	G1P1	Yes	Yes	4	Lethargy, poor feeding	23	No	No MRI done
9	39 4/7	Cesarean	3015	7.1	G6P5	Yes, + PM	No	2	Apnea, hypotonia	8	No	Normal
10	40	Vaginal	3100	5.5	G1P1	Yes	No	2	Apnea at home	13	No	No MRI done
11	37 5/7	Cesarean	2807	4.5	G1P1	Yes	No	5	Low temperature at PMD office	35	No	No MRI done

BF, breastfeeding; ED, emergency department; EEG, electroencephalogram; G, gravida; P, parity; PM, pumped milk; PMD, primary medical doctor.

of the 11 were exclusively breastfeeding without any expressed milk provided. An additional 4 of the 11 were directly breastfeeding and also receiving expressed breast milk via syringe or a bottle, and 2 more were receiving formula in addition to direct breastfeeding. The volume of the supplementation of formula and/or expressed breast milk was not reported in the medical records. Six patients had an MRI obtained and only 1 was read as normal. Seven patients had follow-up available in their medical charts. Four of those 7 patients continue to have neurologic sequelae as a result of their hypoglycemic event. As of their most recent appointments, two of the patients are still on antiepileptic medication, one completed a phenobarbital wean after discharge but continues to have generalized hypotonia, and one continues to have visual impairment. Of the 2 who remain on medication, 1 continues to have feeding difficulties and is followed by speech therapy.

DISCUSSION

This case series describes a cohort of 11 term neonates with profound hypoglycemia requiring admission to the NICU within a few days of discharge from their birth hospitals. The majority of cases were vaginal deliveries to first-time mothers. Five of the 11 were exclusively breastfeeding without any expressed breast milk provided. Four of the 11 were breastfeeding and receiving expressed breast milk in the form of a bottle or syringe. Breastfeeding rates in US women continue to increase. The 2014 Centers for Disease Control and Prevention Breastfeeding Report Card stated that 79.2% of women initiate breastfeeding.⁷ The vast majority of infants do well with exclusive breastfeeding with minimal or no supplementation, but the purpose of our case series is to draw attention to the rare infants who have potentially devastating consequences and discuss how to potentially avoid these consequences in the future.

US Baby-Friendly Hospital guidelines state that before discharge, breastfeeding mothers should have their technique assessed by a health care professional with

2 good-quality feeds documented, should receive education on breastfeeding practices, and should be given referral information for lactation support groups along with adequate timing for the visits after returning home with their newborns.⁸ Most birth hospitals now employ lactation consultants, as did all 6 hospitals where the infants in this study were born. However, some hospitals require a physician order for a lactation consult to occur. Although 1 study showed that timing of discharge had no effect on the feeding outcomes of newborns,⁹ with many hospitals discharging patients at 24 hours of life, not all mothers will receive adequate lactation support before going home. However, all of these mothers should have 2 good-quality feeds observed by a health care professional, in accordance with US Baby-Friendly Hospital guidelines. The American Academy of Pediatrics policy statement states that infants who are discharged at ~24 hours of life should have a follow-up with a health care provider within 24 to 48 hours.¹⁰ We therefore would recommend that with early discharge, a home health visit or primary medical doctor visit occur within 24 to 48 hours of discharge and that a glucose level be obtained at this visit in any infant with feeding difficulty and/or lethargy.

Five patients had seizures reported. One had documented twitching, but the electroencephalogram was negative for seizure activity. Only 6 of the 11 patients had MRIs obtained and 5 of the 6 were abnormal. We would recommend obtaining brain MRIs in all infants who present with profound hypoglycemia and seizures. We would also strongly encourage obtaining a brain MRI in those infants who did not have seizures but had a glucose level <20 mg/dL with any neurologic symptoms. Abnormalities on MRI would determine which infants warrant closer monitoring for neurologic and developmental sequelae. Knowing the presence and degree of brain injury may allow earlier referral to services, such as early interventions and supportive therapies.

In conclusion, providing mothers with increased education, assessments, and support from a multidisciplinary level on breastfeeding techniques for their

newborns will promote success. In addition, the multidisciplinary involvement will allow for identification and diagnosis of inadequate lactation and allow for treatment with alternative feeding plans in those mothers who have inadequate breastfeeding at the time of newborn hospital discharge. This process may help limit these rare but potentially devastating events. Following these patients through school age will be beneficial in tracking their outcomes given that many studies have not gone beyond a few years of life.

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