

Early feeding and neonatal hypoglycemia in infants of diabetic mothers

SAGE Open Medicine
I: 2050312113516613
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sagepub.co.uk/journalsPermissions.nav
DOI: 10.1177/2050312113516613
smo.sagepub.com


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Abstract

Objectives: To examine the effects of early formula feeding or breast-feeding on hypoglycemia in infants born to 303 A1-A2 and 88 Class B-RF diabetics.

Methods: Infants with hypoglycemia (blood glucose < 40 mg/dL) were breast-fed or formula-fed, and those with recurrences were given intravenous dextrose.

Results: Of 293 infants admitted to the well-baby nursery, 87 (30%) had hypoglycemia, corrected by early feeding in 75 (86%), while 12 (14%) required intravenous dextrose. In all, 98 infants were admitted to the newborn intensive care unit for respiratory distress (40%), prematurity (33%) or prevention of hypoglycemia (27%). Although all newborn intensive care unit patients received intravenous dextrose, 22 (22%) had hypoglycemia. Of 109 hypoglycemia episodes, 89 (82%) were single low occurrences. At discharge, 56% of well-baby nursery and 43% of newborn intensive care unit infants initiated breast-feeding.

Conclusions: Hypoglycemia among infants of diabetic mothers can be corrected by early breast-feeding or formula feeding.

Keywords

Hypoglycemia, infants, diabetic, mothers

Date received: 3 October 2013; accepted: 15 November 2013

Background

Infants born to diabetic mothers (IDM) are at higher risk of neonatal morbidities including hypoglycemia.¹⁻⁴ Since cord blood glucose levels do not identify infants at risk of hypoglycemia,² clinicians must rely on blood glucose screening. Early formula feeding (FF) or breast-feeding (BF) may facilitate glycemic stability in infants born to women with diabetes and prevent or correct neonatal hypoglycemia.^{1,3-5} While FF is readily available, maternal complications or neonatal morbidities that affect IDM often precludes BF. Regrettably, recognized barriers to BF among nondiabetic populations (i.e. low socioeconomic status, obesity, smoking, low level of education, race, prematurity, neonatal morbidities and maternal separation) also affect pregnancies complicated by diabetes.⁶⁻¹⁰ The effects of early BF on hypoglycemia and the long-term benefits to mothers' and infants' health make BF the best choice, especially for women with diabetes.¹¹⁻¹³

Objective

To examine the association between early FF or BF in women with diabetes and the incidence and management of neonatal hypoglycemia.

Subject and methods

This retrospective cohort investigation (2008–2009) was approved by the Institutional Review Board of Wexner Medical Center at The Ohio State University. Demographic and clinical information was obtained from hard copies and electronic medical records. The study population consisted of women with diabetes and their infants delivered at ≥ 34 weeks of gestation (gestational age (GA)), a point in gestation in which most infants are able to orally feed.^{14,15} Pregnancies affected by major or fatal malformations were excluded. In cases of twin

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gestation, only the first born infant was reported. Gestational (Class A1-A2) and pregestational (Class B-RF) diabetes mellitus were diagnosed according to clinical and laboratory criteria and grouped using the modified White's classification.¹⁶ Women with chronic hypertension and/or superimposed preeclampsia were included. Obesity was defined by a pre-pregnant body mass index (BMI) of 29–34 kg/m² and extreme obesity by a BMI \geq 35 kg/m².¹⁷ Upon arrival to labor and delivery, women's feeding preference for their infants (BF, FF or undecided) was ascertained by the nurse.

Depending on the condition of the mothers and their infant following delivery, mother–infant interactions (holding, skin-to-skin contact, BF and postpartum visitation) were encouraged. After delivery, stable infants were transferred to the well-baby nursery (WBN) for routine care, while those who required specialized attention were admitted to the newborn intensive care unit (NICU). Early feeding was defined as FF or BF within the first 2 h after birth.

Screening for neonatal hypoglycemia (blood glucose < 40 mg/dL) was done via serial point of care (POC) testing (Accu-Chek[®]) or by plasma glucose measurement in the laboratory (Beckman Coulter AU5800, Beckman Coulter Inc., Brea, CA, USA) starting within the first hour of life. WBN infants with hypoglycemia were immediately breast-fed or formula-fed followed by repeat testing in 30 min. Symptomatic infants or those with recurrent hypoglycemia (especially with blood glucose \leq 25 mg/dL) were treated with intravenous (IV) dextrose (4–6 mg/kg/min). All NICU infants were given IV dextrose upon admission. Type, frequency and amount of each feeding were recorded. Given that women who breast-feed only 1–2 times per day are likely to stop BF soon after delivery,¹⁸ we defined BF as initiated if at the time of discharge \geq 50% of the feedings were direct from the breast or by expressed breast milk.

Statistical analysis

Comparisons between the groups and subgroups were made with Student's t-test for continuous and Chi-square or Fisher's Exact test for categorical variables. Significance was established at a *p* value \leq 0.05. Univariate and multivariate logistic regressions were used to determine maternal and neonatal variables (diabetes class, primiparity, BMI, smoking, GA, mode of delivery, birth weight, gender and admission to NICU) predictive of neonatal hypoglycemia.

Results

Our study population consisted of 391 women (176 Class A1, 127 Class A2 and 88 Classes B-RF) and their infants (Table 1). In all, 98% of the pregnancies involved singletons. The seven twin pregnancies were dichorionic diamniotic. In all, 24% of the mothers were obese, and 31% were extremely obese. All 176 Class A1 women were on diet control, 78 Class A2 were given Glyburide[®], whereas 49 Class

Table 1. Study population.

	No.
Number of patients	391
<i>Maternal characteristics</i>	
Intended to breast-feed, n (%)	224 (57)
Intended to feed formula, n (%)	80 (21)
Undecided feeding preference, n (%)	87 (22)
Mothers \leq 30 years old, n (%)	214 (55)
Primiparous, n (%)	131 (34)
Class A1, A2 diabetes, n (%)	303 (77)
Class B-RF diabetes, n (%)	88 (23)
BMI < 29 kg/m ² , n (%)	178 (44)
BMI = 29–34 kg/m ² , n (%)	93 (24)
BMI \geq 35 kg/m ² , n (%)	120 (31)
Smoking, n (%)	80 (20)
Cesarean delivery, n (%)	181 (46)
<i>Race</i>	
White, n (%)	183 (47)
African American, n (%)	87 (22)
Hispanic, n (%)	62 (16)
Asian, n (%)	22 (6)
African, n (%)	16 (4)
Other, n (%)	21 (5)
<i>Education</i>	
\leq 11th grade, n (%)	87 (22)
High school, n (%)	104 (27)
College or postgraduate, n (%)	200 (51)
<i>Neonatal characteristics</i>	
GA = 34–36 weeks, n (%)	96 (25)
GA \geq 37 weeks, n (%)	295 (75)
NICU admission, n (%)	98 (25)
Well-baby admission, n (%)	293 (75)
Baby discharged home with mother, n (%)	329 (84)

BMI: body mass index; GA: gestational age; NICU: newborn intensive care unit.

A2 and all 88 Class B-RF women were on insulin. There were 40 (10%) mothers with preeclampsia, and of these, 25 required treatment with magnesium sulfate postpartum, and 21 (5%) had chronic hypertension. Of the 391 deliveries, 181 (46%) were by cesarean, of which 95 (52%) were repeat. Common indications for the 86 primary cesarean deliveries included failure of labor to progress, breech presentation, macrosomia and fetal distress. Of all infants, 295 (75%) had growth appropriate for GA, 78 (20%) were large for GA (43 of them weighed \geq 4000 g) and 18 (5%) were small for GA (SGA). Polycythemia (hemoglobin \geq 22 g/dL or hematocrit \geq 65%) affected 5% of all infants. All mothers and their infants survived.

On arrival to labor and delivery, 224 (57%) of the 391 women intended to breast-feed, 80 (20%) intended to feed formula, while the remaining 87 (23%) were undecided. All groups were similar in class of diabetes and in the incidence of preeclampsia and chronic hypertension. For WBN and NICU

Table 2. Time of diagnosis of hypoglycemia for 293 IDM admitted to the well-baby nursery.

White's Class	Number of patients	Hypoglycemia			Treatment	
		Number of patients (%)	Dx at 1 h	Dx at 2–4 h	Per os feed	IV Tx
A1	154	36 (23)	24	12	32	4
A2	110	39 (35)	23	16	37	2
B	23	8 (35)	6	2	6	2
C-RF	6	4 (67)	3	1	0	4
	293	87 (30) ^a	56 (64)	31 (36)	75 (86)	12 (14)

IDM: infants born to diabetic mothers; Dx: diagnosis; Tx: treatment.

^a73 of the 87 (84%) patients with hypoglycemia had only one low glucose reading.

infants combined, and regardless of mothers feeding preference, 208 (53%) of the 391 women initiated BF.

Our univariate regression analysis showed that infants born to Class A2 diabetics had higher odds of having hypoglycemia than Class A1 diabetics (odds ratio (OR) = 1.794, confidence interval (CI) = 1.072–3.004, $p = 0.0262$) and that Class B-RF had higher odds than Class A1 diabetics (OR = 2.335, CI = 1.168–4.666, $p = 0.0164$). Similarly, infants born to Class A2 and B-RF diabetics had higher odds for multiple episodes of hypoglycemia than Class A1 (OR = 3.495, CI = 1.293–9.445, $p = 0.0136$).

WBN admissions

In all, 293 (75%) of the 391 infants were admitted to the WBN for an average hospital stay of 3 ± 1 days. This included 40 late preterm and 253 term infants. Of the 293 infants admitted to WBN, 45% were fed for the first time during the first hour of life, and the remaining 55% during the second. First feedings were with formula except for 33 infants who exclusively breast-fed. Following a vaginal delivery, these 33 women (26 Class A1, 6 Class A2 and 1 Class B), breast-fed their infants in the delivery room. Two of the 33 infants developed hypoglycemia, which was corrected by repeated BF in one infant, while the other required IV dextrose.

Of the 86 episodes of hypoglycemia, 56 were noted during the first hour of life (Table 2). Blood glucose values were ≤ 25 mg/dL in only 6 of the 86 (12%) episodes. All infants were promptly breast-fed or formula-fed. Of the 87 hypoglycemia episodes, 75 (86%) were corrected by early feeding, while 12 (14%) required IV dextrose. Of the 87 hypoglycemia episodes, 73 (84%) were single low glucose occurrences, whereas the remaining 14 (16%) were multiple. At discharge, 77 of 293 infants (26%) were exclusively breast-fed, 88 (30%) were breast-fed with formula supplementation, while the remaining 128 (44%) were taking formula.

NICU admissions

Of the 391 infants, 98 (25%) were admitted to the NICU (Table 3). The most common diagnosis was respiratory

distress 40 (40%). Two of these infants required mechanical ventilation and surfactant administration. The remaining 38 had transient tachypnea of the newborn, 26 needed nasal continuous positive airway pressure (CPAP) (median = 1 day, range = 1–4 days) and oxygen (median = 1 day, range = 1–6 days), while the remaining 12 infants required neither. A total of 31 (33%) infants were admitted to the NICU for prematurity; however, only 6 of them required gavage feedings (median = 3 days, range = 3–9 days). The remaining 26 (27%) infants were admitted for prevention of hypoglycemia (5 were Class A1, 6 Class A2, 5 Class B and 10 Class C-R). On admission to the NICU, all infants were started on IV dextrose. In all, 39 infants were fed during the first 2 h, but early feedings were not possible for the 40 infants who had respiratory distress and for 19 infants for other reasons. Due to the condition of mothers or infants, early BF was not possible in the NICU, thus all first feedings were formula. Of the 98 NICU infants 22 (22%; 15 late preterm, 5 respiratory distress and 2 infants from the prevention group including 1 SGA) developed hypoglycemia. Of the 22 (73%) episodes, 16 were single low glucose occurrences. At the time of discharge, 23 of 98 infants (23%) were exclusively breast-fed, 20 (21%) were breast-fed with formula supplementation, while the remaining 55 (56%) were taking formula.

Blood and plasma glucose screening

Screening and monitoring glucose concentrations for the 293 infants admitted to the WBN required 1680 POCs and 34 plasma glucose determinations over the first 72 h. Median number of tests per infant was 6 (range = 1–17) (Table 4). Approximately half of all blood samples were taken during the first 6 h of life; thereafter, the rate of sampling declined to 5% by the end of the second and 2% by the end of the third day of life. During the three days of monitoring of these patients, 7% of the values were <40 mg/dL, 40% were between 40 and 59 mg/dL and 53% ≥ 60 mg/dL. Of the 1680 POC values, 34 (2%) were verified by plasma glucose testing. One of the 34 results showed values < 40 mg/dL, while the remaining 33 showed values similar to those of the POC.

Table 3. Time of diagnosis of hypoglycemia for 98 IDM admitted to the newborn intensive care unit.

White's Class	Number of patients	Hypoglycemia			Admission diagnosis		
		Number of patients (%)	Dx at 1 h	Dx at 2–4 h	Respiratory distress	Late Preterm	Hypoglycemia prevention
A1	22	2 (10)	0	2	11	6	5
A2	17	3 (18)	3	0	4	7	6
B	19	3 (16)	3	0	8	6	5
C-RF	40	14 (35)	7	7	17	13	10
	98	22 (22) ^a	13 (59)	9 (41)	40 (41)	32 (33)	26 (27)

IDM: infants born to diabetic mothers; Dx: diagnosis.

^a16 of the 22 (73%) patients with hypoglycemia had only one low glucose reading.

Table 4. Blood and plasma glucose results from 293 IDM admitted to the well-baby nursery.

Glucose values (mg/dL)	Time intervals from birth (h)						Total No. (%) ^a
	~1–6	7–12	13–18	19–24	25–48	49–72	
<25	6 (0.01)	0	0	0	0	0	6 (0.1)
25–39	81 (10)	16 (5)	12 (5)	0	0	0	109 (6)
40–59	386 (47)	138 (40)	85 (35)	51 (30)	18 (19)	10 (27)	688 (40)
60–89	322 (39)	185 (52)	134 (55)	108 (64)	68 (73)	26 (73)	843 (49)
≥90	29 (4)	9 (3)	14 (5)	9 (6)	7 (8)	0 (0)	68 (4)
Total	824 (48)	348 (20)	245 (14)	168 (10)	93 (5)	36 (2)	1714

IDM: infants born to diabetic mothers.

^aNumber of samples and (%).

Table 5. Blood and plasma glucose results from 98 IDM admitted to the newborn intensive care unit.

Glucose values (mg/dL)	Time intervals from birth (h)						Total No. (%) ^a
	~1–6	7–12	13–18	19–24	25–48	49–72	
<25	6 (1.5)	0	0	0	0	0	6 (0.4)
25–39	24 (6)	6 (3)	0	0	0	0	30 (2)
40–59	118 (30)	29 (12)	18 (11)	12 (9)	23 (9)	18 (8)	218 (16)
60–89	193 (49)	137 (59)	123 (68)	78 (66)	131 (73)	111 (75)	773 (56)
≥90	53 (13)	65 (27)	45 (21)	67 (25)	83 (19)	37(17)	350 (26)
Total	394 (29)	237 (17)	186 (14)	157 (11)	237 (17)	166 (12)	1377

IDM: infants born to diabetic mothers.

^aNumber of samples and (%).

Screening and monitoring glucose concentrations for the 98 infants admitted to the NICU required 1238 POC and 139 plasma glucose determinations over the first 72 h. Median number of tests per infant was 16 (range = 3–29) (Table 5). In all, 29% of all blood samples were taken during the first 6 h of life; thereafter, the rate of sampling declined to 17% by the end of the second and 12% by the end of the third day of life. During the three days of monitoring of these patients, 2% of the values were <40 mg/dL, 16% were between 40 and 59 mg/dL, while remaining 82% were ≥60 mg/dL. Of the 1377 POC values, 139 (10%) were verified by plasma glucose testing. Five of the 139 results showed glucose

values < 40 mg/dL, while the remaining 134 showed values similar to those of the POC.

Discussion

The incidence of gestational as well as pregestational diabetes continues to rise across the world.^{16,19} Thus, it is anticipated that neonatal morbidities, namely, hypoglycemia, will also increase. The effects of early BF on hypoglycemia and the long-term benefits to mothers' and infants' health makes BF the best choice, especially for those with diabetes.^{11,12} The fact that 55% of our patients were obese or extremely

obese cannot be ignored since the higher the pre-pregnant BMI, the lower the likelihood of BF.^{20,21} Furthermore, obese women with antenatal or intrapartum complications (i.e. prolonged labor, prematurity, emergency cesarean delivery) experience a significant delay in onset of lactogenesis.²⁰

Determining what blood glucose concentration defines hypoglycemia in the neonatal period remains controversial.⁴ At birth, blood glucose concentration in the infant is determined by the maternal glucose levels.²² The rate of fall in blood glucose levels following delivery occurs earlier and is more pronounced among IDM.²² For many years, we have used a working definition of hypoglycemia (blood glucose < 40 mg/dL) similar to that recently proposed by the American Academy of Pediatrics (AAP).²³ Blood glucose screening was initiated at approximately 1 h of life in asymptomatic IDM or earlier if signs suggestive of hypoglycemia are present.¹ Like others, we believe that early oral feedings, whether BF or formula, could prevent or correct neonatal hypoglycemia; however, the high incidence of cesarean deliveries as well as other maternal or infant complications often interfere with BF.^{3–5,20} Since most asymptomatic late preterm and term infants are capable of direct BF or bottle,^{14,15,24} early feedings should be encouraged.

Our data demonstrate that hypoglycemic episodes in the WBN occurred between 1–4 h of life and more importantly that the majority were corrected with early BF or FF. It is also possible that the low recurrence of hypoglycemia may be an additional benefit of early feedings. The low incidence of hypoglycemia among IDM who were exclusively breastfed is encouraging but remains preliminary.^{3,5,24} Since maternal infant interactions are more likely in the WBN, it is not surprising that BF initiation rates were higher there than for those infants admitted to the NICU.

The rate of admission to NICU for comparable groups of IDM from our own institution showed a decline from 47% to 25% in just 10 years.¹ It is possible that this trend resulted from better maternal blood glucose control and from an institutional commitment to enhance maternal infant contact as well as BF. Respiratory distress, prematurity and prevention of hypoglycemia are consistently recognized as NICU admission diagnoses.^{1,4} The high incidence of transient tachypnea observed here may relate to the rate of cesarean deliveries, while the decline in respiratory distress syndrome (RDS) suggests better timing for delivery. The prompt resolution of respiratory distress and the successful initiation of oral feedings among late preterm infants may create a potential for shorter NICU stays and an earlier return to the WBN. In the past, most infants whose mothers were on insulin (Classes A2, B-RF) were routinely admitted to the NICU for prevention of hypoglycemia by early administration of IV dextrose.¹ Considering that most IDM Classes such as A1, A2 and B do very well with early feedings in the WBN, we now discourage preventive admissions to NICU of asymptomatic IDM other than from classes C-RF. Recent publications also support admission of IDM to transitional or

intermediate care facilities to promote bonding, BF and attachment.^{25,26} A decrease in the number of NICU admissions and shorter NICU stays may improve today's low BF initiation rates.

Our regression analysis showed that neonatal hypoglycemia is more likely to occur among infants born to Class A2 and B-RF diabetics. The fact that these observations do not identify specific infants at risk of hypoglycemia highlights the need for and value of neonatal screening programs. In 2011, the AAP provided a practical guide for the screening and management of neonatal hypoglycemia for late preterm infants, term infants and IDM.²³ Our experience supports these guidelines as it relates to the management of asymptomatic IDM during the first 24 h of life. Unfortunately, the AAP guidelines do not strongly recommend BF or address the problems of symptomatic IDM who required admission to an NICU.

Monitoring of blood and plasma glucose concentrations in a population of infants at risk of hypoglycemia should continue until glucose values are consistently above hypoglycemic levels.^{1,2,4,23} Continuous monitoring of glucose in neonates, although promising, is still far from routine use or more importantly may provide worrisome results without reliable clinical implications.²⁷ POC testing albeit not as reliable as plasma glucose measurement still provides a fast, practical tool for clinical use.^{1,2,4,23}

Our data showed that at the WBN, glucose monitoring was dramatically reduced by 18 h of life, yet sampling continued although none of the remaining 297 POC tests yielded values < 40 mg/dL. Among infants admitted to the NICU who receive IV dextrose, closer monitoring of glucose by POC or by plasma testing may not be avoidable. However, the fact that during the first 3 days of life 81% of the values were higher than 60 mg/dL and only 2% were lower than 40 mg/dL raises a valid concern about unnecessary sampling. Once or twice a day, reliable laboratory measurements may be preferable to frequent but inaccurate reagent strips.^{3,23}

Limitations of our investigation are those inherent to retrospective studies. Also due to the study design, we limited our observations to late preterm and term infants free of major congenital malformations.

In conclusion, in most cases, neonatal hypoglycemia in IDM can be corrected by early BF or FF. The low rate of recurrences suggests that early feedings may prevent hypoglycemia in this population. In order to eliminate unnecessary sampling, institutions should review their screening practices for hypoglycemia once stable glucose levels are achieved. A judicious decrease in the number of NICU admissions for the prevention of hypoglycemia as well as the prompt return of these infants to the WBN may improve BF initiation.

Declaration of conflicting interests

The authors declare that there is no conflict of interest.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

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